

Fat influences decisions taken by brain cells for production and survival

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Scientists at Karolinska Institutet in Sweden have identified two molecules that play an important role in the survival and production of nerve cells in the brain, including nerve cells that produce dopamine. The discovery, which is published in the journal *Nature Chemical Biology*, may be significant in the long term for the treatment of several diseases, such as Parkinson's disease.

The same scientists have previously shown that receptors known as "liver X receptors" or LXR, are necessary for the production of different types of nerve cells, or neurons, in the developing ventral midbrain. One these types, the midbrain dopamine-producing neurons play an important role in a number of diseases, such as Parkinson's disease.

What was not known, however, was which molecules stimulate LXR in the midbrain, such that the production of new nerve cells could be initiated. The scientists have used mass spectrometry and systematic experiments on [zebrafish](#) and mice to identify two molecules that bind to LXR and activate it. These two molecules are named cholic acid and 24,25-EC, and are [bile acid](#) and a derivate of cholesterol, respectively. The first molecule, cholic acid, influences the production and survival of neurons in what is known as the "red nucleus", which is important for incoming signals from other [parts of the brain](#). The other molecule, 24,25-EC, influences the generation of new dopamine-producing [nerve cells](#), which are important in controlling movement.

One important conclusion of the study is that 24,25-EC can be used to

turn [stem cells](#) into midbrain dopamine-producing neurons, the cell type that dies in Parkinson's disease. This finding opens the possibility of using cholesterol derivatives in future [regenerative medicine](#), since new dopamine-producing cells created in the laboratory could be used for transplantation to patients with Parkinson's disease.

"We are familiar with the idea of cholesterol as a fuel for cells, and we know that it is harmful for humans to consume too much cholesterol", says Ernest Arenas, Professor of Stem Cell Neurobiology at the Department of Medical Biochemistry and Biophysics at Karolinska Institutet, who led the study. "What we have shown now is that cholesterol has several functions, and that it is involved in extremely important decisions for neurons. Derivatives of cholesterol control the production of new neurons in the developing brain. When such a decision has been taken, cholesterol aids in the construction of these new cells, and in their survival. Thus cholesterol is extremely important for the body, and in particular for the development and function of the brain."

More information: 'Brain endogenous liver X receptor ligands selectively promote midbrain neurogenesis', Spyridon Theofilopoulos, Yuqin Wang, Satish Srinivas Kitambi, Paola Sacchetti, Kyle M Sousa, Karl Bodin, Jayne Kirk, Carmen Saltó, Magnus Gustafsson, Enrique M Toledo, Kersti Karu, Jan-Åke Gustafsson, Knut R Steffensen, Patrik Ernfors, Jan Sjövall, William J Griffiths, and Ernest Arenas, *Nature Chemical Biology*, Advance Online Publication 23 December 2012, [doi: 10.1038/nchembio.1156](https://doi.org/10.1038/nchembio.1156)

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