

New steroid discovery could improve Parkinson's treatment

Scientists at Swansea University and the Karolinska Institutet in Stockholm have identified two steroid-type molecules that play an important role in the survival and production of nerve cells in the brain.

The discovery, published in the journal *Nature Chemical Biology*, could help in the development of new treatments for neurological diseases such as Parkinson's disease.

Professor William Griffiths, chair in mass spectrometry at Swansea University, is leading a BBSRC-funded project to develop an integrated platform for the quantitative and structural determination of steroid metabolites in biological systems. He said, "We believe that the identification of these

[two] molecules represents an important step toward understanding the role of lipids in brain development and toward the development of new therapies for neurological disorders such as Parkinson's disease."

Previous work from the Karolinska group showed 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 brain. One of these types, the midbrain dopamine-producing neuron, plays an important role in a number of diseases including Parkinson's disease.

However it was not known which molecules stimulate these receptors, so that the production of new neurons could be initiated.

Towards cell replacement therapy

The collaboration between the BBSRC-funded scientists in Swansea and the Karolinska group identified two steroid-type molecules that bind to and activate LXR receptors in mice and zebrafish.

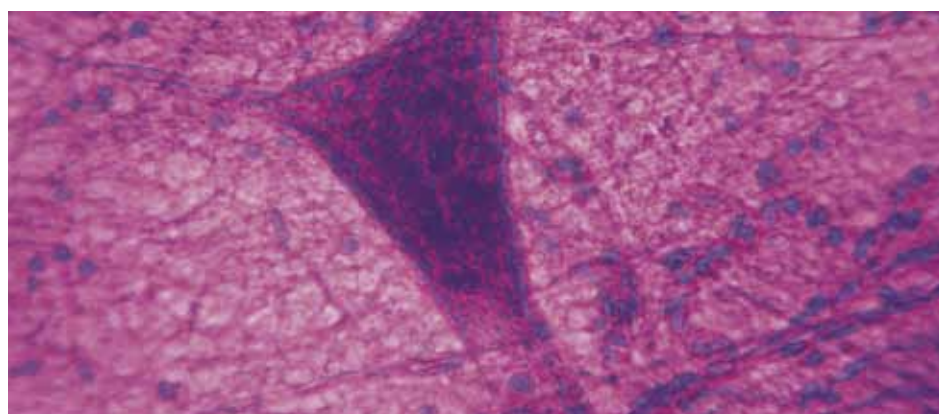
One of these molecules, 24(S),25-epoxycholesterol, can be used to turn stem cells into midbrain dopamine-producing neurons, the cell type that dies in Parkinson's disease.

The other molecule identified, 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.

Co-Investigator Dr Yuqin Wang said, "This finding opens the possibility of using steroid-type molecules in future regenerative medicine, since new dopamine-producing cells created in the laboratory could be used for transplantation to patients with Parkinson's disease. This is an exciting area for further research."

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Professor William Griffiths, Swansea University



Two steroid-like molecules influence neurons in the brain.

Further Reading

Brain endogenous liver X receptor ligands selectively promote midbrain neurogenesis. *Nature Chemical Biology* DOI:10.1038/nchembio.1156

Next steps

- Identify regulators of neurogenesis, or promoters of neuronal survival, for other cell types in the nervous system
- Develop synthetic LXR agonists with the properties of neurogenesis, or which promote survival, towards specific neuronal types
- Exploit synthetic LXR agonists in the treatment of neurological disease

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Discovery pipeline

