

Researchers found a way to treat ischemic pathologies

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A team of researchers from CIC bioGUNE, Spain, alongside a team from Paris' Cardiovascular Research Centre (INSERM U970) have developed a new area of research which looks extremely promising as regards the development of new therapeutic responses to ischemic pathologies and cardiovascular diseases in general.

The results of this research project, which was initiated in 2005 and is supported by Bizkaia:Xede and the Basque Government's Etortek programme, were published in the prestigious scientific journal *Circulation*.

By activating a protein called HIF, the strategy is to stimulate revascularisation and the repair of the damaged organ following ischemia caused by the obstruction of a blood vessel preventing normal blood flow. These obstructions occur, for example, in the event of thrombosis in a limb, myocardial infarction or a stroke. In this sense, it is important to highlight the fact that cardiovascular diseases are the principal cause of death throughout the world (in the European Union, they account for 40% of all deaths, a figure equivalent to 2 million deaths per year).

In general, cells tend to respond to the lack of oxygen caused by poor blood flow by activating HIF. However, in the case of an ischemic pathology, HIF is not sufficiently activated.

Dr Berra, <u>Cellular Biology</u> and Stem Cell Unit's leader, stated that they



decided to over-produce HIF following ischemia as an attractive therapeutic alternative. For their research purposes, they used an ischemic model provoked in a mouse leg through ligation of the femoral artery. In other words, they closed off the femoral artery and stopped the blood flow to the limb. When this happens, the leg develops necrosis and after a time, the mouse dies.

The aim was to artificially help stimulate the production of HIF after the femoral artery had been closed off. And they saw that when they did this, the mouse's leg revascularised and no longer entered into a degenerative process.

How is this high level of HIF production achieved? HIF is a protein which, when not required, degrades constitutively and this degradation is regulated by enzymes called PHDs.

These enzymes hydroxylate HIF and, as a result of this hydroxylation, the protein degrades. Therefore, when these enzymes are inhibited, HIF cannot degrade and so accumulates. To inhibit PHDs, they use siRNAs, explains Dr Berra.

Source: Elhuyar Fundazioa

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