# Biochemical Surveillance

# 15

# Genetics

## 1. Introduction

There are few technologies more controversial, more intimate, or more telling than DNA testing and analysis. DNA is a biological structure that contains a type of genetic 'blueprint'* of our bodies, our individual characteristics, our strengths and weaknesses, our health, our ancestors, our race, and our living relatives. These essential attributes of our organic structure are coded into most of the cells in our bodies. Recently scientists have developed ways of unraveling this code and identifying or inferring important characteristics of an individual from tiny hair roots, teeth, or drops of saliva or blood.

Compared to many other types of surveillance, DNA evidence is easy to collect. You don't need advanced electronics skills and you don't have to set up complex equipment to get it. It doesn't cost anything to gather saliva, or hairs from a brush or a comb. The easy acqui-

*The genetic blueprint analogy is useful but not precise as it implies that the pieces of the genetic puzzle are stored in microscopic boxes that you can open and assemble like building blocks. The growth of an organism is a sophisticated chain of events, though, which are incompletely mapped out in the germ stage. The unraveling of the 'message' contained in DNA, and the process of cell reproduction is more like a bootstrapped, self-modifying computer program than an erector set, but for understanding DNA sampling and analysis from a lay point of view, the blueprint term provides a familiar starting point, and readers seeking a better understanding can consult references listed at the end of this chapter. The above photo illustrates gel electrophoresis being used to reveal gene sequences. [Courtesy of Pacific Northwest National Laboratory.]

sition of DNA samples, compared to many other types of information, makes this technology a significant information-gathering tool.

DNA analysis is a recent science and its use is not yet strongly regulated outside of law enforcement applications. When new technologies arise, there is usually a 'window of opportunity' during which public access is open and unlicensed, and during which certification standards for laboratory procedures are lenient. When automobiles first appeared, there were few traffic laws, and newer vehicles like snowmobiles, are loosely regulated compared to cars. DNA testing and analysis are still in this 'honeymoon' phase. In contrast, there are many laws safeguarding individuals from having their phones tapped, and there are some laws controlling the use of DNA in law enforcement, but there are as yet few regulations protecting individuals from having their DNA sampled by a stranger or relative without their knowledge. Samples can easily be sent through the mail to a commercial lab for analysis, and the resulting profiles can be stored in a computer database indefinitely.

North Americans live in a society that values freedom, and excessive regulation is considered to be contrary to this philosophy. In addition, lawmaking may lag, not because it significantly hinders individual freedoms, but because a technology is not understood by the ordinary individual and thus is not considered highly vulnerable to abuse. In the case of genetic surveillance, a DNA test can cost less than a night on the town and almost anyone can take a DNA sample and send it to a private company. Consequently, in our capitalist economy, DNA collection and analysis firms are now offering a wide range of services. We do not yet know all the possible problems that may result from this open system, but in terms of surveillance, there are currently novel opportunities for information gathering.

DNA technology has created a new field of genetic surveillance, with powerful ways to spy on plants, animals, and humans. It allows them to be identified, tracked, monitored, and sometimes held accountable for their whereabouts. DNA proponents and opponents are lining up on both sides of a privacy controversy that is likely to remain an issue for a long time. Law enforcement officials have been lobbying for broader DNA collection powers, while private rights advocates have been lobbying for greater protection for individuals, whether or not they have been convicted of criminal activities.

DNA sampling and analysis are becoming simple and inexpensive, yet there is an enormous amount of information that can be derived from a small amount of tissue. Consequently, a DNA profile is vulnerable to abuse on an unprecedented scale. Some futurists have proposed that this will lead toward a highly stratified society based on DNA characteristics, with genetically 'superior' humans procuring the best opportunities. Is this unlikely? Consider the fact that the Police Superintendents Association in England has called for the entire population to be DNA sampled. Consider also that current immigration regulations require that all applicants submit to medical tests, including HIV screening. Blood is routinely drawn for these tests. It may only be a matter of time before immigration officials suggest that we add DNA profiling to the blood tests already being conducted.

On the electronics side, administrators are promoting the development of computer network connections between government agencies. Many new centrally funded government databanks are being established. The growth of the Internet has motivated agencies to standardize their databases so there can be widespread sharing of data. We may be less than five years from a system in which immigration files, police files, and motor vehicle license files are fully cross-referenced, aiding law enforcement officials, but at the same time, blurring the line between private citizens and convicted felons. In a standardized database, they all look the same, and all data entry systems are vulnerable to file corruption, data entry error, spying,

or sabotage by hackers or disgruntled employees. There are known instances where hackers have accessed sensitive data in banks and government agencies, and 'published' the information on the Net. Once this type of information is uploaded, it is impossible to 'get it back' or quell its redistribution. It only takes minutes for digital data to be replicated and broadcast to millions of computers around the world.

A stratified society based on DNA characteristics has been chronicled in the science fiction movie Gattaca. Even though Gattaca depicts a futuristic society, much of the technology in the film is already available. The prediction that DNA will be used to control access to jobs, benefits, even mates, is not far-fetched. There are already about 6,000 firms which report that they require DNA samples as a condition of employment, and insurance companies have already begun assessing the technology as a screening tool. In spite of the possible repercussions, DNA profiling is likely to be a growth industry, given that the motivations for obtaining individual DNA profiles are many: paternity confirmation, genetic testing of newborns for treatable and untreatable diseases, identification of remains, and public safety.

It is important for everyone seeking to understand surveillance technologies to grasp patterns of legislation related to DNA profiling and the basic concepts of DNA collection and analysis. DNA testing has been in general commercial use since the mid-1990s and is spreading rapidly. It is now regularly used in law enforcement and social service activities, and no doubt in espionage, in ways that may eventually impact every person on the planet.

## 1.a. What is DNA and How is It Used?

DNA is a microscopic, information-carrying structure that is contained in nearly all living cells. More than one type of cell structure contains DNA. Although it degrades over time, DNA persists for some time after the death of the organism, and depending on where in the cell it is found, it can sometimes be recovered days or centuries later. When subjected to an exhaustive analysis, DNA can tell us a great deal about an individual's familial relations, physical characteristics, and health. The research in this area is recent and it is expected that our knowledge of DNA's relationship to biological evolution, growth, and health will increase dramatically in the coming decades.

### The source of DNA

In sexual reproduction, a new individual develops from the coming together of genetic material from a male and a female. The *genes* in the DNA influence the form and characteristics of the new organism. As it develops, some genes are expressed and others are suppressed, and some interact in complex ways not yet fully understood.

Some of the better-known areas of the human genome, such as gender and certain physical characteristics, can be predicted with a high degree of probability from a small sampling of DNA. As such, DNA testing is quickly being adapted in investigative and surveillance applications as a means of determining information about a specific individual (human, animal, or plant) and where the person may have been. DNA samples taken in espionage operations or at crime sites are gaining acceptance in courts of law and scientific circles as compelling, if not definitive, evidence.

### Using DNA

There is great concern about the ethics and legality of sampling genetic codes–and rightly so. A full understanding of DNA requires a scientific background. As our society becomes more complex, it becomes harder to convey the ramifications of a new technology in lay language. In legal debates about the admissibility, regulation, and constitutionality of DNA

sampling, the DNA information is frequently compared to an inked fingerprint. This is a misunderstanding of the phrase *DNA fingerprinting* and an alarming comparison. Comparing a *fingerprint* to a *DNA print* or *profile* in terms of information content is like comparing a house number with the whole history of a house, its inhabitants, contents, structure, materials, and more.

In this volume, the phrase *DNA fingerprinting* is used to specifically mean matching a minimal type of DNA representation used for *identification only*. DNA fingerprinting refers to the use of what has sometimes been called *junk DNA*,* which is a form of 'noncoding' DNA, to discern a pattern that is compared to a reference pattern. (DNA analysis prepared for paternity testing should be called a DNA *parental profile*, not a *DNA fingerprint*.)

## 1.b. Beyond Human DNA - Meta-Analysis

*In the context of surveillance, when blood samples are drawn for DNA analysis, other medical information or organisms may sometimes be derived from the sample.*

The information potential of DNA samples goes far beyond identification of an individual and his or her physical characteristics. In cryptologic surveillance one learns that much of the *intelligence* that can be derived from a coded message involves information outside the content of the message itself–information such as when the message was sent, how it was sent, who sent it, etc., all of which can be exceedingly important.

The same principle of macro-evaluation applies to intelligence derived from DNA testing. For example, one could observe the DNA of other organisms in a sample of a person's blood. Further information about the activities and of the donor and where he may have been can sometimes be deduced. For example, if particular strains of malaria or HIV, or other detectable pathogens, are found in the sample and can be analyzed and traced to a matching or related population in some part of the world, information about the individual's travels or activities may be revealed. In the surveillance industry, this secondary information may be of greater relevance than the particular genetic makeup of the individual sampled.

For example, someone smuggling narcotics out of South America might deny ever having been to that continent, but may carry a particular strain of organism found there, perhaps malaria or other types of infections. Conventional blood tests may reveal general information about the organism without a DNA test, but the specificity of the DNA used in conjunction with a reference database might someday be used to pinpoint where the person contracted the organism with a precision not possible with current blood tests. This extrapolation of information from a sample may not interest a judge in a paternity case, but may greatly interest a government surveilling a suspected international spy or smuggler.

## 1.c. DNA Matching

*DNA matching* is the most basic level of DNA analysis, in which a DNA pattern is processed in a lab or with a mobile kit and compared to reference samples to see if any of the references correspond to the same pattern as the sample in question. In law enforcement, this reference-comparison process is already used for fingerprints and mug shots. In wildlife research, unique skin markings are commonly used to create photographic databases of whales and dolphins so they can be identified if they are seen later in other regions.

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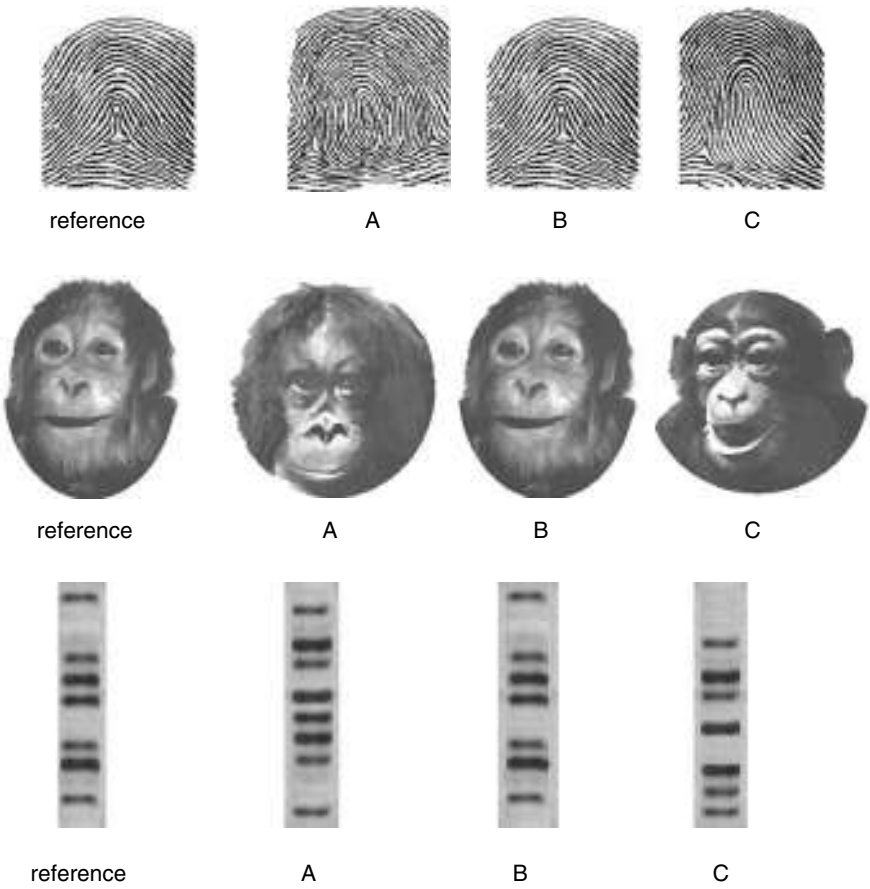
* While *DNA fingerprinting* in and of itself may not be considered invasive of a person's rights, *junk DNA* is not as innocent as the name may imply, and the sample from which it was derived may remain for an extended period in cold storage in some laboratory. There may also be an image or fuller analysis kept in a computer database. These related sources of information may be vulnerable to future use or abuse.

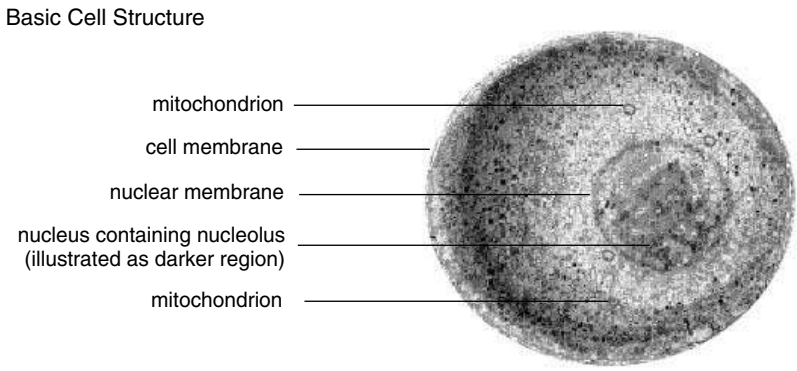



The phrase *DNA matching* should be used instead of *DNA fingerprinting* to refer to the most basic identification procedures. In the top series of images, a traditional fingerprint is compared with three others to determine whether there is a match. In the second series, a 'mug shot' is matched by seeking out identifying facial features. In the third series, an X-ray 'photograph' of DNA fragments is compared to the other patterns. A full DNA analysis provides a broader range of information and should be termed *profiling* rather than *fingerprinting*. [Classic Concepts illustrations ©2000, used with permission.]

# 2. Types/Variations

## 2.a. Nuclear DNA

DNA is the abbreviation for *deoxyribonucleic acid,* a material that is found in living, reproducing organisms. DNA is in nucleated cells throughout the body, and the DNA pattern in a living person's saliva, for example, is the same as that in his or her hair roots or portions of the blood. There is no DNA in mature red blood cells, but it is present in white blood cells. Nuclear DNA is in chromosomes, which in turn are in the nucleus of a cell. Nuclear DNA comes from both the mother and the father, which is why it is preferred for many types of DNA analysis. As cells decay, the DNA contained in those cells decays as well. Nuclear DNA is particularly subject to decay and is not found in bodies that have been dead for some time unless they have been specially preserved.




## 2.b. Mitochondrial DNA

Mitochondrial DNA (mtDNA) is found in multiples in any given cell and, depending on conditions, may survive much longer than nuclear DNA. It can be recovered from structures that decay more slowly, like bones and teeth. Mitochondrial DNA comes almost entirely from the mother and does not provide information about the father.* Mitochondrial DNA does not contain as many bases (less than 17,000 in humans) as nuclear DNA, but mtDNA exists in more copies in the cell than nuclear DNA. The patterns derived from its analysis are not as broad or unique as those derived from nuclear DNA, but their specificity and usefulness can be improved with contextual information. Mitochondrial DNA's survivability makes it an important research tool for identification within a limited population, for analyzing ancient racial lineages, for studying historic population growth in humans, and for determining the maternal relationships in threatened species.

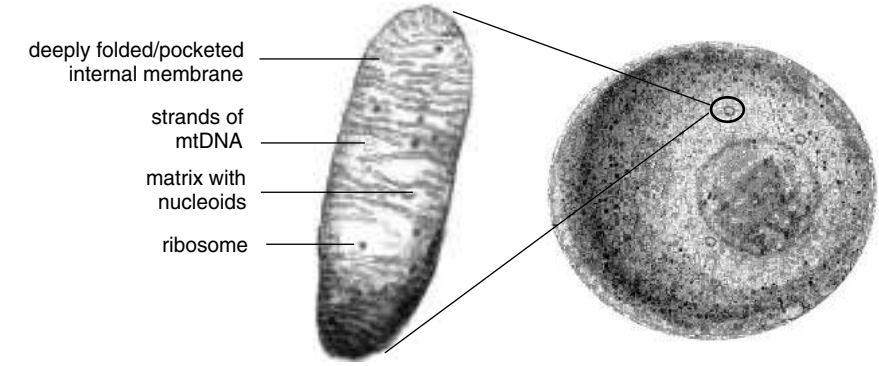
With the exception of identical twins, each person's DNA is unique and different, though patterns that link relatives with a high degree of probability can be detected. If two generations are available for testing, a great deal can be discovered about familial relationships. A genetic pattern, derived from analyzing a DNA sample, is called a *genotype* and can be symbolically represented in a number of ways. A diagram resembling a bar code, called an *autoradiograph*, is commonly used to represent the patterns in a DNA sample, especially for basic *DNA profiling*.

For general understanding, the DNA molecule is symbolically illustrated as a double helix with connecting strands resembling a spiral staircase. DNA contains a large number of *base pairs*, that is, a pair of bonded *nucleotides* on opposite strands of the DNA. The bases are commonly called A, T, G, and C. Base pairs can be C-G or A-T. There are so many millions of these that unique sequences are found in individuals. It would be too time-consuming to examine all the base pairs in a sample, but enough is known about the patterns and repetitions in base pairs to select portions of the DNA that are known to vary from one person to the next and to concentrate on examining these.

Since these patterns vary less among family members than they do among unrelated individuals, they are useful for the identification or exclusion of familial kinships. The likelihood of two individuals being related is usually expressed as a percentage probability. In paternity tests, the offspring or father is generally said to be 100% excluded from being related or is related with a probability that usually ranges from about 99.6% to 99.9%.

*There appears to be a cell-death process that occurs at conception that reduces the mtDNA contribution from the father to virtually nothing.

Basic Mitochondrian Structure




The infolded structure on the left is a cutaway, simplified view of a mitochondrion showing its relative location in the cell on the right (multiple mitochondria exist outside the cell nucleus). Mitochondria are mobile, flexible cell organelles. In mammals, they are passed down through the maternal line (human sperm contains only about 100 mitochondria, compared to about 100,000 from the mother). They are usually elongated, though some may be round. The convoluted inner structure is a greatly infolded membrane. Associated with the membrane is a matrix containing nucleoids (free areas within the matrix), which in turn contain bodies of DNA. This mitochondrial DNA (mtDNA) is useful as it may degrade more slowly than nuclear DNA. [Classic Concepts diagrams, pages 15-6 and 15-7 ©1999, used with permission.]

Details of the structure of the molecule and the various components of DNA can be found in biological texts and forensic texts on DNA sampling and analysis and are not described in depth in this reference. Instead, this chapter focuses mainly on concepts and procedures essential to the basic understanding of *DNA identification* as it pertains to surveillance. Those involved in the surveillance industry typically turn the samples over to specialists (or a computer program) for analysis.

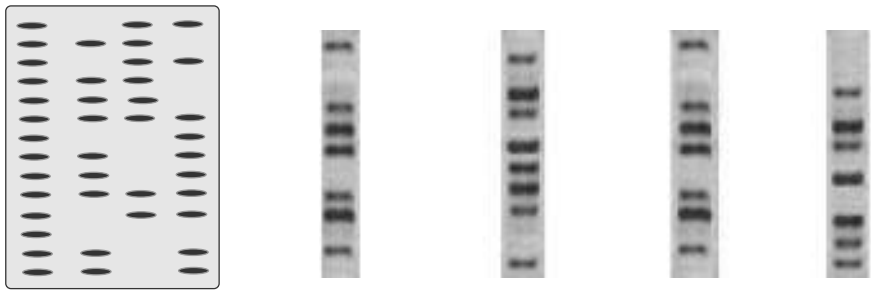
There are many ways to represent genetic coding. DNA sampling results are symbolically or photographically represented, usually in ladder-like bands that are created by processing the DNA fragments so that they are sorted according to size. The portions selected for basic identification of an individual are those which tend to vary widely from one person to another. This information is statistically and experimentally derived.

The human genome includes over three billion ($3x10^9$) base pairs. This is a number greater than most of us can conceptualize. Obviously not all of these are 'active' in the creation of an individual, but exist as potentialities. Of more than three billion base pairs in a human cell, approximately 15,000 genes are expressed at any one time from a typical tissue sample. We are still trying to unravel the complete genetic code and The Human Genome Project (HGP) was initiated as an international collaborative project specifically for this purpose.

The Human Genome Project has the goal of determining the complete human genetic sequence. While this information does not wholly predict or describe an individual's genetic makeup, it does provide significant information about general organization in humans, and particular patterns of organization in related humans or humans with similar characteristics or afflictions.

DNA patterns exist in all living, growing organisms, thus plants, fish, birds, dogs, horses, and people all have DNA characteristics distinct to their species. The DNA pattern in a controlled plant species confiscated in a smuggling operation can potentially be traced back to its source. Recovered children, who have been kidnapped at a very young age, can be reunited

with their biological parents. DNA varies from individual to individual, but inherited characteristics can be mapped in family lines, providing information about sibling and parental relationships.



There are many ways of representing DNA patterns, but the most common means is a ladder-like film of dark and light bands resembling a bar code, called an *autoradiograph*. In a common process called gel electrophoresis, DNA fragments are transferred from a gel surface to a membrane, subjected to radioactive probing, and recorded on X-ray autoradiograph for viewing and storage. Common applications include *DNA parental profiling* for determining paternity or other relationships, or *DNA matching*, comparing several patterns to a specific reference pattern for a match. [Classic Concepts diagram ©1999, used with permission.]

# 3. Context

*DNA testing is recent, and all the possible applications of the technology have not yet been developed. It is not difficult to procure samples for DNA testing; a cheek swab, drop of blood, glob of saliva or semen, or a handful of hair roots or feathers is often sufficient for basic testing. While contamination is possible, the use of sterile gloves and a sterile swab for each sample, and storage in a sterile envelope, vial, or other container, can substantially reduce the risk of contamination. Since collection procedures can be quickly learned, many people can be trained to obtain and handle noninvasive samples, particularly cheek swabs.*

Although DNA sampling can be done by laypersons, invasive procedures, like drawing blood, should be carried out by trained professionals. DNA database entry is usually carried out by skilled or semi-skilled workers. DNA analysis is usually handled by forensic scientists with at least a Bachelor of Science degree and a background in Chemistry and Biology and extra training pertinent to DNA analysis. However, portable 'briefcase' systems sometimes provide preliminary computer analyses onsite which can later be verified by fuller analyses by trained specialists in a lab.

The stability of typical DNA samples is relatively good. Uncomplicated storage procedures can preserve them for weeks or months. More sophisticated embalming or freezing techniques can preserve them for years and sometimes for centuries. Mitochondrial DNA survives longer than nuclear DNA, and while it only carries information from the maternal line, this information may be decades or centuries old, and can be very useful.

