Vitamin D found to influence over 200 genes, highlighting links to disease

The extent to which vitamin D deficiency may increase susceptibility to a wide range of diseases is dramatically highlighted in research published today. Scientists have mapped the points at which vitamin D interacts with our DNA - and identified over two hundred genes that it directly influences. The results are published today in the journal *Genome Research*.

It is estimated that one billion people worldwide do not have sufficient vitamin D. This deficiency is thought to be largely due to insufficient exposure to the sun and in some cases to poor diet. As well as being a well-known risk factor for rickets, there is a growing body of evidence that vitamin D deficiency also increases an individual's susceptibility to autoimmune conditions such as multiple sclerosis (MS), rheumatoid arthritis and type 1 diabetes, as well as certain cancers and even dementia.

Now, in a study whose funders include the Medical Research Council (MRC), the MS Society, the Wellcome Trust and the MS Society of Canada, researchers at the University of Oxford have shown the extent to which vitamin D interacts with our DNA. They used new DNA sequencing technology to create a map of vitamin D receptor binding across the genome. The vitamin D receptor is a protein activated by vitamin D, which attaches itself to DNA and thus influences what proteins are made from our genetic code.

The researchers found 2,776 binding sites for the vitamin D receptor along the length of the genome. These were unusually concentrated near a number of genes associated with susceptibility to autoimmune conditions such as MS, Crohn's disease, systemic lupus erythematosus (or 'lupus') and rheumatoid arthritis, and to cancers such as chronic lymphocytic leukaemia and colorectal cancer.

They also showed that vitamin D had a significant effect on the activity of 229 genes including IRF8, previously associated with MS, and PTPN2, associated with Crohn's disease and type 1 diabetes.

"Our study shows quite dramatically the wide-ranging influence that vitamin D exerts over our health," says Dr Andreas Heger from the MRC Functional Genomics Unit at Oxford, one of the lead authors of the study.

The first author of the paper, Dr Sreeram Ramagopalan from the Wellcome Trust Centre for Human Genetics, adds: "There is now evidence supporting a role for vitamin D in susceptibility to a host of diseases. Vitamin D supplements during pregnancy and the early years could have a beneficial effect on a child's health in later life. Some countries such as France have instituted this as a routine public health measure."

The main source of vitamin D in the body comes from exposing the skin to sunlight, although a diet of oily fish can provide some of the vitamin. Research has previously suggested that lighter skin colour and hair colour evolved in populations moving to parts of the globe with less sun to optimise production of vitamin D in the body. A lack of vitamin D can affect bone development, leading to rickets; in pregnant mothers, poor bone health can be fatal to both mother and child at birth, hence there are selective pressures in favour of people who are able to produce adequate vitamin D.

This new study supports this hypothesis, having found a significant number of vitamin D receptor binding sites in regions of the genome with genetic changes more commonly found in people of European and Asian descent. It is probable that skin lightening as we migrated out of Africa resulted from the necessity to be able to make more vitamin D and prevent rickets: vitamin D deficiency led to pelvic contraction resulting in increased risk of fatality of both mother and unborn child, effectively ending maternal lineages unable to find ways of increasing availability of the vitamin.

"Vitamin D found to influence over 200 genes, highlighting links to disease." PHYSorg.com. 23 Aug 2010.
www.physorg.com/news201791554.html

"Vitamin D status is potentially one of the most powerful selective pressures on the genome in relatively recent times," says Professor George Ebers, Action Medical Research Professor of Clinical Neurology and one of the senior authors of the paper. "Our study appears to support this interpretation and it may be we have not had enough time to make all the adaptations we have needed to cope with our northern circumstances."

More information: Ramagopalan SV, Heger A, Berlanga AJ, Maugeri NJ, Lincoln MR, Burrell A, Handunnetthi L, Handel AE, Disanto G, Orton S, Watson CT, Morahan JM, Giovannoni G, Ponting CP, Ebers GC, Knight JC. A ChIP-seq-defined genome-wide map of vitamin D receptor binding: Associations with disease and evolution. Genome Res doi:10.1101/gr.107920.110

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