

Stroke gene discovered

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A Dutch-German medical research team led by Harald Schmidt from Maastricht University, Netherlands, and Christoph Kleinschnitz, University of Wurzburg, Germany, has discovered that an enzyme is responsible for the death of nerve cells after a stroke. The enzyme NOX4 produces hydrogen peroxide, a caustic molecule also used in bleaching agents. Inhibition of NOX4 by an experimental new drug in mice with stroke dramatically reduces brain damage and preserves brain functions, even when given hours after the stroke.

These findings will be published next week in the online, open access journal *PLoS Biology*.

Stroke researcher, Christoph Kleinschnitz, Germany's Young Scientist of the Year 2008, explains "[Ischemic stroke](#) is the second leading cause of death worldwide. Today, only one approved therapy exists. The effectiveness of this therapy is rather moderate, and, importantly, it can only be used in about 10% of patients; the other 90% are excluded due to contraindications. Thus, there is a huge medical need for better stroke therapies. One such candidate mechanism is oxidative stress. However, approaches to apply antioxidants have failed in clinical stroke trials. This study proposes an entirely new strategy by inhibiting the relevant source of [hydrogen peroxide](#) and preventing its formation."

Importantly, elimination of the NOX4 gene in mice did not result in any abnormalities and therefore no obvious side-effects are to be expected from a future NOX4 inhibitor drug. This could be demonstrated with the detailed systemic phenotyping analysis by the team of the German

Mouse Clinic at the Helmholtz Zentrum München, Germany.

The identification of NOX4 as an enzyme with a key role in killing [nerve cells](#) after a stroke in mice makes NOX4 inhibition currently the most promising new therapeutic approach in this often deadly or disabling disease in humans. Pharmacologist, Prof. Schmidt suspects that the findings "May have implications for other disease states in which hydrogen peroxide or related oxygen radicals are suspected to play a major role but where antioxidant or vitamin therapies have failed. Inhibiting now the source of hydrogen peroxide or oxygen radicals may represent the long-sought solution to treating also heart attacks, heart failure, cancer, and other forms of nerve cell degeneration such as in Parkinson's or Alzheimer's disease."

More information: Kleinschnitz C, Grund H, Wingler K, Armitage ME, Jones E, et al. (2010) Post-Stroke Inhibition of Induced NADPH Oxidase Type 4 Prevents Oxidative Stress and Neurodegeneration. PLoS Biol 8(9): e1000479. [doi:10.1371/journal.pbio.1000479](https://doi.org/10.1371/journal.pbio.1000479)

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