The following information on DNA testing is skewed toward commercially available or patented technologies, as these are the ones most likely to be accessible to surveillance professionals. Human DNA-testing is also emphasized and information on wildlife testing for law enforcement or conservation purposes is surveyed in less detail. For a more abstract theoretical background and pure research in this area, see the numerous resources listed at the end of the chapter.

## Assessing Samples

Before looking at the information inherent in specific gene sequences, the species from which a sample has originated should be known or discovered. Murder suspects are sometimes apprehended on the basis of pet hairs found on their clothing. A crime scene may yield samples from spattered blood, but until it is analyzed, it is not usually known if the blood came from a victim, a witness, a criminal, or the family dog.

Research exists on the DNA patterns of many species, viral, botanical, avian, primate, etc. This knowledge, combined with various analytic techniques, including *protein electrophoresis, enzyme-linked immunosorbent assay,* or *radioimmunoassay* processes, allows one species to be distinguished from another. These techniques can be cumbersome, however, as they require that separate tests be performed on the suspected species to exclude it as a contributor. In 1995, Hershfield described a method of isolating nucleic acid from a biological sample and determining the interspersion pattern of repeats of a sequence in the isolated nucleic acid. This pattern could then be compared to known patterns of the microsatellite nucleotide sequence in selected organisms to determine the species.

Once the basic characteristics of a sample have been identified, and contaminants removed or neutralized, it can be further processed. There are two distinct methods of DNA testing and analysis in the field of forensics that have been widely adopted as they are more efficient than historic means of processing DNA:

- **polymerase chain reaction** (PCR) - This is currently the most commonly used group of methods for preparing a sample for analysis. PCR is less discriminatory than RFLP (described next) but it is a useful type of analysis which can be carried out with smaller samples that may not be in perfect condition, e.g., crime scene samples. The DNA molecule is extracted and replicated, thus providing copies of the original DNA in a process called *amplification* to assist in 'seeing' and evaluating the characteristics of the sample. Care is taken to try to amplify regions in the DNA which show greater variability among individuals, known as *polymorphic* regions. This is generally done in a test tube that is subjected to cycles of heat and cold. With PCR, results can be obtained fairly quickly. Larger, purer samples yield better results. Depending on the results, PCR may be followed up by RFLP. Amplification may be hindered by certain substances in the sample, such as hemoglobin in whole blood. Such substances need to be filtered or inactivated before replication can take place.

After initial processing, a sample can be *typed*. There are commercial kits and typing *strips* for examining genetic loci. *DQ alpha* is a common typing process.

- **restriction fragment length polymorphism** (RFLP) - This is a highly discriminatory type of analysis requiring a somewhat larger sample that is in good condition. The DNA molecule is extracted and cut or *restricted* at specific pre-determined sites by using an enzyme. The resulting fragments are separated by a process called gel electrophoresis in which they are sorted by application of an electric current to the gel medium through which the fragments are drawn. At this point a *blot* is usually made, and a *probe* applied to reveal the patterns in the DNA (blots and probes are described in more detail later). Traditionally, the sizes of the DNA fragments are determined manually, though automated procedures are now favored. The final pattern is represented on a membrane as a 'bar code' which is usually transferred to X-ray film. Analysis may take several weeks. RFLP may be used in situations where speed is not essential, or where a more accurate appraisal is important. It can also be used as a follow-up to the quicker PCR analysis, depending on the circumstances.

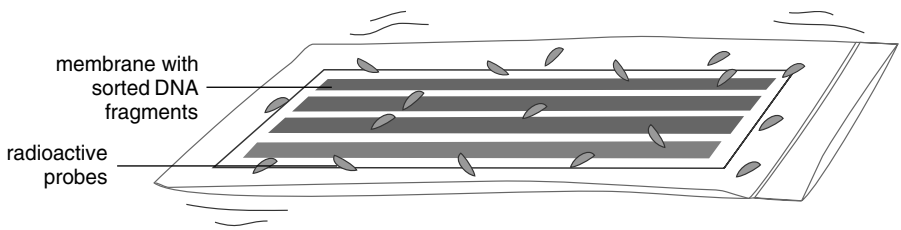
Commercial improvements to basic DNA processes are always being sought, motivated in part by the huge backlog of unprocessed samples stored in law enforcement evidence archives. By the mid-1980s, researchers had developed a means of increasing the concentration of a segment of target DNA without the need to purify or synthesize nucleic acid sequences unrelated to the desired sequence [Mullis et al., 1987]. A decade later, some of the problems of using replicated materials were overcome and specific target DNA could be detected without amplification through site-specific enzymatic cleaving [Dahlberg et al., 1992]. Many aspects of laboratory amplification and detection were improved at this time.

Surveillance occurs on a global scale, with samples often being gathered in foreign countries. The use of the PCR method can have secondary benefits in cases where export restrictions prevent transport of the original sample; one of the synthetic PCR-replicated samples may be sent instead. A thermal cycler is a portable device for replicating a DNA sample which can be used for international export without violating regulations.

DNA technology is still young, and these methods are some of the earliest best solutions to efficient processing of samples. However, they are not without their drawbacks.

In PCR, there is always the danger of amplifying non-target fragments, depending on the quantity of the sample, the number of cycles of amplification performed, and environmental factors such as temperature [Erlich, 1989].

Specific nucleic acid sequences are usually detected by a process called a *hybridization reaction* or simply *hybridization*. While this process has become an important tool, it is not a perfect one. A mixture of DNA may only yield a low concentration of the sought-after target sequences; probe and target sequences are not necessarily perfect complements of one another and do not yield all possible probe-target complexes. Nevertheless, it remains a useful tool.




Radioactive probing of DNA fragments aids in locating target sequences. In many common 'blotting' procedures, the membrane containing the DNA fragment pattern can be reprobed with different markers. Radioactive probes are gradually being superseded by fluorescent probes. [Classic Concepts diagram ©1999, used with permission.]

There are many ways of processing DNA samples. Not all will be discussed here, but examples of some common techniques are given to provide a basic understanding of what happens to a collected sample when it reaches the processing lab.

### Southern Blot

The Southern blot is a well-known process of sample preparation, evolved from Edwin M. Southern's technique of identifying specific nucleic acid sequences. He developed these techniques in the mid-1970s. Blotting provides a stable replica of the distribution of the DNA fragments within a gel medium (after electrophoresis), and information on sequence organization.

Carrying out a Southern blot involves separating out the DNA from other materials in the nucleus of a cell. This can be done with pressure, or with chemicals. The DNA is then chemi-

cally 'cut' into pieces of different sizes using enzymes with consistent effects on the DNA. A process of *gel electrophoresis* is then used to sort the DNA pieces by size. An electrical charge is applied to the mix to attract the DNA fragments. Smaller fragments travel more readily through the gel medium, leaving the longer fragments behind. The DNA is then denatured by heat or chemicals into single strands. The DNA strands are then mounted on a membrane in a process called 'blotting' for handling and analysis.

A radioactive DNA strand can be used as a 'probe' to aid in the analysis of the DNA sample. Subsequent exposure to X-ray film reveals areas in which the radioactive probe binds, indicating the occurrence and frequency of patterns within the sample. The fixation required for this process may take several hours to several days. While still a well-known technique, the use of radioactive probes is giving way to other methods, such as the use of fluorescent probes.

### Short Tandem Repeat (STR) Analysis

Repeat markers such as *short tandem repeats* (STRs) were first described in the mid-1980s. STRs are end-to-end repeating blocks of DNA with less variability in the length of the fragments. STR is sometimes known as STMS (sequence-tagged microsatellite site). Use of these structures for nuclear DNA analysis is faster and less complicated than conducting a RFLP analysis.

In STR, particular areas of DNA selected for high population variability are examined for patterns and unique characteristics that distinguish one person from another, or which bear similarities to others in a given population. In STR, a small area in the DNA chain is targeted and amplified using the PCR reaction. In the mid-1990s, systems for analyzing more than one STR at the same time were developed. A couple of years later second generation multiplex (SGM) was introduced, which utilizes six different areas of DNA. This provides a higher level of discrimination than previous systems when used in conjunction with database population profiles.

Mass spectrometry is one of the more recent technologies to utilize STR fragments. STR analysis is sometimes appropriate in situations where there is not enough sampled material in sufficiently good condition to perform a Southern blot.

Many companies are now using STR systems for paternity testing and crime suspect DNA-print matching.

## 4. Origins and Evolution

*Our understanding and use of DNA technology are incredibly recent. Humans walked the Earth for about a million years without understanding how our bodies express specific physical traits. Even when scientific strides were being made in the Renaissance, social and religious prohibitions prevented the hands-on study of the human reproductive system, or any tampering with its functions, for many more decades. The systematic study of cell reproduction is less than 300 years old, and was at first grasped in only the most general way by leading philosophers and scientists.*

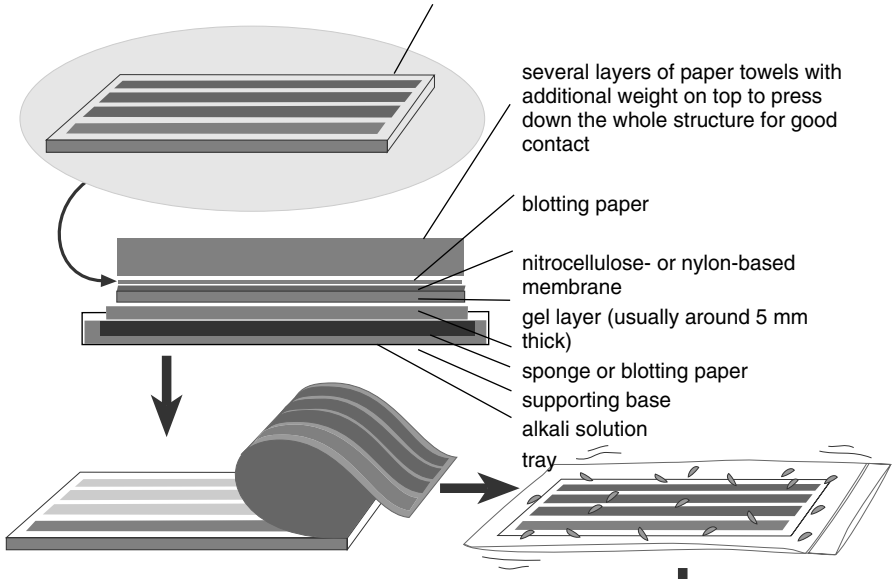
*General public awareness of the biological mechanics of sexual reproduction is less than 100 years old, and public awareness and commercial use of DNA did not become widespread until the mid-1990s.*

Due to social prohibitions on human experimentation, early scientists turned to other forms of life to study cellular structure and reproduction. They may not have realized it at first, but plants, insects, and marine animals are excellent experimental subjects; their cells can be quite large and many engage in sexual reproduction. Scientists have unraveled many important

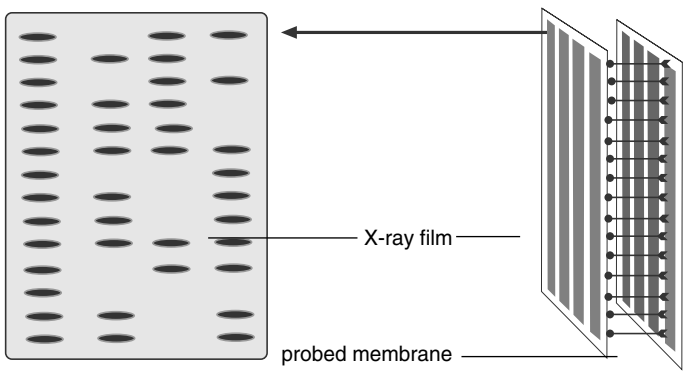
This is a much simplified illustration of a gel electrophoresis and blotting process. Lab techniques vary, and newer methods are beginning to supersede gel electrophoresis, but this has traditionally been a widespread means of processing DNA.

*A gel layer is subjected to electrophoresis to cause the DNA fragments to separate (smaller fragments move more readily through the gel).*

*The fragments are 'blotted' onto a membrane. Good contact between the layers is important, as is the prevention of air bubbles.*




*The membrane bonded with the DNA is removed from the layer of gel and subjected to probing in a buffer medium to hybridize the DNA.*




*After probing, the membrane bonded with the DNA is placed adjacent to X-ray film, where the radioactive decay exposes the film to form a 'picture' of the placement of the fragments. The membrane can then be cleaned and reprobed and the imaging repeated several times.*

DNA fragments are 'sorted' by gel electrophoresis and blotting and embedded in a medium so that the results can be probed and recorded on X-ray film for handling, analysis, and storage. [Classic Concepts diagram ©1999, used with permission.]

genetic fundamentals by studying plants and animals. The vessel cradling the genetic code, the *nucleus*, is present in some form in all these living things.

An overview of historical milestones in cell biology and genetics, and application of this information to DNA profiling, are provided next to give a backdrop to DNA sampling and the evolution of the technology. A summary chart of milestones is provided for quick reference. Following this is a practical section on collecting and handling DNA sample materials.

### Understanding Cell Structure

*Conducting DNA surveillance hinges on collecting useful cell samples. Thus, it is helpful to have a basic understanding of cell structure.*

Antony van Leeuwenhoek

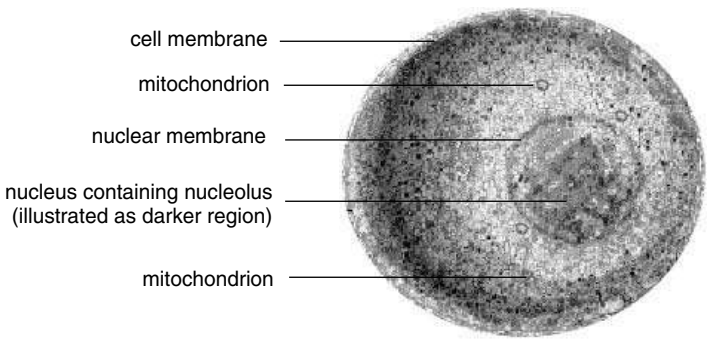
Most cell structures, particularly DNA, are too small to see with the unaided eye. Many of them are transparent, making them hard to recognize or distinguish from one another. Our detailed understanding of cell structure can be attributed to the invention of the microscope in the 1600s by Galileo (adapted from the telescope), Kepler, and Malpighi. Important strides in microscopy were made by Robert Hooke (1635-1703) and Antonie van Leeuwenhoek (1632-1723) in the late 1600s.

Van Leeuwenhoek greatly improved the single-lens microscope and used it to identify and study spermatozoa. The microscope is an indispensable laboratory tool which is routinely used for cell biology (cytology) and DNA sample assessment and preparation.

Left: A historic 1665 single-lens microscope, designed by Robert Hooke, was a significant invention that permitted scientists to discover microscopic cell structures and tiny living organisms. Right: Modern versions of the microscope are still indispensable laboratory tools, especially the electron scanning microscope. NASA uses microscopes extensively in space-related research, which includes searching for signs of life in samples from asteroids and other planets. [Carpenter, "The Microscope and its Revelations," copyright expired by date; NASA/LRL news photo, released.]

A few scientists stand out as being significantly ahead of their time in studying reproductive processes. Regnier de Graaf (1641-1673) described human testicles toward the end of his short life. He also studied female reproductive structures and coined the term *ovary*. The Netherlands botanist Rudolph Jacob Camerarius (1665-1721) observed in 1694 in *"De sexu*

*plantarum epistola"* that plants can reproduce sexually. Another forerunner, Lazzaro Spallanzani (1729-1799), experimented with frog semen and discovered that filtering the liquid could prevent its ability to fertilize frog's eggs, thus indicating that something contained in the liquid, not the liquid itself, must be responsible for fertilization. It took about 100 years for general scientific understanding to catch up with these discoveries. The evolution of DNA science from that time on follows a fairly orderly history from discovering basic cell structures and functions in the early 1800s, to developing theories to explain and predict heritability in living organisms in the mid-1800s, to developing commercial technologies in the 1980s. Trailing behind are ethical and social structures to understand, contain, and regulate the technology. These are ongoing developments.




This simplified drawing of a cell illustrates the basic structures that contain DNA. Historically, the biological structures related to genetics could not be studied in detail until microscopes and staining techniques were developed that could reveal the tiny, transparent contents of cells. [Classic Concepts diagram ©1999, used with permission.]

Once the microscope came into general use, great strides were made in cytology. In the early 1800s, Lorenz Oken (1779-1851) observed that organic beings originate from and consist of vesicles or cells. In 1831, Robert Brown (1773-1858) published *"On the organs and modes of fecundation in Orchideae and Asclerpiadae"* describing an important cell structure associated with fundamental building blocks. He observed an opaque area which he called an 'areola, or nucleus of the cell.' Matthias Jakob Schleiden (1804-1881) enlarged on the work of Brown and emphasized the importance of the nucleus as essential to the structure of the cell, calling it a *cytoblast* in his 1838 paper "Beitrage zur Phytogenesis." Within a year, a significant paper by Theodor Schwan, a professor at the University of Louvain, called attention to the importance of nuclei in animal tissues.

Most of these scientists didn't fully comprehend the role of the nucleus, thinking that perhaps new organisms budded from its surface, but the observations of Oken, Brown, Schleiden, and Schwan represent important pioneering steps in unraveling the mysteries of inherited traits within living organisms through the discovery of basic cell structure.

### Charting Cell Structure and Exploring its Functions

*Looking at further historical discoveries in detailed cell structure helps clarify the aspects of the cell that are related to DNA. This understanding of cells is useful in the DNA sampling process, as not all cells in the body contain nuclear DNA (as examples, hair shafts and mature red blood cells do not contain nuclear DNA).*

Some of our understanding of cells comes from plant studies. In 1835, a German botanist, Hugo von Mohl (1805-1872), observed viscous fluid with a granular texture within cells that were sometimes in motion (motion in cells had been observed for about 60 years). He ob-

served filamentous streams within the structures.

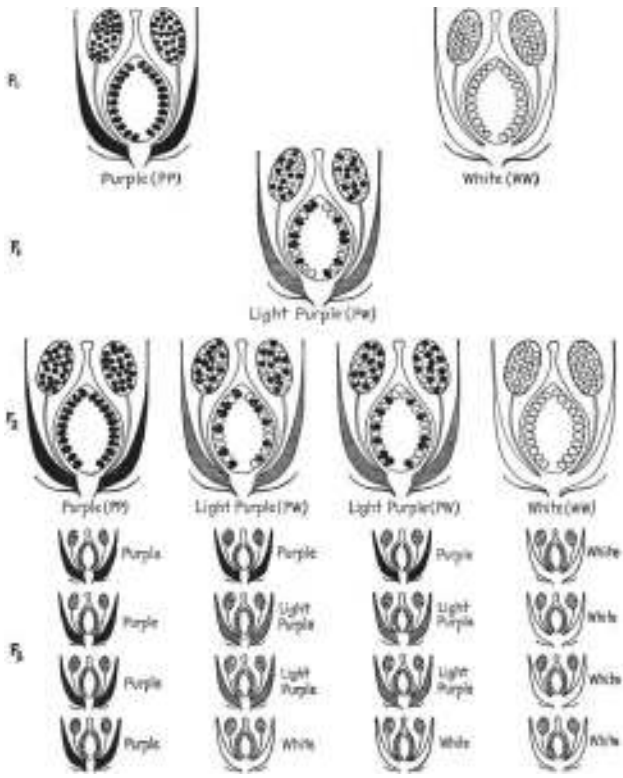
Around this time scientists noticed, with the help of microscopes, that the cell wall was not always present in small organisms, but that the same kinds of substances could be found within cell walls. They realized this was a clue, and subsequently directed their attention to these structures.

In 1848, Hofmeister observed the process of cell division in plants, and rod-like bodies within their cells.

By 1860, German physiologist Rudolph Virchow (1821-1902) had asserted a principle of the continuity of life by cellular division, roughly "All cells arise from cells," thus making an important contribution by establishing that the cell is a key reproductive unit with the potential to generate a new organism.

### New Theories and Procedures to Understand Heritability

*Now that basic cell structure and reproduction were being unraveled, scientists developed theories for the hows, whens, and whys of cell reproduction, and how these might apply to our understanding of human origins. Many of these theories were met with disbelief or strong opposition, particularly in religious circles.*




Gregory Mendel's work in plant inheritance was a strong influence in genetics. This 1922 interpretation of Mendel's Law of Inheritance illustrates color traits in plants that are passed from the parents ($P_1$) onto their offspring through three successive generations ($F_1$, $F_2$, and $F_3$). [From "Botany Principles and Problems," Sinnott, 1923, copyright expired by date.]

In 1859, British naturalist Charles Darwin (1809-1882) introduced a significant work "The Origin of Species" and sought to explain natural selection and inheritance. Other scientists, like Erasmus Darwin before him, and one of his contemporaries, Alfred Russel Wallace (1823-1913), were seeking to explain our roots as well, but Darwin's writings managed to touch a sensitive chord and he is the best remembered theorist of the time.

In 1866, Gregory Mendel (1822-1884), an Austrian cleric, published an important paper "Experiments in Plant Hybridization" in which he credits the earlier work of various researchers Gärtner, Pisum, et al., but points out the lack of a general theory, and the importance and difficulty of framing statements of general laws governing inheritance in organic forms. In his paper he describes his long experiments with plants and offers important observations regarding the stable patterns of heritability of traits among the offspring. Subsequent scientific research included studies of patterns of heritability in humans. Researchers now wanted to know where this information was stored and how it could be accessed and perhaps controlled. The works of Mendel came to the attention of the mainstream of science when they were independently rediscovered at the turn of the century by Hugo DeVries, Erich Von Tschermak, and Carl Correns.

### Cell Division and Fertilization

*The equal contributions of the mother and the father to the genetic makeup of human offspring is an important consideration in DNA analyses, particularly as they relate to parental profiles. Understanding basic cell division can help clarify this aspect of DNA testing.*

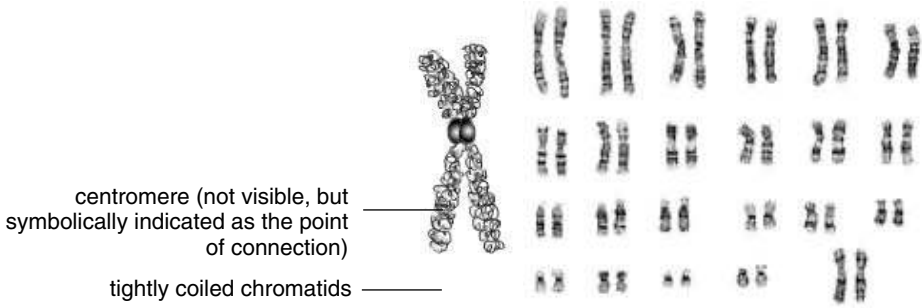
*By the late 1860s, there were many scientists who accepted the dual role of sperm and egg cells in reproduction, but most of them still assumed that the sperm was performing some sort of chemical stimulation of the female egg, and did not yet credit the genetic material inserted by the action of the sperm. Microscopes had been a big boon to cell research, but the limits of their usefulness were being reached because they were unable to show transparent structures.*

The brothers Oscar Hertwig (1849-1922) and Richard Hertwig (1850-1937) conducted research together at a marine station in France. Around 1876 and 1877, Oscar Hertwig described the fertilization process in terms of the 'conjugation of two different sexual nuclei' from the male and the female, thus bringing the theories one step closer to our present understanding. In 1879, Hermann Fol, also working with marine animals, graphically illustrated the process of a sperm penetrating an egg, based on his observations of starfish.

