Healing molecule discovery could reduce limb amputations for diabetes patients

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Scientists have discovered new insights into a molecule which is part of the body's tissue repair system, in a finding which could help treat non-healing wounds and injuries, such as diabetic foot.

The number of limbs amputated because of diabetes is at an all-time high of 20 each day in England alone. Intense research around the world is being carried out to discover new treatments that could help avoid such life-changing operations and reduce medical costs for society.

A study led by the universities of Exeter and Bath, and published in the journal *Antioxidants and Redox Signalling* has made great strides in understanding how the molecule deoxyribose-1-phosphate stimulates the formation of new blood vessels.

It has long been known that the formation of new blood vessels is critical during the body's response to tissue damage. Now, thanks to this project jointly funded by Biotechnology and Biological Sciences Research Council (BBSRC) and the Medical Research Council, the understanding of how deoxyribose-1-phosphate works could open new avenues of treatment in encouraging the body to heal- a discipline known as regenerative medicine.

Dr Giordano Pula, of the University of Exeter Medical School, led the team. He said: "We're very excited to provide new insights into how this crucial molecule works to stimulate the formation of blood vessels in people. We now hope to be able to use this knowledge to trigger the

formation of new blood vessels in patients where this is required for tissue regeneration, such as diabetic foot."

This study demonstrates that deoxyribose-1-phosphate activates an enzyme called NADPH oxidase 2 (NOX2). This in turn leads to the stimulation of the transcription factor called NFkB, which is responsible for turning on genes specifically involved in the formation of new blood vessels.

Among the genes activated in the chain of events leading to blood vessel formation, the vascular endothelial growth factor receptor 2 (VEGFR2) play a central role. This is a key target in regenerative medicine, and the team hope that this discovery will provide a cost-effective treatment for manipulating blood vessel formation.

Dr Pula's team is now planning to focus their investigation on the ability of deoxyribose-1-phosphate to stimulate skin repair by increasing the vascularisation of wounds and non-healing ulcers. The team hopes this work will lead to new applications for treating conditions such as diabetic foot.

The paper, Direct activation of NADPH oxidase 2 by 2-deoxyribose-1-phosphate triggers nuclear factor kappa B-dependent angiogenesis, is now published in the journal *Antioxidants and Redox Signalling*.

More information: Dina Vara et al. Direct activation of NADPH oxidase 2 by 2-deoxyribose-1-phosphate triggers nuclear factor kappa B-dependent angiogenesis, *Antioxidants & Redox Signaling* (2017). DOI: 10.1089/ars.2016.6869