The genetics of white finger disease

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Vibration-induced white finger disease (VWF) is caused by continued use of vibrating hand held machinery (high frequency vibration >50 Hz), and affects tens of thousands of people. New research published in BioMed Central's open access journal *Clinical Epigenetics* finds that people with a genetic polymorphism (A2191G) in sirtuin1 (SIRT1), a protein involved in the regulation of endothelial NOS (eNOS), are more likely to suffer from vibration-induced white finger disease.

VWF (also known as hand arm vibration syndrome (HAVS)) is a secondary form of Raynaud's disease involving the blood vessels and nerves of arms, fingers and hands. Affected fingers feel stiff and cold and loose sensation for the duration of the attack, which can be very painful. Loss of sensation can make it difficult to carry out manual activities. Initially attacks are triggered by cold temperatures but as the disease progresses attacks can occur at any time.

Little is known about what causes the restriction in blood flow, however researchers from Germany investigated the role of SIRT 1 by looking at polymorphisms (naturally occurring variations in DNA sequence) in people affected by VWF.

SIRT1 regulates activation of other genes by controlling how tightly DNA is wound in the nucleus. Tightly wound DNA cannot be 'read' and consequently cannot be used to make new protein. SIRT1 is known to regulate vasodilation by targeting eNOS, a nitric oxide synthase within the cells lining the inside of blood vessels, which regulates smooth muscle contraction, and hence the diameter of the vessel, and the amount

of blood that can flow through it.

Of 113 polymorphisms tested, in the gene coding for SIRT1, only four actually affected the protein, the rest were non-coding or false positives. Of these four, only one was different between people with VWF and unaffected controls. A single nucleotide at position 2191 can either be an A or a G. In the unaffected population 99.7% had the A, but amongst the patients with VWF, almost a third had the G.

Dr Susanne Voelter-Mahlknecht from the University of Tuebingen, who led this study, explained, "While this does not mean that only people with the G version of the gene for SIRT1 will get VWF, it can be used to identify a set of people who would be at risk of VWF if they used vibrating hand held tools. Testing for this variant before starting to work with vibrating machinery could prevent years of pain and disability."

More information: Sirtuin1 single nucleotide polymorphism (A2191G) is a diagnostic marker for vibration-induced white finger disease Susanne Voelter-Mahlknecht, Bernd Rossbach, Christina Schleithoff, Christian-Lars Dransfeld, Stephan Letzel and Ulrich Mahlknecht, *Clinical Epigenetics* (in press)

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