In spite of mounting scientific evidence to support heritability from one generation to the next, there were still people who opposed the idea of nuclear continuity through descendants. Many still thought of family traits as being inherited in some mysterious manner through blood, a belief that resulted in terms like *blood relatives* and *bloodlines*. It was not until William Henry Perkin (1838-1907) made great strides in the synthetic creation of dyes, that microscopy provided the means for the next stage of discovery, starting around the 1870s.

Eduard Adolf Strasburger (1844-1912) made essential contributions to cell science when he used dyes to 'illuminate' various cell structures and plant cells undergoing mitosis. This allowed him to observe the *union of nuclei* during the process of fertilization.

In 1879, Walther Flemming (1843-1905) was studying dividing cells and observed the formation of what would later be termed *chromosomes*, though he didn't yet understand their function. Microscopic dyes allowed Flemming to observe the progressive stages of cell division. In 1882 he published "Cell Substance, Nucleus, and Cell Division." This important work described the results of his studies of cell mitosis, describing the role played by chromosomes in cell division. In 1888, the chromatic threads in the cell nucleus were termed *chromosomes* by Waldeyer.




These simplified drawings illustrate the general configuration and shape of human chromosome pairs. These chromosomes are roughly the same shape, but differ in size, and are typically sorted by size for identification purposes.

New scientific discoveries always seem to generate controversy. In the 1880s, August Friedrich Leopold Weismann (1834-1914) challenged the *blending and rejuvenation* theories of reproduction. In 1892, he described his own theories in "Keimplasma Theorie" (Germ Plasm Theory) about the continuity of life through the self-reproducing nature of cells through chromosomes. He also described how the genetic material in the egg and sperm are halved and then become a full germ plasm again when they combine with one another in the fertilized egg.

Up to this time, many people wanted to believe that a mother's biology somehow determined the sex of her offspring. Henry VIII had several wives killed because they did not bear him a male heir. Clarence E. McClung (1870-1946), an American Biology professor, wrote a key paper that described how chromosomes were involved in sex determination in a species of grasshopper. He was assisted in his research work by Walter Stanborough Sutton.

### The Rise of Modern Genetics

*In the early 1900s, many of the key concepts and techniques involved in the emerging science of genetics were being developed and put into practical use.*

Thomas Hunt Morgan (1866-1945) had enormous influence in early genetics research, not only through his own research, but also through the research of his students, who were inspired by his example. Morgan did some important work in the study of inheritance in fruit flies (Drosophila Melanogaster), confirming Hugo De Vrie's (1848-1935) observations from plants that mutations can occur, and that inheritance is not absolutely scientifically predictable. Morgan's experiments established the important role of chromosomes in heredity and motivated researchers to locate particular gene locations. In 1901, he authored "Regeneration" and in 1926 "The Theory of the Gene." In 1933, he became the first biologist to win a Nobel Prize.

In 1902, Walter Sutton observed the process of cell division and published a paper on chromosome morphology. The following year, Theodor Boveri (1862-1915) and Sutton independently observed that each gamete receives only one chromosome from each original pair and Sutton proposed that the offspring get genetic material from each parent. Within the context of Mendel's studies, he suggested that heritable 'factors' were located on chromosomes and called them *genes*.

In 1902, William Bateson (1861-1926) authored "Mendel's Principles of Heredity: A Defence." In 1905, he made an important demonstration that some characteristics are not independently inherited, thus introducing the concept of 'gene linkage' which led to projects to

map the genes and describe their order and relationships. Bateson coined the term *genetics*.

In 1905, Edmund Beecher Wilson (1856-1939) and Nellie Stevens proposed that separate X and Y chromosomes determine the sex of a human offspring. Thus, two X chromosomes resulted in a female and one Y chromosome resulted in a male, an observation that was subsequently replicated by other scientists. Wilson had previously written "The Cell in Development and Inheritance" in 1896.

Archibald Garrod made some important connections between the work of Mendel and the biochemical pathways of reproduction and speculated on inborn metabolic causes for human diseases that swept away superstitions about 'bad air' and 'impure thoughts' as primary causes of illness and birth defects.

In the early 1900s, structures and nomenclature were specified in more detail, and processes explored more closely. In 1909, Danish botanist Wilhelm Johannsen (1857-1927) described a distinction between genotypes and phenotypes. In 1903, he first mentions the terms 'gene', 'genotyp', 'phenotyp' in the context of the breeding of beans.

In 1909, Archibald Garrod described the heritability of four metabolic diseases and interest in the speciality continues today, with the study of inheritance of serious diseases being a priority in many DNA research labs.

Genetics was introduced as a field of study at Columbia University in 1910.

Thomas Hunt Morgan demonstrated in 1915 that genes are the structures responsible for the transmission of traits. His research group also established the existence of 'sex-linked' traits, traits that are passed onto the offspring by one parent or the other or both, but which manifest in a particular gender (examples include hemophilia, pattern baldness, and color blindness). Morgan promoted a chromosome theory of heredity.

### Genetics and Gene Mapping

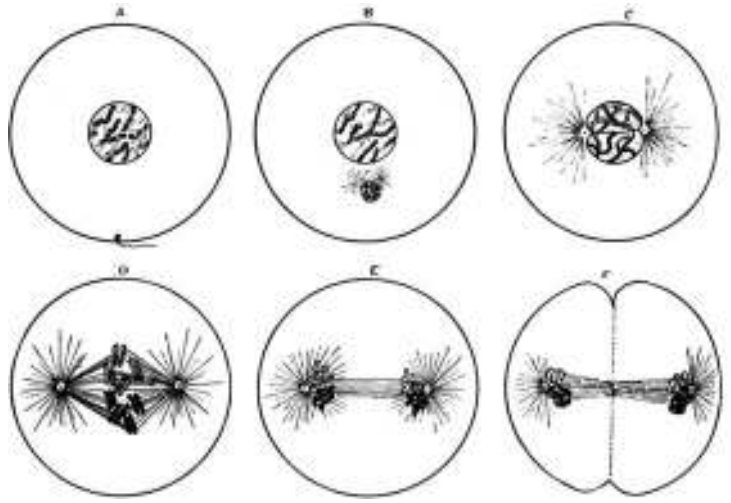
*Technology and discovery go hand in hand. The desire to know motivates us to create better tools for 'seeing,' and better tools result in unanticipated discoveries. Just as the microscope played an essential role in the understanding of cell structure and function, X-ray technologies played an important role in the discovery of DNA.*

Just as dyes allowed us to see previously unknown cellular components, X-ray crystallography extended our 'vision' by revealing structures through the diffraction of light. This technology was developed in large part by the father-son team of William Henry Bragg (1862-1942) and William Lawrence Bragg (1890-1971). Practical use of their invention came in the mid-1930s. X-ray examinations are now used to reveal patterns in DNA. In 1915, the Braggs received a Nobel Prize for their work.

In 1913, Alfred Henry Sturtevant (1891-1970), a student of Thomas Morgan, constructed the first gene map by analyzing fruit fly matings and their results. This made it possible to follow and predict patterns of heritability.

With the introduction of genetics courses into the universities, the pace of research accelerated and the desire for intercommunication of the various discoveries increased. In 1916, the "Genetics" scientific journal was established by George Harrison Shull, a Princeton genetics professor, to meet this need.

In 1918, Herbert M. Evans declared that human cells contain 48 chromosomes (he was almost right).



The process of fertilization and cell meiosis as depicted in 1922. A) The sperm penetrates the egg. B) Having dropped its tail, the sperm moves toward the egg's nucleus. C) Interaction of the nuclei from sperm and egg. D) The splitting of chromosomes from sperm and egg. E) Separation of the chromosomes. F) Cell division. At the time this was drawn, genetics had recently been introduced to university curricula, and the nature of the gene was beginning to be explored and described. [Henry Holt and Co., copyright expired by date.]

In 1921, Hermann Joseph Muller (1890-1967), another of Thomas Morgan's students, described the nature of the gene in a theoretical paper that was very prescient. In the mid-1920s, he discovered that X-rays could increase mutation rates in fruit flies, indicating that the occurrence of mutations could be influenced in somewhat predictable ways. Muller's work was honored in 1946 with a Nobel Prize.

### Genetics Development and Social Impact

*In terms of its historical significance to surveillance, one of the most important landmarks in the application of the knowledge of genetics to human freedom and political control occurred in 1924, when the U.S. Immigration Act used genetics as a political lever to exclude poorly educated immigrants from southern and eastern Europe stating 'genetic inferiority' as a justification. This clear example of the abuse of political power is the reason why many people fear the potential misuse of DNA sampling and genetics databases.*

In 1926, Thomas Hunt published "The Theory of the Gene" describing the physical basis for genetics, based on breeding experiments and his observations with optical microscopes. Around this time, scientists increasingly began to turn their attention to the intimate structure of DNA and its influence on physical traits.

In 1931, Barbara McClintock demonstrated that gene order in chromosomes can change by rearrangements, and that particular traits in maize are related to genetic distribution. In 1947 she reported on 'transposable elements,' now known as 'jumping genes.'

*The increased understanding of heritability of traits resulted in public attention being focused on people with undesirable traits, as interpreted by political powers of the time. As a result of this line of thinking, by 1931, compulsory sterilization laws had been implemented by the U.S. Government. Two years later, Germany instituted even more pervasive sterilization, labelling individuals as 'defective.' These historical precedents underline the impor-*

*tance of carefully evaluating the legal ramifications of DNA technology.*

In 1934, Desmond Bernal demonstrated that very large molecules could be studied with X-ray crystallography.

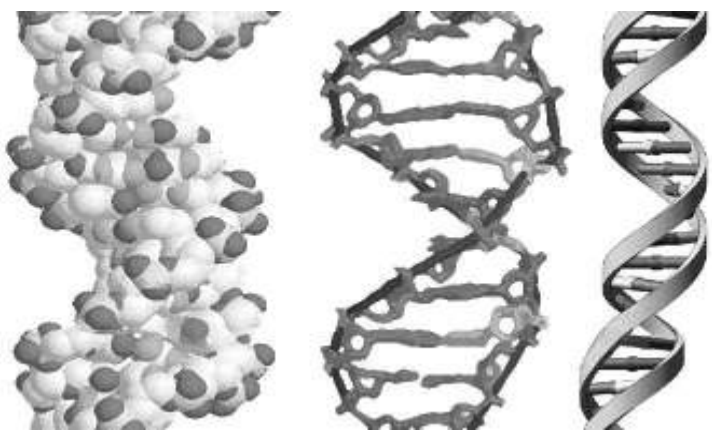
Toward the end of World War II, Maclyn McCarty, Oswald Avery, and Colin MacLeod were conducting research on pneumonia bacteria. They published their findings in "The Journal of Experimental Medicine" on 1 February 1944. This paper discussed thread-like DNA fibers that carried hereditary information, an important precedent, promoting further research into the characteristics and components of these biological fibers.

### Visualizing and Modeling DNA

*With the evolution of radio electronics, and the introduction of transistors in the 1940s, many new instruments that could aid scientists in detecting the structure and function of cells were developed over the next several decades. One of the most significant inventions around this time was Vladimir Zworykin's (1889-1982) adaptation of the electron microscope, originally developed in Germany in the early 1930s. It quickly became a practical and exceedingly important tool for research in molecular biology and biochemistry related to genetics. During the 1950s, scientists began to delve deeply into the detailed components of cell structures.*

In 1950, Erwin Chargaff (1905- ) reported the proportional components of DNA, now known as Chargaff's Rules. He observed the relationship between A and T (adenine and thymine) and between G and C (guanine and cytosine). His research was important to the subsequent development of models of the structure of DNA. Practical applications of inheritance in breeding were developed at about the same time. The principles of artificial insemination were known and had been described in print by the 1920s, but it was not until 1950 that artificial insemination became commercially routine in livestock breeding.

In 1952, Alfred Day Hershey and Martha Chase stated that genes consist of DNA, thus establishing a link between DNA and heritability. The electron microscope made it possible to study the anatomical structures of cells, including the *ribosomes*.



Three symbolic representations of the double helix structure of a DNA molecule. Forming a hypothetical model of DNA was an important step toward understanding the molecule, and synthesizing it in the laboratory. [Classic Concepts diagrams ©1998, used with permission.]

In the 1950s, Oliver Smithies developed a starch gel electrophoresis process for separat-

ing proteins, which eventually led to practical tools for processing DNA for analysis, such as the Southern blot which is now commonly used.

In London, Maurice Hugh Frederick Wilkins (1916- ) and Rosalind Elsie Franklin (1920-1958) conducted X-ray diffraction experiments that revealed the presence of two curving, related strands forming the basic structure of a DNA molecule. This technology constituted another important milestone in research and practical applications.

In the 1950s, James Dewey Watson (1928- ), and Francis Harry Compton Crick (1916- ) built on the work of Wilkins and Franklin and the chemical data of Chargaff, and published a more comprehensive descriptive model for DNA's double-helix structure. This important tool for visualizing DNA earned Watson, Crick, and Wilkins a 1962 Nobel Prize.

One way to confirm a biochemical model is to replicate it in the lab. Despite the complexity and microscopic scale of DNA, Arthur Kornberg (1918- ) confirmed Watson and Crick's theoretical description of DNA and successfully synthesized it in 1956, earning a 1959 Nobel Prize.

In 1956, Tijo and Levan stated that humans have 46 chromosomes rather than the 48 reported by Evans in 1918.

### Laboratory Tools and Manipulation of DNA

*When Arthur Kornberg synthesized DNA in the lab, he opened up vast new roads in DNA research with practical applications in surveillance technology and general investigative sciences. The late 1960s to the late 1970s was a time during which laboratory synthesis and manipulation of DNA made it possible to develop general procedures for replicating and studying DNA, and set the stage for practical DNA profiling methods.*

In 1958, Matthew S. Meselson and Franklin W. Stahl confirmed the 'splitting' of the double helix shape lengthwise to allow nucleotides to link with each half of the chain, forming two duplicates of the original structure. Important lab techniques now began to stem from such discoveries. Hybridization processes, which are now used for detection of specific nucleic acid sequences, were observed and reported in 1960 by Mannur and Lane and Doty et al. By 1970, it was possible to isolate discrete fragments of DNA.

Also in the late 1950s, Crick and his co-workers were exploring a 'messenger' molecule, ribonucleic acid (RNA), that is essential to transmitting DNA information.

In 1968, Victor A. McKusick described the repetitive nature of DNA and defined the first gene place. In 1970, Hamilton Smith and Daniel Nathans discovered a DNA-cutting enzyme. Enzymes which can 'cut' the DNA in certain locations and *ligasen* which can rejoin DNA, became important laboratory tools. Cutting DNA is now an essential procedure in laboratory processing of DNA.

In 1973, Herbert Boyer (1936- ) and Stanley Cohen (1922- ) created the first recombinant DNA molecule using the restriction endonuclease *EcoRI* and the plasmid *pSC101*, opening up a new level of genetic engineering and biotechnology.

*1975 saw the practical application of immobilization techniques used in conjunction with restriction enzymes. Development of processing and analytic tools such as the Southern blot were underway.*

Frederick Sanger (1918- ) and Alan R. Coulson (1947- ) presented a practical gene-sequencing technique that employed *dideoxynucleotides* and *gel electrophoresis.* In 1977, Walter Gilbert (1932- ) and Allan M. Maxam presented a gene-sequencing technique that employs cloning and gel electrophoresis. Gel electrophoresis, a means of sorting DNA fragments in a gel medium, is still widely practiced. Modern DNA profiling was falling into place.

## Applying Laboratory Methods to Unraveling the Genome

*The most significant genetic research of the last twenty years has been the unraveling of the structure and function of individual human genes, and the database organization of this knowledge to better understand gene expression, interaction, and influence. The motivation to chart the human genome is in large part fed by our desire to eradicate or cure psychologically or physically painful conditions or life-threatening illnesses of a genetic origin. However, in the process of exploring the medical aspects of human genes, we are also uncovering many more complex social issues. Understanding the human genome is closely allied to DNA analysis, as the results of an analysis can be related to the growing body of work elucidating the genome, thus uncovering characteristics of a socially volatile nature.*

Fred Sanger is credited as the first person to sequence an entire human gene, in 1978, and DNA evidence was first introduced into courtrooms at about the same time. In 1980 he was co-awarded a Nobel Prize with Paul Berg and Walter Gilbert.

## Exploring the Human Genome

In 1980, David Botstein et al., suggested the use of DNA information as markers for exploring the human genome. Gene mapping became an important goal and tool of DNA researchers. At about the same time, automated sequencing was developed.

In 1983, Kary Banks Mullis (1944- ) developed the polymerase chain reaction (PCR), an important tool for amplifying a DNA molecule which is now widely used both in laboratories and in portable DNA analysis kits.

In 1984, Alec J. Jeffreys of Leicester University developed *DNA 'fingerprinting*.' This was initially used in forensics in the U.K. in 1986 for investigating violent crimes. By 1987, DNA technology had made its mark on the legal system, a suspect had been convicted of a violent crime with the assistance of DNA evidence. The following year, in the United States, DNA was used to assist in convicting a criminal of rape. From this time on, there has been increasing acceptance of DNA evidence in court proceedings.

In the late 1980s, *fluorophore labels* began to supersede *radioisotope labels* for labeling DNA fragments for the purpose of DNA base sequencing. The fluorophore method permits analysis of DNA up to a length of about 500 base pairs (above this length, analysis is difficult due to reduced signal intensity). About the same time, the FBI began investigating the feasibility of using mitochondrial DNA for human-identity testing.

## The Human Genome Project - HGP

*In October 1990, the historically significant Human Genome Project (HGP) was officially launched, with James Watson as the first director. This project was initiated with the goal of mapping the entire human genome, and is expected to complete the task to the 'working draft' stage sometime around the end of 2002.*

By 1993, French researchers had completed a physical map of the human chromosomes. A year later, an international team published the first linkage map of the human genome.

In the early 1990s, following the work of Alec Jeffreys, practical methods for 'fingerprinting' a DNA sample, that is, determining whether it matched or didn't match a given example, were developed, with more precise and efficient quantification procedures for DNA profiling arising a few years later.

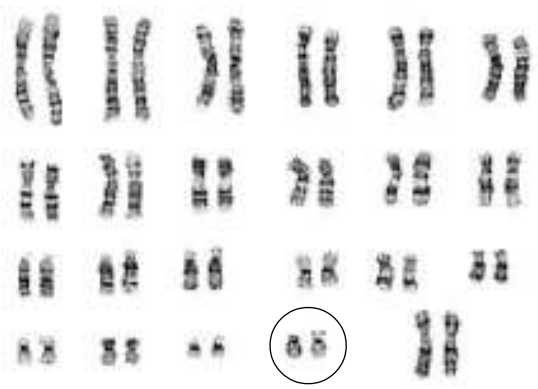
Ranajit Chakraborty, a professor of population genetics, designed DNA-sampling strategies which were used in analyzing hundreds of DNA-typing databases. He manages a repository of forensic DNA databases for more than six countries including India, Australia, Brazil, etc.

**Some Key Developments in the Evolution of DNA Technology**

| | |
|---|---|
| late 1400s | Leonardo da Vinci observes that skin color is influenced by both the mother and the father and Michelangelo writes letters to his brother advising him to find a wife with a good constitution and good traits that can be passed on to the children. These facts indicate that at least an intuitive understanding of heritability existed among the educated by Renaissance times. |
| mid-1600s | De Graaf studies reproductive anatomy and coins the term *ovary.* |
| late 1600s | Microscope technology is advanced by Hooke and Leeuwenhoek. Leeuwenhoek uses his microscope to study spermatozoa. |
| mid-1700s | Spallanzani studies frog semen and discovers that something contributing to fertilization can be filtered out of the semen. |
| 1831 | Robert Brown observes a cell nucleus. |
| 1835 | Hugo von Mohl observes a granular texture in cells. |
| 1848 | Hofmeister observes plant cell division and rod-like structures within the cells. |
| 1859 | Charles Darwin publishes "The Origin of Species." |
| 1866 | Gregory Mendel describes stable patterns of heritability in plants. |
| 1879 | Hermann Fol observes and graphically illustrates a sperm fertilizing an egg. |
| 1902 | William Bateson researches 'gene linkage.'<br>Sutton proposes that genetic material is inherited from each parent. |
| early 1900s | X-ray crystallography is developed. |
| 1916 | The "Genetics" scientific journal is launched. |
| 1920s | Thomas Morgan experiments with fruit flies and establishes the role of chromosomes in inheritance. |
| 1940s | The emergence of modern microscopes, electronics (especially the transistor) and electron microscope technology. |
| 1950s | Watson and Crick create a conceptual model of DNA. |
| 1956 | Kornberg confirms the Watson-Crick theoretical model and synthesizes DNA. |
| late 1950s | Technologies are developed for manipulating DNA. |
| 1960 | DNA profiling techniques are refined and hybridization is introduced. |
| late 1960s | Gene-cutting enzymes are applied to DNA sequencing techniques. |
| late 1970s | DNA evidence is introduced into court room trials, but is initially treated with some skepticism. |
| 1980s | DNA profiling lab techniques are developed and refined. Acceptance in courtrooms is increasing, though not yet secure. |
| 1990 | The Human Genome Project is established. |
| mid-1990s | DNA testing becomes commercially available to public consumers. Privacy and law enforcement issues associated with DNA are debated. |
| 1999 | Human chromosome 22 is decoded by a joint international effort. Iceland turns over its genetic heritage to a private company. |

By June 1996, after about four years of investigating protocol and validity, the FBI began conducting mitochondrial DNA forensic examinations.

By December 1999, an international team of researchers had sequenced an entire human chromosome (#22) containing 33 million base pairs as part of the Human Genome Project. The chromosome was found to have over 500 genes, with about 42% noncoding DNA. This significant achievement will be remembered as a milestone, and will facilitate the sequencing of the remaining chromosomes.



The first human chromosome to be fully decoded was chromosome #22, one of the smallest. This historic feat was accomplished by the end of 1999 in a collaborative international effort. [Classic Concepts diagram ©1999, used with permission.]

### Consumer Access and Awareness

*By the late 1980s, DNA profiling was a commercial commodity and accepted law enforcement tool. By the mid-1990s, the proliferation of DNA testing, and the increased use of DNA information in the legal system, sparked public concern about privacy and the ethical uses of DNA.*

As a result of public outcry from civil rights organizations, the Genetics Confidentiality and Nondiscrimination Act was introduced to the Senate in 1996. It was developed to safeguard the ownership of genetic information and the privacy of individuals. Similar bills were introduced in other areas. These legal restrictions have a direct influence on surveillance activities, limiting their scope and availability.

In the mid- to late-1990s, gel electrophoresis methods were refined and made quicker by using capillary rather than glass plates. Simultaneously, techniques using successive hybridization that did not require electrophoresis were being developed. Commercially available, reasonably priced DNA testing was offered to consumers around this time.

Commercial services proliferated in the early 1990s, and the motivation to produce faster, cheaper, more portable DNA analysis tools increased in the mid- to late-1990s. Realtime analysis of DNA fragments in DNA sequencing processes became commercially available using a fluorescent process around 1998. Approximately 10,000 to 20,000 bases per day could be analyzed with newer systems. Acceptance of automated systems was quick, given that there was a significant backlog of samples in law enforcement storage facilities that had not yet been analyzed.

Consumer acceptance of DNA testing rose dramatically in the late 1990s, in large part due to paternity testing on daytime talk shows. As with many historical developments, television

has had a substantial impact on public awareness (that is not to say that television has provided a well-rounded portrayal, but rather that it focuses public attention on specific aspects). In conjunction with this, the cost of a basic paternity test gradually dropped below $300 (this includes two samples, the alleged father and offspring). DNA research in the commercial sector is now heavily focused on automation and cost-saving measures. Law enforcement officials actively use the technology, and DNA databases are springing up everywhere. Home kits for personal DNA banking are in development.

A portable, battery-operated DNA analysis system has been developed at the Lawrence Livermore National Laboratory. Dean Hadley tests the suitcase-sized system for use in a variety of genetics profiling applications including forensics, paternity testing, remains identification, food and water analysis, and tests for pathogenic bacteria on the battlefield. [LLNL news photo by Joseph Martinez, released.]

By the late 1990s, realtime field analysis tools, such as those developed by the Lawrence Livermore Laboratory, began to make it possible to analyze a sample outside of the lab, a boon in situations where transport is difficult or impossible, or where confidentiality is desired.

### Commercializing a Genetic Heritage

The genetic heritage of the people of Iceland has been of particular interest to those studying genetics and those seeking to promote its ethical use. More than a little controversy has been associated with Icelandic DNA. Since the Vikings colonized Iceland in the 9th century, the settlement has been one of the more isolated and, hence, more genetically pure of the Scandinavian regions. In addition to this, the people of Iceland are organized and tidy and keenly committed to keeping detailed and careful records. A universal health-care system has been in place since the early part of the 20th century, and genealogical research is avidly pursued. A large percentage of the population, numbering a little over a quarter of a million, is able to trace its lineage back many generations and able to read the old texts.

Seeking to preserve and promote its genetic legacy, the Icelandic parliament voted to give medical and DNA records from the entire populace to an Icelandic biotechnology company named Decode. This company was given exclusive marketing rights for the information for

a period of 12 years and permission to create a centralized database. While this move clearly may provide important research information for the study of human origins, genetic patterns, and medical conditions, it also has significant ethical ramifications and raises concerns about what someone might do with the knowledge that a person has certain genetic weakness or latent illness.

In the case of complex issues and sciences that are still evolving, like DNA science, some of the ethical concerns cannot even be known in advance.

# 5. Description and Functions

*DNA samples will vary in their quality, purity, and quantity. What follows is a general overview of procedures for sampling and laboratory evaluation.*

## 5.a. Permissions

Regulations for DNA use vary. Citizens and medical practitioners are not significantly restricted in their use of DNA. The DNA collection of some armed forces personnel is mandatory. DNA collection by law enforcement officials is regulated much the same way as other search procedures. Thus, depending on the situation and the person doing the collecting, the first step in getting a sample may be to inform the donor of his or her rights, and to get permission from the donor or donor's guardian for a sample, or to procure a court order or 'search warrant' for taking samples from an involuntary donor.

If a person being sampled is involved in a family or legal dispute, it is particularly important to verify the identity of the donor with *all* of the following: picture ID, a signature, and preliminary questioning. There are documented cases of imposters, some of them look-alikes, showing up to provide DNA samples for paternity disputes or on behalf of fugitive criminals. It will never be known how many of these imposters have gotten away with this fraud, and there are still clinics that need to improve their screening and verification procedures.

## 5.b. Collecting Samples

*This section gives a general overall description of tissue collection, as there are variations in requirements from one lab to the next. For a practical understanding, it is recommended that a course of instruction be taken that includes hands-on demonstrations. Samples can be divided into two general categories: those that are given voluntarily or with permission of a guardian, and those that are collected without consent of the individual (individuals who are dead; who have committed a crime; who are being surveilled without their knowledge; or plants or animals which cannot give informed consent).*

When tissue donations are given voluntarily, it is customary to use a blood draw or buccal (cheek) swab or, in the case of a rape victim, it might be a vaginal or anal swab. Blood collection or other invasive procedures should be done by trained professionals. For full analysis, it is valuable to take samples from more than one body site. It is often necessary to take the sample in the presence of a witness, with signatures, for it to qualify as admissible evidence. In the case of involuntary samples, DNA tissue is especially subject to contamination. It is recommended that sterile gloves be worn, and sterile glass vials, tissues, swabs, and envelopes be used whenever possible, with fresh gloves for each sample taken. Materials that can contaminate samples include chemical residues, dirt, grease, and some dyes (e.g., denim dyes).

It must always be remembered that human body fluids may contain dangerous viral or bacterial materials that can be contracted or spread by the person taking the sample (tubercu-

losis, HIV, streptococcus, etc.). Exercise good judgment in acquiring and handling body fluids. In the case of large fluid samples such as urine or mouthwashes, it may not be practical or necessary to transport and store the entire sample, a few ounces may be sufficient.

Changes occur in our cellular structure as we age or are affected by various illnesses. Genetic material is quite stable and resilient, but mutations can occur. *Germ line* mutations are likely to occur throughout an individual as this is a type of mutation that happens early in the reproductive process or growing stages of a new organism. *Somatic cell* mutations can happen during reproduction, or later in development, with the changes present only in cells developing after the mutation. Thus, a somatic cell mutation may not be present in all body cells, and a sample taken from a cell mutation site could differ from a sample from another part of the body. For practical purposes, these mutations are rare, and surveillance professionals gathering samples can concentrate their attention on getting as many good quality samples as possible, leaving micro-analysis of the tissues to a trained lab professional.

When sampling plant tissues, it is generally easier to obtain enough material to satisfy the needs of the lab. Collect as much as is practical and store it in a sterile container. Depending on the type of plant, samples can be dried, vacuum-sealed, or frozen, if they need to be transported. Animal tissues may be more difficult to collect in sufficient quantity, especially those that are associated with violent crimes such as murder, and rape, as they may be scarce or difficult to see. Blood traces can sometimes be located with chemical reagents, but the chemicals that reveal the stains may also alter them so that they can't be processed for DNA. In some cases, ultraviolet light can be used to reveal stains and other traces of body fluids. It is vital to collect as much good tissue as possible, as not all the samples may be from the same individual, and some may be of poor quality. Sometimes more than one test needs to be performed. Skin scrapings from a window sill or from under a victim's fingernails should be collected, but the chances of getting a good sample are slim. The tissue is usually too sparse, or too contaminated to be useful, but it may be the only thing available, and therefore should still be collected with care.

Scrapings can be put on clean dry paper which is folded before placing it in an envelope. Avoid putting the debris directly in the envelope, if possible.

### Body Fluids

The saliva on an envelope, cigarette, or stamp may not be sufficient for a sample, but it should be collected nevertheless. If the saliva is associated with a large object, it is usually not necessary to send the whole object (unless it is to be used as evidence), but rather to cut out the relevant section with a margin of a few inches, and transport the portion containing the sample. Saliva samples kept in a wet condition tend to deteriorate rapidly; freezing may be appropriate; and air drying seems to be effective in prolonging the usefulness of the sample.

Blood and semen on a blanket or clothing can be treated in a similar fashion. As long as the entire object is not needed as evidence, the sample can be cut from the garment with a border of several inches and then packaged for transport. Blood is usually collected wet and transported wet or frozen. Body tissues are usually frozen. Certain types of preservatives are sometimes used with blood samples. Formaldehyde should not be used for tissues collected for DNA analysis.

Stains can be swabbed using a sterile swab lightly moistened with distilled water. The sample should be air dried with good ventilation before placing it in a container.

If a large object which has been spattered with fluid or tissue is being transported, and it is not practical to remove or cut out the sample, cover the sample area with clean dry paper securely taped around the edges. If there is a danger of exposure to moisture, put the whole

object in a waterproof container or bag before transport. Nonabsorbent objects should generally be kept at room temperature.

In most cases, when sampling animal tissues, it is preferable to collect nuclear DNA, which has genetic material from both maternal and paternal lines, e.g., hair roots contain nuclear DNA, while hair shafts do not. Nuclear DNA degrades quickly, so blood drops and semen should be collected as soon as possible. For hair samples, it is desirable to get about 80 head hairs and about 50 pubic or other body hairs, but information can occasionally be derived from very small samples of five or more hairs. Contrary to popular belief, single hairs, or a few skin scrapings are rarely sufficient for a lab analysis, at least not at the present time. If good nuclear DNA samples are not available, sometimes mitochondrial DNA (mtDNA) can be analyzed. The remains of victims of transportation disasters, wars, fires, or individuals from past civilizations are analyzed using mtDNA, usually from teeth or bones.

### Bones and Teeth

Bone samples of a few inches in length are best if taken from long bone and are usually transported at room temperature (unless fragments of tissue are attached to the bone, in which case it may be best to freeze the tissue). Teeth can be sent at room temperature, or the pulp removed and sent refrigerated.

Fetal cell samples for genetic testing must include a sample of the mother, to distinguish the child's DNA from that of the mother.

Do not expose samples to heat or bright sunlight, as this may degrade them, and air dry with sufficient ventilation (a low-power fan may be used) to avoid fungal or bacterial contamination.

Each sample should be carefully labelled with the probable source, the collection site, the date and time of collection, the method of collection, and the initials or name of the collector, taking care not to contaminate the sample with the labeling materials. If there are unusual conditions present, such as extreme temperatures or possible chemical contamination in an industrial setting, these should be noted as well.

## 5.c. Transporting Samples

Sterile blotters, swabs, envelopes and glass vials are generally provided for the temporary storage and transport of DNA samples to a lab or storage facility. Labs often provide these in kit form.

In the absence of professional storage containers, clean containers made of glass or stainless steel can be used, with paper or plastic bags as a second choice. If contaminating foodstuffs or other substances are present in a container, clean it thoroughly, add water and microwave for a few minutes and pour out as much of the water and debris as possible. Swab with alcohol and air dry. This isn't a perfect solution, but it can help reduce the level of unwanted materials prior to putting in the sample. Hair samples can be transported in a clean envelope with the flap folded or taped (not licked).

It is usually desirable to purify and dry samples before transport, if the technical expertise and equipment are available at the collection site.

Plastic is not recommended for storing samples, as chemicals in the plastic may leach into the sample, but acid-free solid plastic or vacuum-pack bags can be used for some types of samples if glass or stainless steel containers are not available.

Samples are usually transported dried or frozen. If they have been stored for a while before transport, the general rule of thumb is to transport them in the same state they have

been stored in up to the time of transport. In other words, if they are frozen, keep them frozen (using dry ice if needed); if they have been kept liquid for a while after collection, then keep them liquid (rather than freezing them); and if they are air-dried, keep them air-dried. It is very important to prevent rehydration of dried samples, or thawing of frozen samples until they are ready to be used.

Samples are usually frozen at a temperature of about -20°C although temperatures of -7° to -15°C have been successful with some substances.

Unless a sample is being analyzed onsite, it must be transported to a testing facility. Portable testing kits for use at a scene, such as a crime scene, are now available and will increase in use as the technology improves and prices drop. However, portable kits may provide only a minimal, preliminary evaluation. If an onsite analysis is carried out, it is generally followed up with lab tests for confirmation or further analysis.

Transport of liquids or frozen materials may require specialized facilities, whereas the transport of hair samples through the regular postal system is practical and convenient in some circumstances. Potentially infectious or contagious materials that may be present in blood samples require special care and supervision to prevent them from contacting outside agents.

Blood can be dried onto filter paper, but without carefully controlled conditions, some breakdown of the DNA is likely to occur with this process. It is especially important to protect dried blood drops from rehydration.

Sometimes samples are purified before they are transported, but more commonly purification occurs after transport to a lab. Purification has been accomplished with a number of materials including silica gel or glass particles. Gordon, Stimpson, and Hsieh (1993) have developed a process to 'pull' the liquid through a filtering system while still retaining the desired cells, so that transport can be more efficiently carried out and on-site centrifuging avoided. Padhye, York, and Burkiewicz (1995) have suggested an improved method of using a *mixture* of silica gel and glass particles in combination with an aqueous solution of chaotropic salts to isolate DNA or RNA.

## 5.d. Assessing Samples

*When received at a lab, the samples will be stored until they are ready for assessment and analysis. The following steps in the assessment and preparation of DNA fragments are a brief generic description only, as the processing of samples varies, depending on the type of tissue, the age of the tissue, its quantity, and the type of analysis being performed.*

The technician will first read the notes associated with a sample, and give it a visual inspection. The notes can help indicate whether it is a mixed or relatively pure sample, and should describe the origin of the sample. The notes may also indicate the possible presence of contaminants or unusual environmental conditions at the point of origin. This may be followed by a microscopic examination to confirm the composition of the sample and whether there is sufficient good tissue to continue with processing. It is important to determine whether it is a pure or mixed sample and, if mixed, identify and isolate the individual components. This is followed by the extraction of a portion of the sample from its container or substrate.

Hair samples may be cleaned with detergent in an ultrasonic bath to remove contaminating residues. The tissues are then usually combined with an extraction solution and ground up to release the DNA from the surrounding cellular material.

Bones (including teeth) are cleaned and sometimes sanded. The inside of the tooth is generally used. A sample is extracted and finely ground. The resulting powder or extract is treated with a chemical solution to release the DNA.

Blood samples stored on blots can be cut away or punched from the blotting medium and the balance of the sample returned to storage for future use. Chemical sterilization and filtering can then be carried out.

Materials may be centrifuged to encourage separation of the various materials into layers. DNA remains soluble in the top layer and other cellular components are filtered out. The DNA sample is then subjected to a purification process ready for further processing, usually by the common PCR or RFLP methods.

If they results are successful, they are recorded or the process may be repeated until a good result occurs. Remaining pieces of tissue are stored for future reference.

## 5.e. Analyzing Samples

*If you have not already done so, it is valuable to read the sections on PCR, RFLP, and Southern blotting (Section 3.a.) to understand the different means by which DNA fragments are separated, bonded, and recorded for visual analysis by a trained professional. Once records of the sample have been made, these records can be stored in files, or scanned and recorded in a computerized database, which may include a software analytical system.*

*When processing and sequencing DNA, the information is evaluated in the context of the situation. For example, if the samples were submitted for paternity testing, the DNA patterns of the alleged parent and child will be evaluated to see whether they 'match' (share key characteristics) with a high degree of probability.*

Many sequencing methods, subprocedures, and apparatus have been developed, and there are likely to be more as our understanding of the science improves. They are too numerous to discuss in depth here, but some evolutionary examples that provide an overall understanding of basic methods and some of their advantages and disadvantages include

- *Sanger (dideoxy) sequencing method* - a well-known, frequently used method that uses enzymatic elongation procedures with chain-terminating nucleotides. The size of DNA fragments is determined by gel electrophoresis. Careful preparation of samples is required and the process is somewhat time-consuming [Sanger et al., 1977].
- *Maxam-Gilbert sequencing method* - Chemical cleavage to generate fragments that are randomly cleaved. Chemical reactions which exhibit specificity of reaction to generate nucleotide-specific cleavages. Careful preparation of samples is required [Maxam and Gilbert, 1977 and 1980].

These two important earlier methods generate fragments that are ordered by length. They have limitations related to errors and to the number of DNA segments that can be processed at one time. A number of alternative methods have been explored, including hybridization.

The creation of clones of the original DNA is an important aspect of sequencing. A larger sample provides more material for processing, and clones can sometimes be exported in circumstances where the original sample cannot. There are several ways to replicate or amplify and sequence DNA samples:

- *shotgun method* - a technique for digesting a DNA sample at random by ultrasonic vibration, preparing DNA fragments by subcloning, sequencing each fragment, and using overlaps to determine the full-length base sequence. The full-length base sequence is determined before the portion of the DNA that corresponds to the extracted DNA is known [Maniatis et al., 1989]. Analysis of a DNA length 10 to 20 times longer than the length of the DNA being sequenced must be obtained, a process requiring substantial time and care.

- *primer-walking method* - a huge intact DNA is used as a sample. The base sequence is first determined. For each sequencing, a primer is then synthesized to determine the DNA sequence of a contiguous portion. The process starts at one end of the sample and is sequential. While more efficient than the shotgun technique, it nevertheless requires very careful preparation of a primer for each sequencing process. The purification process is time-consuming [Matsunaga et al., 1997].
- *nested-deletion method* - fragments from a DNA sample are enzymatically digested, yielding different-sized fragments. The fragments are then sequenced according to longer length. A priming site is obtained in the process, and thus does not need to be repeated for each sequencing process. As in the primer walking method, the purification process is time-consuming [Maniatis et al., 1989].

Since the implementation of these three general methods in the late 1980s, other processes intended to streamline and simplify sequencing processes have been experimentally introduced, for example:

- *fragment-walking method* - direct sequencing of a DNA sample that is digested with a restriction enzyme. An oligomer with a known sequence is then ligated with the DNA fragment's terminus to recognize each DNA fragment in the mixture. A set of primers is used for a sequencing reaction for discriminating a complementary base sequence. After determining the base sequence of each DNA fragment, the base sequences of respective DNA fragments are reconstructed to obtain the overall base sequence. This has advantages over previous techniques in that it does not require cloning, but may yield digested fragments with long DNA sequences.

Sometimes techniques are combined in order to improve efficiency. For example, Matsunaga et al. (1997) have proposed the use of the fragment-walking method as a means to prepare DNA fragments for use with the nested-deletion method, followed by DNA sequencing. This hybrid approach streamlines the process by bypassing some of the operations for nested-deletion subcloning, and some of the difficulties in fragment-walking fragment connection.

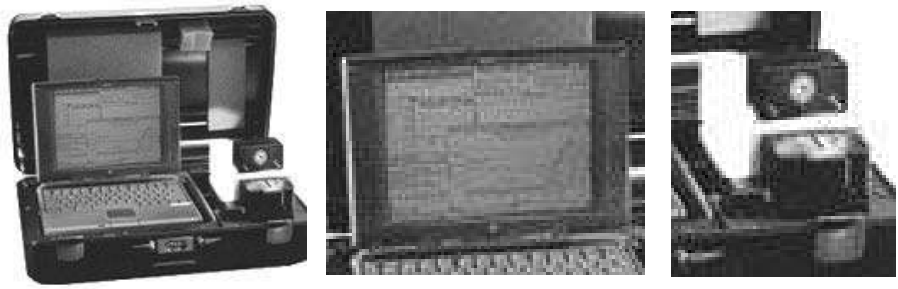
By the mid-1990s there was widespread interest in commercializing and streamlining DNA testing techniques, opening up access outside of academic research to local law enforcement officials, federal agents, private detectives, and general consumers. Some other developments of commercial interest during the 1990s include

- Drmanac et al. - a non-gene-specific hybridization DNA sequencing method using probes (1993). Drmanac has more recently been involved with developing a system to read a base multiple times to improve the accuracy of known and novel DNA substitutions, deletions, and insertions.
- Rothberg, Deem, and Simpson with U.S. Government funding - developed a computerized apparatus for use in conjunction with a data library for identifying, quantifying, and classifying DNA sequences without sequencing. Distinctive signals (e.g., optical signals detected from fluorochrome labels) from short DNA sequences (or their absence), taken together, are used to identify a particular DNA sequence in conjunction with information from the data library. This is important for deriving information from mixed samples or those of unknown origin. Previous probe methods were somewhat effective for single samples, but cumbersome for mixed samples (1995).

- Jones - an iterative and regenerative method for DNA sequencing in discrete intervals using restriction enzyme and hybridization procedures. This is suitable for creating offset collections of DNA segments for providing continuous sequence information over long intervals and for sequencing large sets of segments (1996).
- Kambara and Okano - a gel electrophoresis method and apparatus for DNA and protein detection and DNA base sequencing using a photodetection system. The object of this method is to improve the efficiency of DNA sequencing by allowing two or more samples to be processed at once without sacrificing sensitivity. Improving efficiency over previous single-sample methods has important commercial and research implications (1996).
- Fodor, Solas, and Dower - de novo (new) sequencing of unknown polymer sequences for verification of known sequences and for mapping homologous segments within a sequence. Through automation, sample preparation is streamlined and speed and accuracy of results are enhanced over previous methods (1997).

One of the most common motivations for DNA analysis is paternity testing. Since fathering a child involves tremendous emotional, financial, and social implications and responsibilities, the confirmation or exclusion of paternity has become a substantial industry, and an important tool in legal proceedings. There are a number of ways to identify paternity. Love (1994) has described a means of detecting the presence or absence of multiple nucleic acid sequences. In this method, the multiple presence polymorphic (MPP) probes in a series of separate hybridization tests result in a pattern unique to an individual. This personal identification pattern (PIP) can be compared and contrasted with others within the test population to positively exclude or include within a high degree of probability, the likelihood of paternity.

While gel electrophoresis processing is still widely practiced, non-gel systems employing PCR samples and short tandem repeat (STR) sequences, micropellicular matrix separation of DNA fragments, and computerized displays are now available. These automated systems can create profiles in minutes, as compared to earlier technologies that took hours or days.



This portable, computerized DNA analyzer from Lawrence Livermore National Laboratories (LLNL) is contained in a briefcase, and can be used in the field to perform polymerase chain reaction (PCR) DNA analyses. The PCR chamber and analysis equipment are located on the compartment on the right side of the case. [LLNL news photo, released.]

Recently, Lawrence Livermore National Laboratory (LLNL) has created a 'suitcase' DNA lab which makes it possible to analyze a sample outside of the lab, a boon in situations where transport of the sample is difficult or impossible. This new level of miniaturization makes it possible to do testing and analysis in remote environmental sites, war zones, or crime scenes

in politically unstable environments. Accurate measurements can be attained with flow cytometry, a general-purpose laser light-scattering diagnostic tool for assessing and categorizing biological cells and their components. This technology can be used for detecting biological warfare agents and cell contents such as DNA. The Department of Defense Armed Forces Institute of Pathology is using LLNL's Microtechnology Center's DNA analyzer for identifying human remains in the field, and testing for pathogenic bacteria and other contaminants.

### 5.f. Storing DNA Samples

*Databanking of the information attained from a sample may have legal ramifications. It may be necessary to obtain permission to store the information or, as in the cases of samples taken from American service members, there may be policy stipulations as to how long the information may be retained, such as 50 years beyond the length of the term of service.*

Destruction of DNA information after a specified period of time may be necessary to safeguard privacy. Currently, sample information provided to federal authorities usually reverts back to the state authorities who supplied it, with the onus on the state to destroy the original sampled tissues. As such, there is no centralized monitoring of the actual destruction of the materials, or the method of destruction (usually by incineration, or encapsulation and deposit in a landfill). Procedures for information and sample storage are still evolving with growing support for federal supervision.

In some situations it may be mandatory or ethical to convey the results of the analysis to the donor, whether or not the sampling was voluntary.

DNA samples are stored in clinical settings, forensic laboratories, research facilities, commercial 'DNA banks,' and homes. Samples may or may not be subjected to DNA extraction before storage. Specialized facilities may use special environments and preservation techniques such as transformed cell lines, or freezing, in order to maintain the samples over time.

The easiest method of storage, in the absence of storage equipment, is simple drying. Care should be taken not to contaminate the samples. Sterile containers and gloves are recommended, and in crime scenes in particular, it is recommended that a new pair of gloves be worn for each sample.

In cases of private sector DNA banking, the consumer is always faced with the problem of the firm going out of business, being taken over, or changing its product direction or corporate policies. In addition, private and public enterprises are subject to legislative inducements and restrictions that might require destruction of the samples after a specified date or length of time. There is also the lesser but provocative possibility of profit organizations using semiskilled or unskilled labor to label and store samples, with the subsequent errors or abuse that may occur due to staff turnover, inexperience, or malicious mischief.

Solid storage and transport techniques are still being developed. One example is a patented process by L.A. Burgoyne, an Australian inventor. The use of a solid matrix medium with a protein denaturing agent and a free radical trap is used to protect against the degradation of DNA, and is suitable for blood samples. The free radical trap acts as a DNA-releasing agent to aid in releasing the DNA from the solid storage medium. Pathogenic organisms can be inactivated by the solid medium. The solid medium can be cellulose or synthetic in the form of a compressed pellet. If long-term storage is desired, it can be encased further in a protective material.

Uric acids or urate salts have found to be useful in long-term storage of purified DNA by providing buffering and free-radical protection. Once dried at room temperature, samples

can be put into cold storage at about -15°C to -20°C.

Drying agents such as silica gels and dry sodium carbonate can be used in conjunction with cold storage to remove traces of acid vapors. Vacuum-packing can help reduce oxidation.

### Equipment

*Most of the equipment used for DNA processing and analysis is highly technical and is set up in a laboratory for use by trained professionals. A description of this equipment is outside the scope of this book and the reader is encouraged to contact labs directly for more detailed information.*

*In contrast, the equipment for collecting samples is relatively straightforward, and many labs will ship sampling kits that can be used by laypeople or professionals, depending on the type of sample. Buccal (cheek) swab kits can be used with a minimum of training. Sterile swabs, gloves, transport and storage containers should be used whenever possible.*

FTA™ paper is a commercial dry reagent mixture commonly used for the transport and storage of blood samples. Small amounts of sample can be extracted by 'punching out' a portion from the medium. Sterile tissues, paper, and clean envelopes can be used for dry substances or those that have been collected wet and then air-dried. Dry ice can be used to keep samples cold if they have been previously frozen.

Sterile or well-cleaned tweezers, knives, or scrapers can be used to pick up dried samples to put them into a paper fold, though it is preferable to transport the sample with the object to which it is attached, when practical.

Syringes and pipettes can be used for wet samples. BD Vacutainers™ are commonly used to hold blood samples, and may come with substances that prevent coagulation or inhibit enzymes that could damage the sample. If a sample is scraped, the scraper must be thoroughly cleaned between each sample. If sterilization is not possible, cleaning with detergent and alcohol can help.

Clean scissors or a knife can be used to shorten hair root samples, if the shafts are long. It is usually not necessary to transport more than a few inches of the shaft.

# 6. Applications

*DNA testing is a generic technology that can be applied in many aspects of life. It is used in law enforcement, poaching and wildlife conservation management, social services (especially child-support disputes and genetic counselling), crop evaluation, seed management, dog and livestock breeding, drug control, and many other areas in which information about the lineage, composition, or the whereabouts of an animal or plant is desired.*

*In this section, applications are described in general terms, followed by a selection of specific examples. It is not possible to list all the many applications of DNA analysis and new ones are constantly being developed, but there are enough listed here to convey the breadth of the field.*

## 6.a. General Applications

### Law Enforcement

Law enforcement officials have been quick to see the potential of DNA as evidence of both innocence and guilt. However, because of pre-existing laws concerning identification and search and seizure, the use of DNA technologies is more stringently regulated in law

enforcement than anywhere else. Thus, there are limits for sampling, storage, and court admissibility of DNA evidence. Until recently, only crime scene samples, and samples from convicted criminals could be collected. However, in some jurisdictions, it is now lawful to take samples from suspects, in spite of challenges that this is an unconstitutional violation of a suspect's rights.

Not all suspects may be sampled. Currently, in most countries, suspects of violent crimes, primarily rape and murder, may be sampled. In some areas, burglary suspects may now also be sampled. DNA evidence can exonerate a falsely accused, innocent suspect so that limited resources are not expended in trying to apprehend and prosecute the wrong person. DNA can further be used to provide evidence or confirmation of more likely suspects.

A databank of original samples or a computer database of analyses may be available, in some cases, to determine if a suspect has previous offenses or if the DNA matches another sample from an unsolved crime. National databanks (e.g., CODIS) are being developed for reference. In the U.K., there have been instances where vast numbers of citizens have voluntarily provided DNA samples to exclude themselves as suspects and to aid in pinpointing a murder suspect. Since widespread testing expends large amounts of taxpayer's dollars, some citizens have supported the continued storage of these samples, rather than spending millions on retesting every time there is a violent crime. In other words, in law enforcement, DNA banking may increase as a result of economic pressures, in spite of concerns over privacy.

Certain law enforcement organizations have called for the DNA sampling of the entire populace, with the information to be kept in law enforcement files.

Attorney General Janet Reno has ordered a federal commission to study the legality of collecting DNA samples from millions of Americans who have never been convicted of any crime. This is currently an issue of substantial debate.

### Breeding and Wildlife Conservation and Management

DNA allows animal lineages and pedigree documents to be verified and monitored to a degree of certainty never before possible.

Wildlife conservationists have found DNA sampling to be an invaluable tool in protecting the genetic diversity of threatened species. By breeding individuals that are as genetically different as possible, it is possible to strengthen a species, by improving resistance to disease and avoiding genetically related inherited abnormalities, especially those that are recessive and only express themselves when both parents have the traits. This can improve wild and captive breeding programs. Some rare species are privately owned, and access to these animals is sometimes difficult, but it is hoped that the owners will support DNA profiling for the sake of the continuation of the species.

DNA has been found valuable in determining gender in birds and animals. Some species are not easily sexed by visual inspection. Private and institutional bird breeders especially appreciate being able to know the sex of a bird before paying a high price for it or transporting it to a distant destination.

DNA sampling can be invaluable in providing evidence for the poaching of protected animals, whether wild, captive, or domesticated. A product on the market in another country can now potentially be traced to a specific herd or community of animals in the wild, or in a wildlife park or sanctuary. A decade ago, it was almost impossible to 'prove' this type of case, whereas it may now become routine.

With fish stocks declining dangerously, fishing boats may be subject to closer scrutiny. The sampling of fish debris found in the water of boats suspected of illegal activities can

indicate whether certain species were present in the catches.

The U.S. Fish & Wildlife Service laboratory staff includes a genetics team which uses electrophoretic separation systems, protein analysis, and DNA analysis for a variety of scientific purposes, including species categorization, gender identification, and sample matching or exclusion. [U.S. Fish & Wildlife news photos, released.]

DNA sampling is used to chart the lineages of pedigreed animals, or animals bred for specific purposes like research. Litters with mixed parentage (i.e., more than one father) can be verified, as can fraudulently bred animals, or those which have been excessively line-bred. Fraud in the dog-breeding community has recently been revealed by DNA testing. 'Dogprints' designed to verify the parentage of an animal are becoming a routine part of the documentation that accompanies a purebred. Similar systems are being put in place for alpacas and cattle, and may soon be commonplace. In the past, brands and tattoos have been used to confirm the identity of an animal. Perhaps someday these will be replaced by tiny implantable microchips that can transmit stored DNA information about the animal's identity and characteristics.

In many areas, dog pedigree information has been confirmed or refuted with DNA evidence such as microsatellite (STR) DNA typing. Many cases of fabricated pedigrees (those in which one or both of the parents turn out to be unregistered dogs), or pedigrees listing the incorrect parent (usually the father) are now being investigated, and fraudulent breeders are being required to compensate purchasers of dogs from questionable litters.

Dog pedigrees can be used for other reasons not related to the breeding of dogs. It has been suggested that DNA could be used to locate dog owners who don't clean up after their dogs. Given the backlog of DNA testing needed for more important law enforcement activities, one would hope this suggestion of a 'poop patrol' remains a low priority compared to DNA testing for violent crimes. The idea, however, indicates that city database records for dog tags may someday be cross-referenced or supplemented with DNA information.

### Archaeology and Anthropology

DNA analysis has been a tremendous boon to scientists studying our past history and evolution, and the evolution and characteristics of plants and extinct species. Since nuclear DNA degrades rapidly, mitochondrial DNA is usually used for these studies. Mitochondrial DNA (mtDNA) is passed through the maternal line and is more stable than nuclear DNA. Because skeletal remains last longer than soft tissue, and mtDNA can be found in bones, it is possible to sample mtDNA that is decades or hundreds of years old. This has produced some sensa-

tional and sometimes surprising discoveries in anthropology and archaeology.

DNA is also being proposed as a way to identify bodies in cemeteries whose origins are no longer known. By forming databases of family DNA patterns, a computer matching system may someday be able to identify an exhumed ancestor in minutes. Given the high degree of interest in charting family trees by amateur and professional genealogists all over the world, it is quite likely that DNA patterns will eventually be part of genealogical databases.

The exhumation of bodies is bound to yield some surprises. Throughout history it has been common for adoptions and out-of-wedlock pregnancies to be 'covered up' due to social stigmas against unmarried women and their children. As a result, many children have been raised by uncles and aunts as their own children. Often the offspring of a very young girl has been raised as a sibling by the young mother's parents, rather than as her child. Still other children have been parented by fathers that were not the husband of a married woman. Human curiosity about our past relations will result in at least a few unexpected revelations when people dig deeper into family histories.

The remains of victims of massacres or dire poverty may someday be returned to their families for services and reburial based on the results of DNA testing. There has been intense interest and research over the centuries in locating the bones and burial place of W. A. Mozart who was reportedly placed in a mass grave. Exhumation and DNA testing has already been used to verify the identity of a slaughtered Russian Czar (described in more detail later), and to study the descendants of Thomas Jefferson's family. Private detectives may someday find themselves investigating not just the extramarital affairs of living relatives, but those of dead relatives as well, especially where large inheritances are involved.

### Tracking and Identification

DNA can be used as an identification tool for tracking wildlife, people, and plants. A sample taken in one part of the world can be matched with a reference specimen in another country in cases of poaching or smuggling.

In cases where the parentage of a child is unknown, DNA testing may be a way of alerting parents that they are related to kidnapped or adopted children. This type of identification can be carried out at a distance without a visual inspection. It can also be used when so much time has passed that it's difficult to recognize a child who was lost in infancy.

Identification of skeletal remains recovered from a crime scene, war zone, or search and rescue operation can be aided by DNA. Forensic anthropologists and dentists have long been involved in assisting with the identification of individuals who have been murdered or killed in a disaster. Now they have additional tools to carry out their work. A complete skeleton can reveal useful clues about sex, age, handedness, race, height, musculature, general health, and sometimes specific illnesses (e.g., rickets), and injuries. This provides information about characteristics which may be sufficient to identify an individual, but the skeleton may not be wholly recoverable, may be mixed with other skeletons, or may be incomplete. Even if a whole skeleton is found, identification may still be uncertain. If the teeth are present, dental work can help in a positive identification. But if the teeth are not present or have not been altered, DNA analysis and matching with an existing specimen, as in a service members database, can provide a positive ID. If an existing specimen is not available, matching with close family members can often provide a positive ID.

As DNA testing kits become more accurate and sensitive to smaller amounts of DNA, DNA may begin to be used to detect traces of unlawful entry by unauthorized persons in hazardous or politically sensitive buildings.

## 6.b. Specific Applications

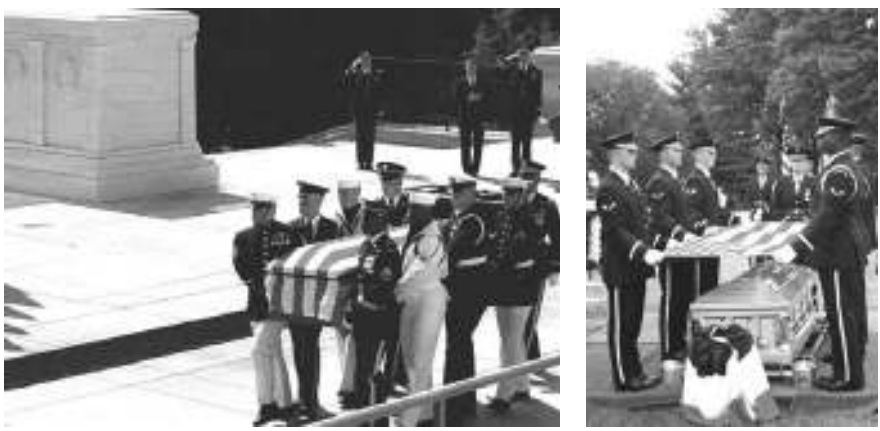
*There are thousands of ways in which DNA can be used to derive information about an individual or a situation, so not all can be described here. However, this section provides some specific examples, some of them high-profile, of how DNA has been used in practical applications.*

### Service Member Remains Identification

The U.S. Government has been collecting DNA samples from service members since 1992, with almost three million specimens being stored in Gaithersburg, Maryland. This information is gathered primarily for the identification of recovered remains. DNA collection from service members is now mandatory, even in cases where the member is not being sent to a war zone.

In 1995, service marines challenged this practice by disobeying an order to submit to DNA sampling under the threat of a court martial. In the lower courts, the action was not found to violate the plaintiffs' constitutional protections. A number of subsequent court cases that deal with very specific challenges to mandatory testing have occurred. In general, the plaintiffs appear to be losing, sometimes due to technical weaknesses in their preparations and arguments rather than the issues themselves, whereas in more widely ranging general constitutional studies, the higher courts, in some instances, are finding in favor of the plaintiffs. As of late 1999, compliance is being tracked over the Internet by U.S. Army leaders.

When the remains of soldiers are found in poor condition, sampling of the nuclear DNA is usually impossible, but mitochondrial DNA, which can be compared with the maternal line, may result in identification.



Left: The disinterred remains of the Tomb of the Unknown Soldier were carried to a waiting hearse at the Arlington National Cemetery en route to the Armed Forces Institute of Pathology. There, at the Walter Reed Army Medical Center, they underwent forensic testing, positively identifying them as the remains of U.S. Air Force 1st Lt. Michael Blassie. They had been interred for 14 years since recovery from Vietnam. Right: After being identified, the remains were buried in a service at the Jefferson Barracks National Cemetery. [U.S. DoD 1998 news photos by Helene C. Stikkel and Scott Seyer.]

The celebrated Unknown Soldier, interred since 1984, was identified in 1998 as Vietnam veteran 1st Lt. Blassie, an Air Force pilot, based on mitochondrial DNA evidence matching tissue donations from his female relatives. Since 1991 about 100 identifications have been

made by the Armed Forces DNA Identification Laboratory (AFDIL), mostly of remains from Asian wars. A decision was made not to inter another service member in the tomb because officials are now confident that the identification of the remaining members can now be successfully undertaken.

Individuals seeking to identify service member remains can order a kit from AFDIL and go to a licensed health professional to take the sample, which can then be sent in for matching.

### Identifying Political or Murder Victim Remains

DNA can be used to unearth information about historical incidents in which the facts have been lost or obscured.

One of the most publicized identification cases involves the use of DNA evidence to confirm that the bones buried in a mass grave after the murder of Czar Nicholas II of Russia in 1918, were indeed the remains of the Czar and some of the members of his family and staff, as reported in 1995. While tentative identification of bones and teeth had previously been undertaken, the DNA evidence produced in this case provided powerful corroborative evidence to existing information and oral reports. It has helped paint a clearer picture of political events of the time.

Royal Canadian Mounted Police (RCMP) forensic experts use wire trays to sift through the remains at a grave site in a village in Kosovo as U.S. Marines provide security. The remains were investigated to help determine war crimes, to establish evidence for breaches of international conventions. [U.S. DoD 1999 news photo by Craig J. Shell released.]

In spring 1999, at the request of the International Criminal Tribunal for the former Yugoslavia (ICTY), Federal Bureau of Investigation (FBI) agents carried out forensic examinations of burial sites identified by NATO to allegedly contain biological and chemical evidence of war crimes. The FBI investigators uncovered human remains of men, women, and

children who had died from gunshot wounds to the head. A forensic anthropologist and four physicians from the Armed Forces Institute for Pathology (AFIP) conducted autopsies near the burial sites. Evidence to support allegations against Serbian forces was found.

This operation did more than establish evidence of war crimes. It also helped identify the remains of even badly decomposed bodies, so that after examination confirmation could be given to families who were unsure of the fate of their relatives. It also provided an opportunity for remains to be returned to the bereaved families.

Top: A tent village is used as a base near the area of the alleged Kosovo massacres. Bottom: FBI investigators sift through the debris to recover remains from grave sites. In addition to human remains, the recovered evidence included shell casings and bullet fragments. The physical evidence was supplemented with photographic records and other scientific examinations. Autopsies of the deceased indicated that most had died from gunshot wounds. [FBI news photos, released.]

### Wrongfully Accused Exoneration

Since DNA evidence can be used to exclude a suspect or incarcerated individual, there is a movement to use this technology to free wrongfully convicted individuals, particularly those serving long jail sentences. Connors et al., have reported through the National Institute of Justice (1996) that a number of individuals, incarcerated mainly for cases of sexual assault and murder, have now been cleared by evidence showing their DNA did not match samples taken at the crime scene. Twenty-eight cases of released prisoners, having served an average of seven years in prison, were reviewed and analyzed for this report. The authors include commentary on the implications for public policy.

In "Law and Human Behavior," Wells et al. (1998) describe how DNA evidence exonerated individuals in 12 additional cases. The authors combined these with the cases cited in the Connors report, bringing the total cases under study to 40. Approximately half of the tissue samples examined came from semen, blood, or hair samples. The authors point out that about 90% of these cases included incorrect eyewitness identification testimony resulting in wrongful convictions. They make recommendations for improving eyewitness identification procedures in order to reduce the incidence of false selections.

The National Academy of Sciences has noted that "...the reliability of DNA evidence will permit it to exonerate some people who would have been wrongfully accused or convicted without it." Scheck and Neufeld report that in sexual assault cases referred to the FBI since 1989, DNA evidence excludes the primary suspect about 25% of the time.

### Transportation Disasters

Families of individuals killed in disasters involving trains, planes, and other forms of transport have traditionally been identified from remains, documents, and dental records. However, there is often insufficient information to make a definite identification by traditional means. Katz et al. (1998) have reported the use of short tandem repeat (STR) and mitochondrial DNA (mtDNA) analysis to assist in identifying the remaining individuals from the 1997 Korean Airlines disaster.

In serious public transit accidents, including aircraft and train disasters, the remains may be seriously charred or crushed. Traditional visual inspection, fingerprinting, X-ray, and dental records-matching may be insufficient for identification. DNA can sometimes aid in these situations. The databanking of flight-crew DNA has been proposed and frequent flyers are being urged to voluntarily provide tissue samples.

### Child Abductions

If at least one family member can be located, a child suspected of being abducted may be identified by means of DNA testing. A number of children abducted in El Salvador have been identified by a joint effort of the Physicians for Human Rights, and the Association in Search of Disappeared Children. In the case of civilian massacres, children of the victims are sometimes abducted and adopted out, or may be kept in servitude. Since many of these children were taken as infants, or as toddlers too young to remember their parents, DNA testing is the only way to verify their family relationships.

Young children have fewer distinguishing characteristics than adults and they grow and change quickly, so if a child is abducted and subsequently murdered, it can be very difficult to make a positive identification from the remains, especially if they are mutilated or badly decomposed. DNA can help provide definitive identification to a grieving family and allow them to come to terms with the loss of a child.

### Pharmaceuticals

In the area of health care, there are many motivations for DNA testing. DNA can be used to predict some potentially devastating conditions and, eventually, drugs or pharmaceutical techniques may routinely correct some of these problems. Thus, those seeking help are likely to support pharmaceutical DNA-testing. This has an enormous potential for good, and also a frightening potential for abuse. Designer drugs may some day be used to target an individual's specific disease-causing agents, but may also be used for very specific and insidious types of chemical war agents. Individuals who test positive for serious illnesses may receive more effective health care, but they may also be denied access to jobs, insurance, and other important necessities for survival.

In war zones, DNA could be used to detect fevers, genetically altered micro-organisms, and other microscopic substances on face masks and other implements used in warfare. In turn, this information could be used to determine exposure risks.

It may not be long before DNA testing at birth becomes routine. There have even been suggestions that hospitals develop computerized databases of infants born with birth defects. The goal of health care is to study and pinpoint genes that cause these abnormalities, but how long will the information stay on file, and how much control will parents and the children tested have over the use of this DNA information?

## 6.c. Commercial Products

*DNA technology is rapidly being commercialized. Many recent DNA patents are for faster, less expensive analysis methods that will speed up production and lower costs. The general public can purchase a variety of products and services, including sampling kits and, very recently, home DNA-banking kits. They can take noninvasive samples at home, or have blood sampled at a local clinic. Samples to be used as evidence require documentation as to the identity of the donor and the witness who oversaw the sample collection.*

### Genetic Counselling

DNA analysis is routinely used in genetics counselling, and research into organ growth and transplantation. The sample may be collected in a doctor's office or a hospital. DNA information is valuable in many situations related to childbirth. Couples planning to have a child can have their DNA screened for hereditary diseases and receive counselling based on the results. Once conception occurs, a fertilized egg may be examined when it reaches the blastula stage and selectively implanted in the mother if it shows no abnormalities or congenital diseases. If the pregnancy is underway, the fetus may be tested *in utero* to detect correctable abnormalities, since it is now possible to do some types of surgical correction during pregnancy. Even though genetics counselling is not a priority for surveillance professionals, there is still an indirect benefit from the commercialization of these services, as public demand for DNA analysis brings down the price of the technology in general, making it less expensive for other purposes.

### Familial or Pedigree Testing

For routine paternity or animal pedigree tests, consumers can take samples to a walk-in laboratory or, in some cases, send them through the postal service. Outside of genetics counselling, the most common commercial services requested by private citizens are paternity tests, and pet and livestock pedigree documents. DNA records of children are also of interest to people whose offspring are at risk of developing a serious illness later in life (it may some day be possible to grow new organs from a person's own tissue). Parents may also want a

DNA record of an adopted child for future reference. Parents of children at risk of being kidnapped may wish to store DNA records, especially those living in unstable political climates.

Costs for the more common DNA tests range from about $50 to $300. Costs for institutional storage of samples for future reference, medical procedures, or research vary greatly, depending on the purpose, the institution, and the length of time the DNA samples or records are stored.

Rosgen in the U.K., and PE AgGen in the U.S. are two prominent DNA service providers. PE AgGen, Inc. runs an animal DNA-profiling facility with locations in California and Europe. The company provides test kits, profiles, and storage for up to five years for a variety of pets and livestock breeds. The cost is about $50 for a dog profile. PE AgGen, originally developed as Zoogen at University of California, Davis, was purchased by PerkinElmer. The company is known for advocating a standardized marker system in the public domain so that registries can be free to use independent labs for profiles. http://www.pebio.com/ab/aggen/

Rosgen Ltd. is a major U.K. provider of animal DNA analysis services, primarily for dogs and livestock. Forensic casework DNA profiles are approximately $200 per sample, dogprints are around $50 each. Genotyping and sequence analysis are available on request.
http://www.rosgen.co.uk/

### Forensics

Law enforcement officials have access to a broader range of services than private citizens, including in-house labs and external specialized labs. In appropriate instances, they also have access to restricted state and national databanks, some of which are publicly funded (e.g., the Combined DNA Index System - CODIS). Lifecodes is a prominent accredited commercial laboratory providing services to law enforcement agencies. It manages one of the largest DNA databases in the world.

For a surveillance professional, access to services will depend on the person's status and affiliations with the law enforcement community. Association with law enforcement provides greater access to labs and databanks, but also involves greater restrictions on who can be sampled and how samples are gathered.

## 7. Problems and Limitations

*Errors can happen in many aspects of DNA collection and profiling. The sample may come from the wrong donor, the processing may be compromised, files may be mislabeled or misfiled, and computer databases may be incorrectly recorded or accidentally or deliberately lost or corrupted. Safeguards against the misuse or abuse of DNA information should also to be taken into consideration. This section surveys some of the most common problems and limitations in the field of DNA analysis.*

### Sampling

*The most common sampling errors involve contamination and a misunderstanding of how much tissue of a particular type must be collected. Fraud is another problem, as it's relatively easy to submit a fraudulent sample, or even a fraudulent donor, if there are no verification systems in place. Section 5 (Description) provides relevant information on gathering and transporting samples that should be understood in conjunction with this section.*

DNA profiling is dependent on the quantity and quality of the samples. If the amount of tissue is too small, or has been contaminated by grease or dyes, it may be useless. Single

hairs, hair shafts, or small skin scrapings (as might be found under fingernails) are not usually sufficient for nuclear DNA testing. A sufficient quantity of sample must be collected, and sterile or clean implements and storage containers must be used. It is important not to trample or overpopulate a crime scene, and to collect and store fluids and tissue as quickly as possible before they degrade. Important court cases, especially those involving murder, have been compromised by the shoddy collection of samples that might have led to a conviction.

One of the limitations of sampling is cost. In the U.K. there have been prominent cases in which a large part of the populace was sampled to apprehend a murderer, but such large-scale operations usually cost millions of dollars. There will always be a trade-off. Storing samples may compromise individual privacy and may prevent some people from voluntarily coming forward with samples. Not storing samples will likely result in repeatedly high costs, usually borne by taxpayers, for carrying out future investigations.

Deliberate substitution of a sample from another individual, or deliberate substitution of another individual for testing is not only possible, but has been documented in a number of paternity suits and even in a well-publicized murder case in which the murderer asked at least two people if they would donate a blood sample on his behalf. One of them agreed, thinking he was helping a friend, rather than considering that he might be harboring a criminal.

### Processing

Many types of processing errors can occur in the lab. Samples can be mislabeled or misplaced, chemicals can be outdated or measured incorrectly. If the original sample is too small for repeat tests, an error or loss of a sample can be disastrous. Labs and law enforcement agencies are concerned about quality assurance in processing DNA samples, and certification programs for technicians and individual labs are being developed and implemented.

Gel electrophoresis and the creation of an autoradiograph on X-ray film are still common ways to process DNA fragments. The visual comparison of autoradiographs created on X-ray film can be subject to error if the intensity or exposure varies from one film to the next. Although time-consuming, creation of multiple films of each sample can help reveal processing errors, but does not overcome all the limitations of using X-ray film. More recent phosphor technologies are said to offer some improvements over older techniques.

Symbolic representations, or X-ray images of DNA patterns, are often filed, scanned, or entered into a database for long-term storage. Incorrect entry into databases can occur, with typographical or factual errors occurring as much as 30% of the time if good proofreading and quality assurance practices are not in place. In the private sector, the turnover in database entry jobs is moderately high, and it is repetitive and tedious work. A number of firms have hired prison workers in the past to save costs on various types of database entry. Also, insecure database entry systems provide opportunity for deliberate sabotage or tampering.

### Storage

DNA degrades over time, particularly nuclear DNA. Mitochondrial DNA, as found in longer-lasting structures such as bones and teeth, may survive for centuries, but even mtDNA eventually degrades. Air-drying, vacuum-sealing, and freezing can help extend the life of a sample, but samples don't last indefinitely, and changes in humidity or temperature can affect storage conditions and lead to destruction or degradation.

It takes a financial investment to store samples in a long-term facility. Storage firms can have hardware failures (freezers breaking down, power outages, etc.) that compromise the samples. Private firms may be the target of business takeovers, sabotage, or bankruptcies. Home storage banks are seldom climate-controlled and frozen samples may thaw in a power

outage without backup generators.

Libraries can provide hindsight clues as to what might happen to data in DNA banks as the demand for storage space increases. Historically, when shelf space limitations precluded the storage of large quantities of books, newspapers, and journals, libraries used microfilm as a means to keep the information on file. Anyone who's used a microfiche reader knows that the records of these documents are substandard compared to the originals. They are sometimes poorly exposed (too light or too dark), difficult to read, and usually awkward to handle. Now that microfiche readers are being sold at auctions due to better computer technology, but we no longer have the originals from which to rescan better images.

Librarians do the best they can with limited resources, and a microfiche is invaluable compared to nothing, but similar compromises could happen with DNA data, with more serious consequences. Just as it's difficult to store vast numbers of books, it's expensive and awkward to store large numbers of original DNA samples. There are already circumstances where DNA samples are being destroyed after they have been scanned or otherwise entered into a database. Thus, there is no way to reprocess the data or to check the computer record against a sample taken in a crime scene. This makes the data even more susceptible to tampering or corruption in the absence of a source of verification. The loss of an individual book is unfortunate, but does not usually have a serious impact. The loss, substitution, or corruption of DNA information, on the other hand, could have life or death consequences for a person involved in a medical or legal dispute, if too much faith is put into the computer data.

### Population Demographics

Our understanding of DNA is still very incomplete. Practical use of DNA profiles is in part based on statistical assumptions. Since DNA analysis extends beyond the matching of one pattern to another, to analysis of statistical relationships with known or reference populations, we need databases of large numbers of profiles or profiles specific to the subgroup being investigated. Without them, an individual profile is often useless. DNA data acquisition requires cooperation, and attempts to encourage voluntary donations have sometimes met with strong resistance.

In 1999, in a controversial effort to get broader demographic information for African Americans, the Attorney General of Ohio requested that staff members from this ethnic group donate voluntarily. While the move may have been well-intended, it clearly was ill-conceived and was roundly criticized. Eventually the request was withdrawn. Thus, the development of useful population statistics that are needed for DNA pattern comparison and research is limited by concerns over privacy and discrimination. Most databases so far have been developed from mandatory testing of military service members and convicted or suspected felons.

Another limitation in developing reference databanks is the concern over commercial use of an individual's unique DNA pattern. One way to get people to agree to allow their DNA patterns to be entered into databanks is to keep the entries anonymous, but this means that if a particular pattern is found to have great commercial value, the person who owns or 'is' that pattern does not directly benefit, and may not even know his or her personal attributes are being exploited.

### Discrimination

Discrimination in the business world with respect to race or health is rampant, in spite of equal opportunity laws. DNA tests could reveal medical conditions or mixed-race backgrounds that are not physically obvious, but which may result in a person being screened out of an existing or potential job. There are reports by the American Management Association that

over 6,000 firms require genetic profiling from job candidates. While recent bills in the Senate are intended to protect private individuals from discrimination based on DNA patterns, it is unlikely that legislation against DNA discrimination will be enforced any more stringently than current legislation against other types of discrimination. The track record so far hasn't been good.

Presently, many health and life insurance companies require a potential insuree to have a medical examination and may try to refuse to insure someone with a debilitating or life-threatening condition. It is likely that insurance companies will want to require DNA sampling as part of that medical examination and may charge higher premiums on the basis of 'medical potentialities' for serious illnesses that may be indicated by their genetic makeup.

There are historical precedents for discrimination that provoke concerns over long-term storage spanning multiple political administrations. In the United States, by 1924, the Model Eugenical Sterilization Law, which discriminated against drug addicts, epileptics, criminals, and the insane, had been passed by 21 states. In 1927, the U.S. Supreme Court supported the widespread use of involuntary sterilization of 'genetically undesirable' individuals. If unanticipated political swings occur in the future, and massive DNA databanks are available, it is conceivable that DNA information might be expropriated for uses other than those for which it was originally collected.

# 8. Restrictions and Regulations

*Before using a technology for surveillance purposes, the professional must be aware of the legal requirements and restrictions associated with the technology, and how its use could impinge on the rights, safety, or privacy of the organization or individuals being surveyed.*

It is likely that laws related to genetic testing will never address all the issues in this complex science and will never fully protect everyone. Consider these three important social dynamics:

- the most significant scientific breakthroughs and their ultimate influence on society are rarely anticipated,
- opportunities for wealth often seduce entrepreneurs into ignoring the damaging consequences of their products, and
- citizens and lawmakers haven't sufficient time nor expertise to understand every aspect of genetic science.

Taken together, these factors have a substantial influence on lawmaking, with the result that genetics-related legislation will probably always be compensatory rather than proactive. This section gives a general overview of federal and state legislation related to DNA testing, issues which have only been under scrutiny for about 20 years. The ramifications of legislation are discussed further in Section 9 (Implications of Use).

Federal and state bills on health privacy have been debated since the early 1980s, with few resolutions and many delays. It is usually difficult to implement wholly new measures, so most of the DNA-related issues introduced to the Senate have taken the form of amendments and additions to existing legislation.

Many public officials have as yet only a novice understanding of DNA technology and its potential effect on society, which is not surprising, since the science is recent and ongoing. Many citizens have no knowledge of it at all. This is part of the reason why the various bills are moving slowly through legislative channels, with many as unresolved or shelved. As it

stands, law enforcement officials are working with federal support to extend their jurisdictions and their databanks, employers and health insurance providers are on an honor system to not use DNA information to discriminate against employees and insurees, and free agents have few impediments to DNA collection and use.

### National Legislative Concerns

Court challenges of DNA sampling have been relatively few, considering the significant number of people in our society who have already been sampled for one reason or another. In cases contesting the constitutionality of mandatory or nonvoluntary DNA sampling, the most commonly referenced amendments are the Fourth and the Fourteenth. The Fourth Amendment to the United States Constitution provides that

> "[t]he right of the people to be secure in their persons, houses, papers, and effects, against unreasonable searches and seizures, shall not be violated ...."

The Fourteenth Amendment to the Constitution provides for protection and due process of law. The First, Fifth, and Ninth Amendments also include explicit guarantees of privacy that are relevant to genetics testing.

In 1989, the National Institute of Justice initiated standards for DNA typing in agreement with the Office of Law Enforcement Standards (OLES) at the National Institute of Standards and Technology (NIST). Further standards were developed through the Technical Working Group on DNA Analysis Methods (TWGDAM).

*The mid-1990s was a time when interest in DNA issues resulted in a number of new Acts and the establishment of DNA-related facilities and databanks.*

In 1993, the *Privacy Protection Act* was introduced to the Senate to establish a Privacy Protection Commission. This sought to grant investigative powers to the Commission, but contained no similar grant of enforcement powers to the Commission itself. The Act charged the Commission with reporting violations of the Privacy Act, yet left private sector activities outside of its jurisdiction.

The *Violent Crime Control and Law Enforcement Act of 1994* included within it the *DNA Identification Act of 1994*. This act of Congress sought to protect genetic information derived from DNA samples held by law enforcement agencies for identification purposes. This law would not be affected by the Genetic Privacy Act. Related to this is the Violent Offender DNA Identification Act introduced five years later, in 1999 (described further below).

Also in 1994, the DNA Advisory Board (DAB) was established under the *DNA Identification Act of 1994* by the Director of the FBI. The DNA Identification Act was contained within the Omnibus Crime Control Act for quality assurance and proficiency testing standards and passed into law in 1995. It provided funding for forensic labs to improve the quality and availability of DNA analysis and for the FBI to establish a national DNA database called the *Combined DNA Index System* (CODIS). Funding was contingent on strict adherence to standards. Board members were appointed by the FBI Director from nominations proposed by the National Academy of Sciences and professional societies of crime labs. Board recommendations resulted in the FBI's Quality Assurance Standards For Convicted Offender DNA Databasing laboratories which came into effect 1 April 1999. The DAB was slated to end in March 2000, but was extended and was still meeting in the summer of 2000. This effort included support from the Scientific Working Group DNA Analysis Methods (SWGDAM).

### United Kingdom

In the U.K., the *Police and Criminal Evidence Act of 1984* (which included handling of fingerprint records) was further amended by the Criminal Justice and Public Order Act of 1994 to introduce compulsory sampling of bodily tissues and fluids, using reasonable force, if necessary, from anyone charged with 'a recordable offence.' Results of the samples, whether or not they are used in the case, would be used for a national DNA database.

### Canada

In June 1995, the Canadian Department of Justice released information on the amendment of the *Criminal Code and Young Offenders Act* which empowered a Peace Officer or other authorized warrant-holder to obtain bodily samples (hair, saliva, blood) for forensic DNA analysis from an individual reasonably believed to have committed a criminal offence, thereby broadening the powers of Canadian law enforcement officials to include suspects not proven guilty. It was stipulated that if subsequent investigation cleared the individual of wrongdoing, the results and the sample were to be destroyed. However, the judge would retain the power to veto this destruction.

### United States

More than a dozen bills were introduced to the U.S. Senate in 1996. These included the Health Insurance Portability and Accountability Act of 1996, designed to protect consumers from discrimination in receiving health insurance, includes provisions that would prevent companies from charging higher premiums for 'at risk' insurees.

In October 1998, the FBI announced the creation of the *National DNA Index System* (NDIS), a database through which DNA profiles could be compared in order to turn up investigative links.

Concerns over discrimination that might affect health care benefits or employment access were clearly growing in the mid-1990s, and a number of relevant bills were introduced in 1997, including the *Genetic Privacy and Nondiscrimination Act and the Genetic Confidentiality and Nondiscrimination Act* which would amend the *Public Health Service Act and the Employee Retirement Income Security Act of 1974*. These measures sought to prohibit health insurance providers from discrimination affecting eligibility, renewal, or benefits, and to prohibit employers from using genetic tests to discriminate against employee rights or benefits. The bills were similar in some ways, both encompassing broader issues than some of the other bills presented that same year, one of which stated:

> ...the circumstances under which DNA samples may be collected, stored, and analyzed, and genetic information may be collected, stored, analyzed, and disclosed, to define the rights of individuals and persons with respect to genetic information, to define the responsibilities of persons with respect to genetic information, to protect individuals and families from genetic discrimination, to establish uniform rules that protect individual genetic privacy, and to establish effective mechanisms to enforce the rights and responsibilities..."

This bill stipulated specific safeguards, namely, that the person being sampled must not only give written consent, but must give fully informed written consent, putting an onus on the agency taking the sample to educate the individual about DNA before taking the sample. It was proposed in the bill that this Act take effect on 1 January 1999. In spirit, this would be a good safeguard. In practice, it is almost impossible to implement fully informed consent in large-scale screening activities. Also, 'informed consent' is usually carried out by handing the donor a complicated sheaf of small print with a place at the end for a signature that attests

to the signer reading and understanding the contents of the document.

At about the same time that these bills were presented to the Senate, a number of states developed similar amendments to individual state privacy-related acts.

### Employer Interests

One might think that a bill that protects the public against discrimination in the workplace or in the provision of health insurance would pass through Congress quickly and easily, but that hasn't been the case. A working citizen might consider it 'obvious' that employers should be barred from receiving confidential medical information from physicians or pharmaceutical companies, but employers have countered that as long as they are paying for employee medical benefits, they have a right to know about an individual's medical history, including the results of a DNA test. Given these conflicting interests, resolution to the benefit of all parties has not been achieved.

In 1997 there were amendments to the Criminal Evidence Act further extending law enforcement powers for obtaining non-intimate DNA samples, without consent, of violent offenders, sex offenders, mentally disordered offenders, and burglary offenders convicted prior to April 1995 and still serving their sentences.

In July 1999, the FBI announced the first 'cold hit' processed through the National DNA Index System (NDIS). A cold hit represents a DNA association between an offender or a crime without an investigative lead. Evidence linked six sexual assault cases occurring in the Washington, D.C. area through NDIS with three sexual assault cases occurring near Jacksonville, Florida. The Florida Department of Law Enforcement then notified the FBI Laboratory of the apparent association of the crimes in different areas. The FBI then turned up five more matches in the Washington, D.C. area and linked the crimes to a deceased individual, Leon Dundas. It appeared as if the system might be instrumental in helping solve violent serial crimes.

In 1998, the U.S. Bioethics Advisory Commission issued a report arguing for tighter controls on tissue and DNA sample banks.

In May 1999, an amendment was proposed to the DNA Detection of Sexual and Violent Offenders Act to add burglary to the list of crimes that require DNA sampling. Up to this time only felony sex offenses, murder, and indecent assault were eligible for mandatory testing.

The same year, the Violent Offender DNA Identification Act was proposed to eliminate local law enforcement agencies' backlogs of convicted offender samples or to have them reanalyzed with better technology, with help from the FBI, the results being recorded in the CODIS databank. This information is also intended to help form a statistical population database (with personal identifying information removed). The act further directed the expansion of the DNA Identification Index to include information on criminal offenses and acts of juvenile delinquency that would be considered violent crimes if committed by an adult.

### International Organizations

*By the late 1990s, international organizations were working out ethics and procedures for dealing with genetics research and technology on a global basis. Given the divergent interests and educational levels of the different countries, this is a major undertaking.*

In 1997, the United Nations Educational, Scientific, and Cultural Organization (UNESCO), on behalf of almost 200 member states, adopted the *Universal Declaration on the Human Genome and Human Rights*, the first international statement of ethics in human genetics research. It is intended to safeguard the public in the area of scientific research, emphasizing consent and nondiscrimination within the context of fundamental human rights and freedoms.

## State Legislative Concerns

*At the state level, legislative concerns were similar to those at the federal level, with the addition of a number of challenges to the legality and constitutionality of mandatory or involuntary sampling of DNA. No clear direction is yet apparent as to whose rights take priority in courts of law. In some cases, law enforcement has successfully won broader powers, in some cases, citizens have won the right to refuse DNA testing. However, there does appear to be a general leaning in favor of empowering military and law enforcement agencies to acquire and store DNA.*

In 1995, two marine service members under threat of court martial refused DNA testing. In court, they challenged the U.S. military's actions in requiring mandatory DNA samples of all service members. The military's principle motivation for testing was to aid in recovery of unidentifiable remains from armed conflicts, yet tests were being required of all service members, whether or not they were being sent to war zones. In initial court challenges, the military's actions in demanding the tests were upheld as lawful.

In 1996, Jason Aaron Boling challenged Roy Romer, Governor of the State of Colorado, on the constitutionality of Colorado Revised Statute 17-2-201(5)(g):

> "... which requires inmates convicted of an offense involving a sexual assault to provide the state with DNA samples before their release on parole, and the Department of Corrections' (DOC) policies implementing that statute...."

The principal argument was that the statute violates the Fourth Amendment prohibition against unreasonable searches and seizures and plaintiff rights under the Fifth, Eighth, Ninth and Fourteenth Amendments. The plaintiff failed to support contentions that he was denied equal rights, and that the state might misuse the information, and his motions were denied.

The DNA Seizure and Dissemination Act enacted by the Commonwealth of Massachusetts has been challenged on constitutional and privacy grounds as well. The Act was put into place on 30 September 1997 to assist criminal justice and law enforcement agencies in identifying individuals and in deterring and discovering crimes. This would give wide-ranging powers affecting not only those convicted of a large number of statutory offenses, but also those convicted of an attempt or conspiracy to commit such acts. It would be incumbent not just on those incarcerated, but also on those on probation or parole. The results of all DNA analyses would become part of the state's DNA database. The Act further would permit officials to use 'reasonable force' in order to obtain samples from uncooperative donors, and the levying of fines and possible imprisonment for those refusing to provide samples.

The Act went into practical use in 1998. On 12 Aug. 1998, Massachusetts Superior Court Justice Isaac Borenstein challenged the DNA Seizure and Dissemination Act and ordered that "... defendants will not participate in the collection, analysis, and/or dissemination of DNA ..." and that "DNA samples already in the possession of the Director of the State Crime Laboratory shall remain sealed, impounded, segregated, and separately stored pending further notice by the Court." Judge Borenstein rejected a state bid for seizure of DNA from seven individuals, stating "... this Court would need to change the existing laws governing Fourth Amendment jurisprudence, and would not only exceed its authority, but adopt a rule that is new, extensive and unjustified under any analysis of constitutional doctrine."

In August 1999, the ACLU of Utah fought against policy that would take DNA samples from arrested individuals prior to conviction. They raised concerns about sampling individuals for minor offenses such as jaywalking, or civil disobedience acts of conscience that might occur at a political demonstration.

In October 1999, the New York State Senate and the Assembly passed a bill to revamp the New York State DNA database. This was significant in that it removed the distinction between criminals and those who have attempted a serious crime. It now covers violent felonies, serious nonviolent offenses (e.g., burglary), and some drug-related crimes. Offenders incarcerated prior to the establishment of the database in 1996 may now be sampled.

In some jurisdictions the onus is on an accused party to explicitly ask that DNA results and samples be destroyed after they have been acquitted or released. Many individuals are not aware of this fact, or that they may only have a few days in which to make the request.

As can be seen from this small sampling of examples, the DNA rights pendulum has not yet come to rest and there are many important issues still to be resolved.

# 9. Implications of Use

### Accessibility

To a surveillance agent, the accessibility of DNA technology is a combination of a number of factors, including ease of use, portability, cost, and the ease of surreptitious collection of samples.

It is relatively easy to collect voluntary DNA samples with cheek swabs, and only somewhat technical to collect blood samples. It's not quite as easy, but it is reasonably routine to collect involuntary or crime scene samples. Analyzing the samples requires technical expertise and equipment, but can be done by labs for a fee or, in some cases, with portable 'briefcase' systems costing several thousand dollars. DNA is moderately easy to collect surreptitiously from saliva (spit), semen (carelessly discarded condoms), and hair roots. The cost of a basic analysis on a couple of samples (as in a paternity test) is now about $300. Simple DNA printing for one individual is less. A full analysis yielding more information, such as genetic defects, may cost several hundred to a couple of thousand dollars, but that is still reasonably low, and demand for genetic counselling will drive costs lower for similar, nongenetics services. Reduced costs of $200 for a complete genetic profile, $75 for a paternity test, and $25 for a livestock or endangered species profile might reasonably be expected by 2002.

While sampling is relatively easy, access to DNA databases is somewhat restricted. Publicly funded national DNA databases are restricted mainly to government and law enforcement officials, but there are databases in research facilities that are open to scientists and instructors, and public databases containing generic information are available on the Internet. It is probable that individuals researching and publishing their genealogies will eventually make DNA patterns available to family members as part of their database histories. Many people's computer systems are wide open to anyone on the Internet when they are searching the Web, especially now that cable modems allow users to economically stay online all the time. Clearly, private individuals are not as security-conscious as corporate agencies (most of whom have firewalls, though even here there are exceptions). Thus, private databases may be vulnerable to unauthorized use.

Database entry is often carried out by lower-paid clerical workers who, in most circumstances, are only loosely supervised. While most of these people are hard-working and honest, they may still be the weakest security link in restricted databases. Low-paid employees are vulnerable to bribery, and young, low-paid employees and interns will sometimes hand over sensitive information because they are unaware of the possible consequences of their actions. Labs without careful verification measures will sometimes sample a 'stand-in,' that

is, someone posing as the person who allegedly is the donor.

Given the ease and cost of sampling, in a couple of years, spying with DNA won't be substantially more difficult or more expensive than spying with video cameras, especially if the technical analysis is done with a briefcase lab, or is available for a reasonable fee through a private company that's not inclined to ask questions about the source of the sample or the purposes for which it might be used.

### Ethics and Regulations

Ethics and regulations have been surveyed in earlier parts of this chapter, and a full discussion of ethics is too large a topic to be covered here since DNA is used in hundreds of fields of study. However, in terms of surveillance agents, regulations for the collection and use of DNA are fairly stringent in law enforcement, but not significantly restricted in the private sector.

DNA technology is not inherently good or bad. It is likely that a lot of good can come from pharmaceutical drugs designed to work with the genetic makeup of individuals, giving them a chance at a longer life and better health. But the same technology can be applied to biological warfare that targets a specific family or ethnic group. Thus, DNA collection on behalf of hate- or protectionist-oriented groups may have some serious repercussions.

As described in earlier examples, most genetics-related bills are not comprehensive. They typically focus on protecting the confidentiality of information in the hands of institutions. Few seek to regulate individual or noninstitutional collection and use of DNA information. Some provisions protect physical access to the individual (e.g., the taking of blood), but few outside of law enforcement address the surreptitious gathering of spit, or hair from a brush, etc. Like any commodity, DNA may eventually be traded on the black market. If scientists find ways to inject DNA into developing embryos, people may buy particular attributes, or use illicitly collected DNA from famous personages, or unwitting parents. Just as there are professional killers willing to take a life for three- to five-thousand dollars, there will likely be professional DNA collectors, willing to gather DNA for a fee. Taking a saliva sample or handful of hair roots from a person's home involves trespass and theft, but gathering it from a sidewalk, washroom, or other public place without the donor's knowledge is pretty easy. Even if it's illegal, it may be hard to prove when an involuntarily sampled donor doesn't know the crime has been committed.

Many legislative bills regarding national databanks are drafted on the assumption that anonymity is sufficient to safeguard the rights of individuals, but this reflects a simplistic understanding of DNA profiling. Anonymity may disappear when a sample shows a profile of unique interest to researchers or pharmaceutical companies. Who will safeguard the anonymous individual from exploitation of his or her unique genetic makeup for experimental or commercial purposes? What happens if an anonymous profile is later matched to one collected for another reason? What if the anonymous profile is evaluated in the context of close relatives, thus divulging the source of the DNA through deduction and inference? Currently there are no protections against these types of exploitation or intrusion.

### Applications

The practical applications of DNA surveillance fit into roughly three categories: a) activities intended to benefit the 'greater good' (law enforcement, medicine, conservation, and defense); b) private information-gathering (by corporations, small detective agencies, and individuals); and c) sinister, underground, or black market surveillance (by unauthorized individuals or agencies).

*Category a* activities have been discussed throughout this chapter and are not repeated here, but *categories b and c* have not been covered in detail, and a few examples are cited to provide some perspective on less-sanctioned surveillance activities.

Private detectives and free agent spies are routinely hired to surveil corporations, allegedly cheating spouses, and individuals suspected of insurance fraud. This is currently done with hidden video cameras, radio transmitters, and sometimes with illegal phone taps. Given that phone call recording is rampant, in spite of tough legislation regulating its use, it's probable that surveillance agents will undertake clandestine collection of DNA in much the same way.

- Free agents collecting saliva, hair roots, or semen, and getting analyses from private labs, currently have few legislative hurdles to hinder them. They can conceivably collect and analyze DNA from motel sheets provided by the motel owners voluntarily or for a fee. They may sample a potential CEO or other employee, or a marriage hopeful who might want to know the genetic makeup of a potential spouse, perhaps a child that is suspected of being fathered through another woman, a deadbeat parent, or an adopted child.
- Supremacist groups might undertake racial 'screening' before admittance into their organizations.
- Enemies might sample a person for vulnerabilities, like a predisposition for alcoholism or heart disease, in order to discredit or harm a person.
- Underground research labs might design a 'smart virus' targeted specifically to be active in people with certain DNA patterns.
- Terrorists might target a specific species of plant, like a food crop, to be decimated by a designer gene that becomes active after the initial growing period.

When you are dealing with the building blocks of life, almost anything is possible and since many of these potential crimes are hard to trace, they will be equally hard to prosecute.

### Strength of Evidence

Strength of evidence depends on its specificity, its accuracy, and admissibility in court. Five years ago there was a lot of debate about the strength and accuracy of DNA evidence. This is partly because other court-related tests are controversial, such as lie detector tests. From a scientific view, however, DNA is strong evidence, particularly in the areas of DNA *print matching* and DNA *family profiling* which are relevant in many legal disputes. Courtrooms are now gradually accepting DNA as 'good' evidence and supporting its credibility. Juries composed of lay people may not yet fully understand the technology, but gradually, as articles are written in the popular press, its applications and implications will be better understood. DNA evidence is now strong enough to exonerate falsely accused incarcerated individuals and is compelling enough to convict many murderers and rapists.

### Freedom and Privacy

*Freedom and privacy issues are probably the most important matters related to DNA surveillance and thus are covered in more detail. Some of the important implications of DNA sampling, storage, and use have already been discussed in Section 7 (Problems and Limitations), including discrimination and the logistics of sampling and storage, and the reader is encouraged to consult Section 7 in conjunction with this section.*

The study and use of DNA technology are likely to grow in spite of concerns about pri-

vacy and commercial exploitation of an individual or family's unique attributes. There are so many stakeholders in the DNA goldrush: medical researchers, pharmaceutical companies, genetics counsellors, parents, potential parents, spies, and law enforcement officials, that the genie is already out of the bottle. Automation and commercialization will cause prices to continue to drop and DNA analysis to become readily available through portable suitcase labs. The cheaper it gets, the more people will use it; the more they use it, the cheaper it will get.

DNA analysis may be the most significant of any surveillance technology in terms of the amount of personal information that can be gathered and pinpointed to a particular location, or even to specific actions of an individual. Tissue samples can reveal not only characteristics of the individual and indirect information about his or her ancestors and siblings, but may also indicate medical conditions or pathogens that can betray a person's activities, general lifestyle choices, or specific whereabouts. This intimate information, taken together with data from other observations, can provide a composite intelligence picture that reveals much more than was ever before possible. Serial murders, for example, may be difficult to track when the killer is constantly on the move. Certain interstate murders might never before have been linked without careful studies of the modus operandus (MO) and sharing of notes with other jurisdictions. With DNA testing of crime scenes where blood or semen might be found, DNA analysis has the potential to immediately connect the murders, thus alerting law enforcement to cases in which cooperation between agencies would be fruitful.

DNA testing is being favored over simple blood type testing in paternity suits, as it provides a far greater set of information, and requires less invasive sampling (suitable for children and animals). It can be performed on infants and in some cases, unborn children or their associated CVS and amniotic fluids. DNA sampling to detect genetic defects is already carried out in many hospitals and birth clinics. It's only a short step to sampling all children at birth, or even before the child is born. The information can be permanently stored, perhaps in a tiny implant on the underside of an arm or leg, one that might have an electronic lead or transmitter for interfacing with a computer network.

The DNA sword is two-sided. Usually the easier it is to surveil, the easier it is to be surveilled. Clearly, law enforcement officials could do their jobs more efficiently if they had a key to every house in the community and, clearly, they could do better crime solving if they had a DNA file for every person in the nation, but is this a good idea or might it result in an insidious, irrevocable erosion of our free society? In the U.K., citizens have made voluntary donations of DNA samples to help fight crime and police agencies have advocated sampling the entire population. There are tax incentives for permanent DNA banking of not just criminals, but ordinary people, as it's expensive to resample the populace each time a crime is committed. In some countries citizens won't even be given a choice. They'll be directed to submit a sample to the state, with strong penalties for noncompliance. Even in the U.S., when service marines refused to submit to mandatory DNA collection, the right of the U.S. military was given precedence over the concerns of the marines.

We should be both awed and concerned at the applications of this technology. Awed at the potential good from genetics counselling and the apprehension of violent criminals, and concerned about trading one set of freedoms for another without any guarantee of overall gain. If we look critically at computer technology, which developed in a flush of hope that automation would provide us with more free time and a better quality of life, we see that the tradeoffs are sometimes greater than originally anticipated. Computers have spawned a global obsession with information-gathering, record-keeping, and publishing that now appears to be

reducing free time, rather than increasing it. We are learning that computer use provides no guarantee whatsoever of an improved quality of life except in a few incidences of medical applications, transportation, or communication with distant business associates or loved ones.

Those particularly concerned about institutional and private abuse of DNA information have argued that DNA is a natural attribute of the person, subject to consent and privacy laws. Governments change and policies change but information databases tend to survive from one administration to the next. History has shown us that data collected for one purpose may be expropriated for other purposes by subsequent administrations. Those who handle the data, or turn it over to office colleagues or superiors, often don't know what it is or how it is used. Everyone involved with DNA technology should be aware that we may be handling 'data' that are more sensitive and more volatile than any technology ever devised.

# 10. Resources

*Inclusion of the following companies does not constitute nor imply an endorsement of their products and services and, conversely, does not imply their endorsement of the contents of this text.*

## 10.a. Organizations

**American Academy of Forensic Sciences** (AAFS) - The AAFS is a Colorado-based society with international activities dedicated to the application of science to law. Members include physicians, physical anthropologists, document examiners, criminologists, toxicologists, and others. http://www.aafs.org/

**American Association of Blood Banks** - This organization has established standards for DNA use in paternity testing, and accreditation for laboratories.

**American Board of Criminalistics** (ABC) - Wisconsin-based organization that oversees a peer-developed, peer-reviewed certification program. http://www.criminalistics.com/

**American Civil Liberties Union** (ACLU) - The ACLU is a prominent, nonpartisan individual rights advocate organization involved in legislation, litigation, and education on issues related to freedom in the United States. Established in 1920 by Roger Baldwin. http://www.aclu.org/

**American Society of Crime Laboratory Directors** (ASCLD) - Founded in 1973 by the Director of the FBI Laboratory and the Director of the FBI, the ASCLD is a nonprofit professional organization concerned with the operations, standards, and ethics of crime laboratory operations. The ASCLD runs a voluntary Crime Laboratory Accreditation Program and publishes the ASCLD Newsletter. http://www.ascld.org/

**Armed Forces DNA Identification Laboratory & Repository** - A subspecialty of the Center for Advanced Pathology (CAP) for consultation, education, and research. It processes identification of remains from Vietnam, Operation Desert Storm, Waco, etc. and collects and stores service member DNA samples, with more than 10,000 currently on file. http://www.cap.org/

**Armed Forces Institute of Pathology DNA Identification Laboratory** (AFIP, AFDIL) - AFDIL is comprised of two lab. sections - mitochondrial DNA, used primarily for analyzing service member remains; and nuclear DNA, which supports the Office of the Armed Forces Medical Examiner in disaster investigation (explosions, air disasters, etc.). http://www.afip.org/

A DNA Registry was established in 1992 to provide identification information for American service personnel and contractors sent to areas which may be dangerous to life. Blood specimens are collected (usually at induction centers), packaged, and frozen. Identifications are said to be based on the lengths of the repeated sequences, information sufficient to identify familial relationships, but not sufficient to provide in-depth medical information about the individual. However, with the original

blood sample on file, it does not guarantee that different types of testing might not occur in the future. Cards are kept on file for the same length of time as other records, currently 50 years. Once service has been completed, an individual may request destruction of the DNA record.

**Armed Forces Repository of Specimen Samples for the Identification of Remains** (AFRSSIR) **Armed Forces Identification Review Board** (AFIRB) - A department involved in identification of the remains of service members, which now uses DNA technology to assist in this task. AFIRB was involved in identification of the memorialized Unknown Soldier.

**Assistant Secretary of Defense for Health Affairs** (ASDHA) - A federal agency responsible for establishment and enforcement of DNA sampling requirements. DNA samples superseded panographic samples as of 1 January 2000.

**Association in Search of Disappeared Children** - A humanitarian organization founded in 1994 to locate children who disappeared in the El Salvador civil war. It works in conjunction with Physicians for Human Rights in using DNA testing as an identification tool to help reunite families.

**Bodymap** - Web-accessible, grant-supported gene expression databases for humans and mice. It is based in Japan. http://bodymap.ims.u-tokyo.ac.jp/

**Celera Genomics** - One of the leading commercial companies in the process of unraveling the human genome and creating a base of genetics information and services for pharmaceutical, biotechnology, and academic research. http://www.celera.com/

**Combined DNA Index System** (CODIS) - A national computer bank of DNA from all states including known and unidentified samples. Initiated October 1998, CODIS requires sampling from 13 gene loci that are specific to identification. (The FBI has had a typing lab in the Hoover Building in Washington, D.C. since 1989.) CODIS is a databank with profiles of evidence and convicted offenders. Access is restricted. Includes state (SDIS) and local (LDIS) indexes. Samples and records for convicted criminals are kept indefinitely.

**Council for Responsible Genetics** (CRG) - Founded in 1983, CRG is a nonprofit professional organization devoted to public awareness and monitoring of technological advances related to genetics. CRG advocates the responsible use of this technology, and publishes an information bulletin. http://www.gene-watch.org/

**Danish Centre for Human Genome Research** - Web-accessible databases at the University of Aarhus for health and disease research. The protein files are extensively cross-referenced to other Internet databases (GenBank, UniGene, etc.). Includes still and video examples of procedures. http://biobase.dk/cgi-bin/celis/

**DNA Advisory Board** - A federal organization which sets standards for the interpretation of DNA evidence.

**EarthTrust** - An organization that supports the ongoing use of DNA testing to end whaling.

**European DNA Profiling Group** (EDNAP) - In 1991 EDNAP was accepted as a working group of the ISFH. Founded in October 1988 in London, it represents over a dozen European countries, providing law enforcement assistance based on cooperation and scientific data and decision-making. http://www.uni-mainz.de/FB/Medizin/Rechtsmedizin/ednap/ednap.htm

**Federal Bureau of Investigation** (FBI) - A U.S. federally funded investigative agency with a number of departments involved in DNA sampling, analysis, profiling and databasing. http://www.fbi.gov/

**Forensic Justice Project** (FJP) - A national, Washington, D.C.-based effort to provide objective, expert evaluation and testimony, and to monitor and review cases handled by the FBI crime lab with the goal of protecting innocent people from the misuse or abuse of forensic sciences. http://www.forensicjustice.org/

**The Forensic Science Service** (FSS) - A U.K.-based, accredited group of laboratories employing over 1,200 scientists. Lab members examine samples, provide expert evidence in court, and engage in scientific research on advanced DNA techniques. http://www.forensic.gov.uk/

**Genetics Society of America** - Established in 1931, this organization promotes academic research and recognition in the field of genetics, and publishes the monthly "Genetics" journal. http://www.faseb.org/genetics/gsa/gsamenu.htm

**Genome MOT** - A genome monitoring project which presents Web-accessible status reports for monitoring the progress of the many large genome sequencing projects, which includes the human genome. http://www.ebi.ac.uk/~sterk/genome-MOT/index.html

**Genome Sequencing Center** - Established in 1993 at the Washington University School of Medicine with a grant from the National Human Genome Research Institute of NIH. The teams each sequence about 7 million base pairs per year. The GSC works in conjunction with the Sanger Centre. http://genome.wustl.edu/gsc/index.shtml

**Human Genome Diversity Project** (HGDP) - A National Science Foundation-supported, international project proposed in the early 1990s to study global human variation, patterns of migration, and reproduction by collecting DNA samples from anonymous members of some 500 defined populations. Ethical and practical matters were being worked out before full-scale commencement of the project. THE HGDP is affiliated with HUGO.

**Human Genome Organization** (HUGO) - A nonprofit, non-governmental organization of scientists involved in the coordination of studies of human genetics, founded by Victor McCusick. HUGO is involved the Human Genome Diversity Project.

**The Human Genome Project** (HGP) - A highly significant international collaborative effort to 'map' the entire human genome. Established in 1991 by the Ministry of Education, Science, Sports and Culture (MESSC).

**The Innocence Project** - An effort which helps free people who have been jailed unjustly. DNA evidence is used to exonerate incarcerated individuals by excluding them as the perpetrators of a crime, usually involving rape or murder.

**The Institute for Genomic Research** (TIGR) - A not-for-profit research institute based in Rockville, Maryland. It conducts research on plant and animal cells and includes a large DNA sequencing lab. http://www.tigr.org/

**International Association of Forensic Science/Scientists** (IAFS) - This organization conducts an annual international professional conference.

**The International Association for Identification** (IAI) - A large professional organization founded in 1915 for individuals around the world engaged in forensic identification, investigation, and scientific examination of physical evidence. The California-based IAI educates through conferences and workshops, encourages research, and promotes communication among members and affiliates. http://www.theiai.org/

**International Criminal Police Organization** (INTERPOL) - An international cooperative organization of crime-fighting police authorities with members in almost 200 countries. Established in 1956 (descended from ICPC), INTERPOL is currently based in Lyon, France. http://www.kenpubs.co.uk/INTERPOL.COM/

**INTERPOL European Working Party on DNA Profiling** - A working group consisting of members from several countries, including Belgium, the Czech Republic, Germany, U.K., Norway, Spain et al. Its members discuss DNA profiling as an investigative tool and make recommendations concerning its use in criminal investigations.

**Lawrence Livermore National Laboratory Forensic Science Center** (LLNL FSC), **LLNL Human Genome Center** (HGC) - Research and commercialization of DNA sequencing techniques and equipment. The HGC has established a number of databanks and sequence tracking systems. LLNL has also been involved in the formation of a Joint Genome Institute for the U.S. Department of Energy with its three Genome Centers at Livermore, Berkeley, and Los Alamos. http://www-bio.llnl.gov/bbrp/genome/genome.html

**Maxxam Analytics Inc.** - Human DNA Department - recently inspected by the Standards Council of Canada in hopes of becoming accredited for paternity and forensic DNA analysis.

**Medlantic Research Institute's Transplant and Immunogenetics Laboratories** - Tissue typing for organ transplants, crossmatching cadavers and living recipients for compatibility, blood serology and viral screening. Designated as the central donor lab for the Washington Regional Transplant Consortium (WRTC) in 1990.

**Mitochondrial DNA Concordance** - Centered at the University of Cambridge, this database provides a cross-referenced list of single nucleotide substitutions in the two hypervariable segments of the mtDNA control region. The purpose is to provide information that is easier to analyze than that found in the GenBank, for example, which has been useful in the forensics field.
http://shelob.bioanth.cam.ac.uk/mtDNA/

**MITOMAP** - A comprehensive human mitochondrial genome database that can be accessed through the Internet. The human mtDNA sequence was determined in the mid-1990s.
http://infinity.gen.emory.edu/MITOMAP/

**National Center for Biotechnology Information (NCBI) GenBank** - A national, annotated, public databank of DNA sequences containing data submissions mainly from scientists. The GenBank is searchable over the Internet. GenBase is part of the International Nucleotide Sequence Database Collaboration project, and as such shares data with the DNA DataBank of Japan (DDBJ) and the European Molecular Biology Laboratory (EMBL). http://www.ncbi.nlm.nih.gov/Genbank/index.html

**National Center for Genome Resources** (NCGR) - A nonprofit center founded in 1994, arising from the Human Genome Project. NCGR supports the research, development, and application of knowledge systems in biology related to technologies that support humankind and the environment. The Center develops and applies computer-based systems for visualizing and analyzing data and disseminates them through collaborations with research institutions, both academic and commercial. Funding is from public and private sources. The center is one of two public repositories in the U.S. for human genomic data. Located in Santa Fe, New Mexico. http://www.ncgr.org/

**National DNA Advisory Board** - Established in 1995, arising from the DNA Identification Act of 1994, to recommend quality assurance standards to the FBI.

**National Human Genome Research Institute** (NHGRI) - Originally established in 1989 as The National Center for Human Genome Research (NCHGR). NHGRI heads the Human Genome Project. It is one of two dozen centers comprising the National Institutes of Health (NIH).
http://www.nhgri.nih.gov/

**National Institute of Justice** (NIJ) - This agency has a research branch awarding $5 million grants in 1999 to speed DNA chip technology.

**National Institute of Justice Commission on DNA Evidence** - Established as directed by the Attorney General to provide recommendations on the use of current and future DNA methods, applications, technologies, policies, and legal issues in the operation of the criminal justice system. Meetings are held about four times per year. http://www.ojp.usdoj.gov/nij/dna/welcome.html

**National Research Council Committee from the National Academy of Sciences** - Has been promoting the use of defined standards for proficiency testing, DNA laboratory work, and statistical calculations and issuing reports.

**The Sanger Centre** - Research in genomes, especially sequencing and analysis. The facility is jointly founded by the Wellcome Trust and the Medical Research Council. (See Wellcome Trust.)
http://www.sanger.ac.uk/

**Scientific Working Group DNA Analysis Methods** (SWGDAM) - With support from the FBI, it includes members from more than 30 laboratories. Originally TWGDAM, it addresses issues related to statistical interpretation, DNA profiling, quality assurance and criteria.
http://www.for-swg.org/swgdamin.htm

**Selmar** - DNA profiling services for law enforcement.

**Stanford Human Genome Center** (SHGC) - Research and education regarding the construction of high resolution radiation hybrid maps of the human genome, and sequencing of large, contiguous genomic regions. http://www-shgc.stanford.edu/

**Technical Working Group on DNA Analysis Methods** (TWGDAM) - Founded in 1988, TWGDAM is hosted and supported by the FBI Laboratory. It is now known as the Scientific Working Group on DNA Analysis Methods (SWGDAM).

**UniGene** - Unique Human Gene Sequence Collection. Records about 40,000 clusters of GenBank sequences representing the transcription products of distinct genes derived from an experimental system. Includes human, rat, and mouse data. http://www.ncbi.nlm.nih.gov/UniGene/index.html

**United Nations Educational, Scientific and Cultural Organization** (UNESCO) - Headquartered in France with about 60 field offices around the world, this multinational United Nations organization was founded in 1945 and currently represents almost 200 member nations. http://www.unesco.org

**U.S. Army Central Identification Laboratory, Hawaii** (CILHI) - Involved in the search, recovery, and identification of skeletal remains of American bodies lost in prior conflicts. Works through use of the Armed Forces Institute of Pathology (AFIP) labs.

**U.S. Army Forces Command** (FORSCOM) - Engaged in cataloguing all active soldiers by the end of 1999 and all reserve soldiers by the end of 2004, as per the Assistant Secretary of Defense for Health Affairs which is the agency responsible for the establishment and enforcement of DNA sampling requirements.

**U.S. Fish & Wildlife Service** - The Fish & Wildlife Service lab in Ashland, Oregon includes a Forensic Science Branch with Genetics and Criminalistics departments. These facilities aid the Service in prosecuting individuals 'beyond a reasonable doubt.' http://www.lab.fws.gov/

**Wellcome Trust Genome Campus** - Hinxton, near Cambridge, U.K. The campus houses the Sanger Centre, the European Bioinformatics Institute (EBI), a branch of the European Molecular Biology Laboratory (EMBL), and the Medical Research Council's Human Genome Mapping Project Resource Centre (HGMPRC).

## 10.b. Print Resources

*The author has endeavored to read and review as many mentioned resources as possible or to seek the recommendations of colleagues. In a few cases, it was necessary to rely on publishers' descriptions on books that were very recent, or difficult to acquire. It is hoped that the annotations will assist the reader in selecting additional reading.*

*These annotated listings may include both current and out-of-print books and journals. Those which are not currently in print are sometimes available in local libraries and second-hand book stores, or through interlibrary loan systems.*

Ballantyne, Jack; Sensabaugh, George; Witkowski, Jan, "DNA Technology and Forensic Science (Banbury Report 32)," New York: Cold Spring Harbor Lab Press, 1990, 368 pages. Discusses legal and policy issues, and the provision of DNA services.

Billings, Paul R., editor, "DNA on Trial: Genetic Identification and Criminal Justice," New York: Cold Spring Harbor Lab Press, 1992, 154 pages. Describes the history of DNA in trial courts, civil liberties, and public policy. Includes an analysis of decisions in various courts and whether juries should consider DNA evidence. Out of print.

Erlich, H. A., Editor, "PCR Technology: Principles and Applications for DNA Amplification," New York: Stockton Press, 1989, 246 pages.

Evett, I.; Weir, B., "Interpreting DNA Evidence: Statistical Genetics for Forensic Scientists," Sinauer, 1998, 278 pages.

Farley, Mark A.; Harrington, James J., editors, "Forensic DNA Technology," Chelsea, Mi.: Lewis Publishers, Inc., 1991. Includes contributions from some of the country's leading experts. Traces the underlying theory and historical development of DNA testing, legal admissibility requirements and courtroom utilization, as well as the history of DNA use in the clinical lab.

Fisher, Barry, A. J. "Techniques of Crime Scene Investigation, 6th edition," Boca Raton, Fl.: CRC Press LLC, 1999. Describes field-tested techniques and procedures, and technical information concerning crime scene investigation. A comprehensive source used by police academies, community colleges, and universities. Recommended by three professional organizations, the International Association for Identification, the American Board of Criminalistics, and the Forensic Science Society, as a text to prepare for their certification examinations.

Frankel, Mark S.; Teich, Albert H., "Ethical and Legal Issues in Pedigree Research," Washington, DC: AAAS, 1993, 216 pages. DNA and pedigree lineage issues. These are currently undergoing substantial change due to the availability of DNA information.

Frankel, Mark S.; Teich, Albert H., Editors, "The Genetic Frontier: Ethics, Law, and Policy," Washington, DC: AAAS, 1994, 240 pages. Out of print.

Inman, Keith; Rudin, Norah, "An Introduction to Forensic DNA Analysis," Boca Raton, Fl.: CRC Press LLC, 1997. Forensic DNA analysis theory and techniques explained so that professionals in other fields and laypeople can understand DNA analysis from sample collection to data interpretation. Describes the legal and scientific advantages and limitations of the various techniques.

Judson, Horace Freeland, "The Eighth Day of Creation: Makers of the Revolution in Biology," New York: Cold Spring Harbor Lab Press, 1996. Historical information in molecular biology. Includes interviews with some of the scientists involved in the discovery of DNA.

Kitcher, Philip, "The Lives to Come: The Genetic Revolution and Human Possibilities," New York: Simon & Schuster, 1996, 381 pages. Covers many aspects of DNA technology, including sequencing, fingerprinting, transcription, translation, restriction, cloning, etc. Includes a historical survey, an evaluation of its impact on our lives, and a good glossary.

Lagerkvist, Ulf, "DNA Pioneers and Their Legacy," New Haven and London: Yale University Press, 1998, 156 pages.

National Institute of Justice, "The National Institute of Justice and Advances in Forensic Science and Technology," a National Law Enforcement and Corrections Technology Center Bulletin, March 1998, 23 pages. Primarily important for providing background information on DNA procedures, legislation, quality assurance and application, but also includes information on latent fingerprinting and authorship of questioned documents. http://nlectc.org/pubs/

National Research Council, "The Evaluation of Forensic DNA Evidence, Washington, D. C.: National Academy Press, 1996. Includes information on population genetics and statistics, case descriptions, and recommendations for handling samples.

Olby, Robert, "The Path to the Double Helix," Seattle: University of Washington Press, 1974. A comprehensive historical presentation. Dover Publications has produced a 1994 reprint, 522 pages.

"President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, Screening and Counseling for Genetic Conditions," Washington, D.C.: U.S. Government Printing Office, 1983.

Sayre, Anne, "Rosalind Franklin and DNA," New York: W. W. Norton & Co., 1975, 221 pages.

Teich, Albert, "Ethical and Legal Implications of Genetic Testing," Conference Proceedings: The Genome, Ethics, and the Law: Issues in Genetic Testing. Washington, D.C.: AAAS, 1992, 124 pages.

Watson, James D.; Stent, Gunther S., Editor, "The Double Helix: A Personal Account of the Discovery of the Structure of DNA," New York: W. W. Norton & Co., 1980, 298 pages.

Zaborskey, Oskar R., "An Evaluation of the Application of DNA Technology in Forensic Science," Washington, D. C.: National Research Council, National Academy Press, 1992, 185 pages.

## Articles


Andrews, L. B.; Jaeger, A. S., "Confidentiality of genetic information in the workplace," *American Journal of Law and Medicine*, 1991, V.17, pp. 75-108.

Annas, George J. "Privacy rules for DNA databanks: protecting coded 'future diaries'," *Journal of the American Medical Association*, 1993, Nov. 17; 270(19), pp. 2346-2350. Discusses the wide-ranging information contained in DNA and how it relates to privacy, obligations, storage, and public policy and rule-making. Annas continues this discussion in "Rules for gene banks: protecting privacy in the genetics age," a 1994 paper presented originally at a 1991 conference on Justice and the Human Genome.

Connors, Edward; Lundregan, Thomas; Miller, Neal; McEwen, Tom, "Convicted by Juries, Exonerated by Science: Case studies in the use of DNA evidence to establish innocence after trial," *NIJ Research Report,* June 1996, 118 pages.

Croteau, Roger, "Experts ID Dog DNA in Mauling," *San Antonio Express-News*, 14 May, 1998. Report in which saliva on a victim's clothes matched a dog accused of the mauling.

Dahlberg, James E.; Lyamichev, Victor I.; Brow, Mary A. D., "Method of site specific nucleic acid cleavage," *U.S. Patent #5,422,253,* filed 7 Dec. 1992.

Drmanac, Radoje T.; Crkvenjakov, Radomir B., "Method of sequencing genomes by hybridization of oligonucleotide probes," *U.S. Patent #6,018,041,* filed 29 July 1997 as a continuation of several other patent filings including *U.S. Patent #5,492,806,* filed 12 Apr. 1993.

Fodor, Stephen P. A.; Solas, Dennis W.; Dower, William J., "Methods for nucleic acid analysis," *U.S. Patent #5,871,928,* filed 11 Jun. 1997.

Gill, P.; Jefferies, A. J.; Werrett, D. J. "Forensic applications of DNA fingerprints," *Nature*, 1985, V.318, pp. 577-579.

Gill, P.; Ivanov, P. L.; Kimpton, C.; Piercy, R.; Benson, N.; Tully, G.; Evett, I.; Hagelberg, E.; Sullivan, K. "Identification of the remains of the Romanov family by DNA analysis," *Nature Genetics*, 1994, V.6, pp. 130–135.

Ginther, C.; Issel-Tarver, L.; King, M. C., "Identifying individuals by sequencing mitochondrial DNA from teeth," *Nature Genetics*, 1992, V.2, pp. 135–138.

Gordon, Julian; Stimpson, Donald; Hsieh, Wang-Ting, "Method and apparatus for collecting a cell sample from a liquid specimen," *U.S. Patent #5,578,459,* filed 24 Nov. 1993.

Hershfield, Bennett, "Method for identifying the species origin of a DNA sample," *U.S. Patent #5,674,687*, filed 29 Nov. 1995.

Isenberg, Alice R.; Moore, Jodi M., "Mitochondrial DNA analysis at the FBI Laboratory," *Forensic Science Communications*, V.1(2), July 1999.

Jones, Douglas H., "Iterative and regenerative DNA sequencing method," *U.S. Patent #5,858,671,* filed 1 Nov. 1996.

Kambara, Hideki; Okano, Kazunori, "DNA sequencing method and DNA sample preparation method," *U.S. Patent #5,985,556,* filed 18 Sept. 1996.

Kass, N. E., "The implications of genetic testing for health and life insurance," 1997, in Rothstein, M.A., Editor, "*Genetic Secrets: Protecting Privacy and Confidentiality in the Genetic Era*," Yale University Press, pp. 299-316.

Katz, D.; Lee, D. et al, "The Application of Mitochondrial DNA Sequence Analysis to the Identification of Remains from a Mass Disaster - KAL Flight 801," *Armed Forces DNA Identification Laboratory,* 1998.

Kusukawa, N.; Uemori, T.; Asada, K.; Kato, I., "Rapid and reliable protocol for direct sequencing of material amplified by the polymerase chain reaction," *BioTechniques*, 1990, V.9, pp. 66-72.

Lewin, Roger "Genes from a disappearing world," *New Scientist,* May 1993, V.138(1875), pp. 25-29. Discusses DNA samples and databanks, genome mapping, investigative methods, impact, risks and benefits, minority groups, and social discrimination. This article includes an inset "Making the most of a human genetic atlas."

Love, Jack D., "Identification and paternity determination by detecting presence or absence of multiple nucleic acid sequences," *U.S. Patent #5,645,990,* filed 22 Nov. 1994.

Maniatis, T. et al., "Molecular Cloning," *Cold Spring Harbor Lab Report,* 1989, V.13, pp. 21-33.

Matsunaga, Hiroko; Okano, Kazunori; Kambara, Hideki, "DNA sequencing method and reagents kit," *U.S. Patent #5,968,743*, filed 9 Oct. 1997.

Maxam, A.; Gilbert, W., "A new method of sequencing DNA," *Proceedings of the National Academy of Sciences,* 1977, V.74, pp. 560-564.

Maxam, A. M.; Gilbert, W., "Sequencing end-labeled DNA with base-specific chemical cleavages," *Methods in Enzymology,* 1980, V.65, pp. 499-560.

McEwen, Jean E.; Reilly, Philip R. "A review of state legislation on DNA forensic data banking," *American Journal of Human Genetics*, 1994 June; V.54(6), pp. 941-958. Discusses confidentiality, criminal law, disclosure, DNA sampling, privacy issues, legislation, and advisory committees.

McEwen J.; McCarty K.; Reilly P., "A survey of medical directors of life insurance companies concerning use of genetic information," *American Journal of Human Genetics*, 1993, V.53, p. 33.

Mirsky, Alfred E., "The Discovery of DNA," *Scientific American,* June 1968, pp. 78-88. Provides an outline of major events and discoveries in the field.

Mullis, Kary B. et al., "Process for amplifying, detecting, and/or cloning nucleic acid sequences," *U.S. Patent #4,683,195*, filed 28 July 1987.

Padhye, Vikas V.; York, Chuck; Burkiewicz, Adam, "Nucleic acid purification on silica gel and glass mixtures," *U.S. Patent #5,658,548,* filed 7 Jun. 1995.

Rothberg, Jonathan Marc; Deem, Michael W.; Simpson, John W., "Method and apparatus for identifying, classifying, or quantifying DNA sequences in a sample without sequencing," *U.S. Patent #5,871,697*, filed 24 Oct. 1995.

Sanger et al., "DNA sequencing with chain terminating inhibitors," *Proceedings of the National Academy of Sciences*, USA, 1977, V.74(12), pp. 5463-5467.

Sensabaugh, George; Kay, D. H., "Non-human DNA evidence," *Jurimetrics Journal,* 1998, V.38, pp. 1-16. Judging the soundness of new methods of DNA analysis, including samples from non-human sources, as evidence. The article is adapted from the 2nd edition of the U.S. Federal Judicial Reference Manual on Scientific Evidence.

Shapiro, E. D.; Weinberg; M.L., "DNA Data Banking: The dangerous erosion of privacy," *Cleveland St. Law Review*, 1990, V.38, pp. 455, 477.

Tahara, T.; Kraus, J. P.; Rosenberg, L. E., "Direct DNA sequencing of PCR amplified genomic DNA by the Maxam-Gilbert method," *BioTechniques*,1990, V.8, pp. 366-368.

Thompson, W. C., "Evaluating the admissibility of new genetic identification tests: Lessons from the 'DNA War'," *Journal of Criminal Law*, 1993, p. 22. The process and procedures related to DNA typing.

Wells, Gary; Small, Mark et al., "Scientific Review of Lineups," White Paper, *Law and Human Behavior,* Dec. 1998.

Wilson, M. R.; Polanskey, D.; Butler, J.; DiZinno, J. A.; Repogle, J.; Budowle, B., "Extraction, PCR amplification, and sequencing of mitochondrial DNA from human hair shafts," *BioTechniques*, 1995, V.18, pp.662–669.

### Journals

"Forensic Science Communications," a quarterly publication by FBI Laboratory personnel. It includes articles on document examination, imaging technologies, evidence and statistics, the recovery, handling and transport of evidence, and other topics related to forensic science (formerly Crime Laboratory Digest). http://www.fbi.gov/

"Genewatch: The Bulletin of the Council for Responsible Genetics," a national newsletter which monitors the ethical, social, and biological impacts of biotechnology, six issues per year. http://www.gene-watch.org/

"Institute for Psychological Therapies Journal," official journal of the IPT, which deals with the private practice of clinical therapies for victims and alleged victims of violent crimes such as sexual abuse and murder. As such, the journal discusses issues related to DNA evidence and exoneration of wrongfully accused individuals. http://www.ipt-forensics.com/

"Journal of Forensic Sciences," the professional journal of the American Academy of Forensic Scientists (see listing under organizations). The JFS editorial base is at the University of Illinois at Chicago.

## 10.c. Conferences and Workshops

*Many of these conferences are annual events that are held at approximately the same time each year, so even if the conference listings are outdated, they can still help you determine the frequency and sometimes the time of year of upcoming events. It is very common for international conferences to be held in a different city each year, so contact the organizers for current locations.*

*Many of these organizations describe the upcoming conferences on the Web and may also archive conference proceedings for purchase or free download.*

*The following conferences are organized according to the calendar month in which they are usually held.*

The International Association of Forensic Scientists (IAFS) "15th International Symposium on Forensic Sciences," sponsored by the Australian and New Zealand Forensic Science Society; Gold Coast, Queensland, Australia, 5-10 March 2000,

Arizona State University SmithKline Beecham Symposium, "Respecting Genetic Privacy," explored the relationship between laws, legal doctrines, and genetic privacy, information, and tissue samples. 12-13 March 1999.

"Bloodstain Evidence Institute Spring Meeting," Corning, New York, 1-5 May 2000.

"International Conference on Forensic Science," Dublin, Ireland, 2-5 May 2000.

"National Conference on the Future of DNA: Implications for the Criminal Justice System," fifth annual conference, New York City, 8-9 May 2000.

"Cambridge Healthtech Institute's DNA Forensics Conference," the fourth annual conference, Springfield, Virginia, 31 May-2 June 2000.

"The Fourth Biennial Conference: International Perspectives on Crime, Justice and Public Order," Budapest, Hungary, 21-26 June 1998. This conference included genetics topics.

The British Council "3rd International Seminar on Advancing the Scientific Investigation of Crime," Durham, U.K., 11-23 July 1999.

"International Congress on Forensic Genetics," 19th annual forensics conference, Münster, Germany, 28 Aug. - 1 Sept. 2001.

"First International Conference on DNA Sampling and Human Genetic Research: Ethical, Legal, and Policy Aspects," Montreal, Quebec, Canada, September 1996.

TIGR "Genome Sequencing and Analysis Conference," Miami Beach, FL, 18-21 September 1999.

"Conference on DNA Sampling - The Commercialization of Genetic Research: Ethical, Legal and Policy Issues," Edmonton, Alberta, Canada, September 10-13, 1998. Re-presented at "The Canadian Bioethics Society 10th Annual Conference: Reflections on a Decade of Bioethics," Toronto, Ontario, October 15-18, 1998. This was the second annual conference. Note that the fifth annual conference (above) was scheduled for May.

Forensic Science Service "First International Conference and Exhibition on Forensic Human Identification," London, United Kingdom. Held at the Q.E. II Centre in London on 24-26 October 1999.

## 10.d. Online Resources

**DNA Tells All–Doesn't It?** A site that specifically looks at crime investigation and other forensic aspects of DNA. This is part of a NISE project funded by the National Science Foundation. http://whyfiles.news.wisc.edu/014forensic/genetic_foren.html

**The Gene School**. An educational site with general information, applications, interactive tutorials, a glossary and other resources related to gene therapy, cloning, the Human Genome, agriculture, and medicine. http://library.advanced.org/tq-admin/day.cgi

Note: If you don't enjoy typing in long Web addresses (URLs), you can access the links on the support site set up by the author for your convenience. http://www.abiogenesis.com/surveil

## 10.e. Media Resources

"Buried Secrets: Digging for DNA," from the *History Channel* History's Mysteries series. An examination of a number of important forensic techniques, including DNA matching, which determines identities of the famous dead, including the Unknown Soldier and descendants of Thomas Jefferson. VHS, 50 minutes. Cannot be shipped outside the U.S. and Canada.

"The DNA Revolution," from the *History Channel* 20th Century with Mike Wallace series. This describes the history of our understanding of DNA and describes some of the current technologies and controversies concerning genetic engineering. VHS, 50 minutes. Cannot be shipped outside the U.S. and Canada.

"Forensic Science: The Crime-Fighter's Weapon," from the *History Channel* Modern Marvels series. This traces the history and development of forensics and looks at various types of evidence (including DNA). VHS, 50 minutes. Cannot be shipped outside the U.S. and Canada.

"Gattaca," feature film by Columbia Pictures with Jersey Film Production, an Andrew Niccol Film. A futuristic story that investigates the possible consequences of DNA testing to stratify and control movement within society. Worth watching as the implied consequences are not unprecedented, and much of the DNA technology illustrated in the film already exists.

"The Wrong Man," from the *History Channel* American Justice series. This looks at the case of Rubin "Hurricane" Carter who was convicted of a crime he apparently did not commit. VHS, 50 minutes. Cannot be shipped outside the U.S. and Canada.

# 11. Glossary

*Titles, product names, organizations, and specific military designations are capitalized; common generic and colloquial terms and phrases are not.*

| | |
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| amplification | a process used to increase the number of copies of a specific fragment of DNA, usually to make it easy to test and analyze the sample |
| autoradiograph | a form of X-ray film image of DNA fragments that have been processed to yield certain patterns that can be studied and interpreted |
| chromosome | a replicating genetic structure in a cell which contains cellular DNA |
| clone | a cell or organism 'copied' from a specific ancestor such that it essentially retains the same genetic makeup as the ancestor |
| DNA | deoxyribonucleic acid, a molecule that contains encoded genetic information |
| double helix | a geometric shape that is used to symbolize the physical relationship of bonded DNA strands |
| gene | a fundamental unit of heredity found in a chromosome |
| genome | the genetic material found in the chromosomes of a particular species of organism |
| marker | an identifiable location on a chromosome which can be monitored through subsequent generations |
| mutation | a heritable change in a DNA sequence that is not typical |
| PCR | polymerase chain reaction |
| RFLP | restriction fragment length polymorphism |
| RNA | ribonucleic acid, a chemical constituent of cells that has a structure similar to DNA |