

MEDIA RELEASE

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The Notch effect steers stem cells into cells of the nervous system

Stem cell scientists at the University of Edinburgh have discovered that Notch, a protein first discovered more than 80 years ago in the fruit fly, directs unspecialised embryonic stem cells to become cells of the nervous system. These unexpected findings pave the way for using lab-grown cells to model disease and test the effects of new drugs, and are published online this week in the open-access journal PLoS Biology^(*).

Embryonic stem cells have the potential to make all 200 cell types in the body. The challenge is to restrain this diversity and uncover the signals that commit stem cells to a single specialised function. Sally Lowell and her colleagues have now established that Notch gives embryonic stem cells the critical push towards becoming cells of the nervous system.

The researchers show that when Notch is activated in embryonic stem cells, up to 90% of the cells in the dish become nerve cells. In any colony of embryonic stem cells, under normal conditions, many never become cells of the nervous system: they spontaneously change into other cell types or remain as embryonic stem cells.

The Notch effect can be observed in both mouse and human embryonic stem cells, and can be created without any recourse to genetic engineering - all it takes is the presence of Notch activating signals in the cells that stem cells grow on.

As individual embryonic stem cells become specialised, they communicate with those around them. Notch is a major means of communication, and has, according to Dr Lowell, "a domino effect: once it is switched on in a small group of cells, it sets off a wave of Notch activation in neighbouring cells, directing them all to become cells of the nervous system."

This research has far-reaching implications for other aspects of stem cell research. Dr Lowell adds, "We expect our findings to shed light on how to make other types of cell, such as muscle or pancreatic cells. If we can identify the processes that Notch blocks in embryonic stem cells we will have a handle on how to get them started, and so drive embryonic stem cells to become other types of cell that are more difficult to grow in the lab".

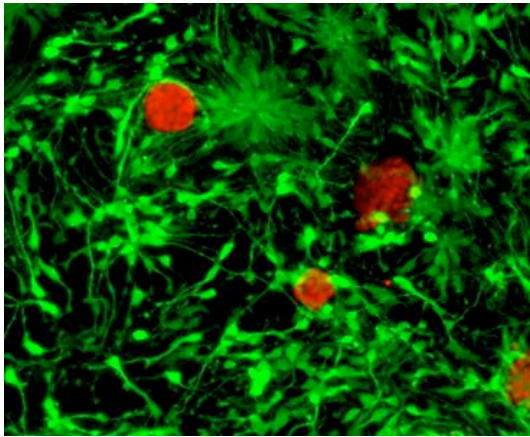
Says Professor Austin Smith, leading the Edinburgh team and coordinating the EuroStemCell consortium, "This discovery gives us another method to generate pure populations of nerve cells – so important for drug screening, disease modelling and potential cell therapies. As in stem cell colonies, communication between EuroStemCell researchers has been crucial to this discovery. Our work would not have been possible without information and materials from colleagues in Cambridge, Paris and Stockholm."

This research was supported by EuroStemCell, the BBSRC, the MRC and The Wellcome Trust.

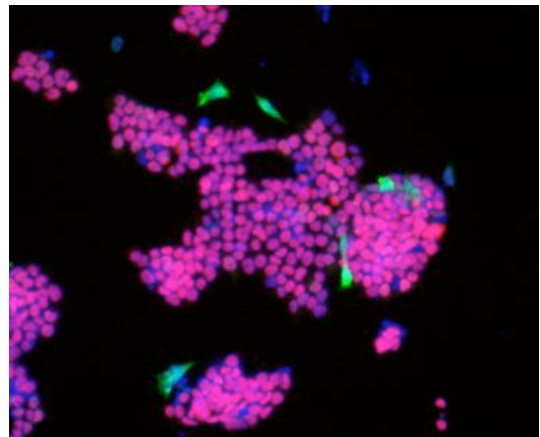
^(*)Lowell S, Benchoua A, Heavey B, Smith AG (2006) Notch promotes neural lineage entry by pluripotent embryonic stem cells. PLoS Biol4(5): e121

PRESS ONLY PREVIEW OF THE ARTICLE:
<http://www.plos.org/press/plbi-04-05-smith.pdf>

-MORE -



When Notch is activated in embryonic stem cells, most turn into nerve cells (green)



When Notch is switched off, most cells remain as embryonic stem cells (pink)

- ENDS -

Notes to Editors:

The Institute for Stem Cell Research (ISCR) is a world-leading multidisciplinary research institute focused on molecular, cellular and developmental biology of stem cells. The ISCR's mission is to acquire an understanding of the mechanisms of stem cell self-renewal and differentiation processes and to provide scientific foundations for the application of cell replacement therapies in the treatment of human disease and injury. Further information on the ISCR is available at www.iscr.ed.ac.uk.

EuroStemCell is a four-year Integrated Project of the European Union's Sixth Framework Programme, and will receive up to €11.9 million in funding from the EU. The 27 participating laboratories are from Scotland, England, Sweden, France, Denmark, Italy, Germany, and Switzerland. They comprise universities, research institutes and 3 biotechnology companies. EuroStemCell's mission is to build the scientific foundations required to take stem cell technology to the clinic. Further information on EuroStemCell is available at www.eurostemcell.org

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<http://dx.doi.org/10.1371/journal.pbio.0040121>
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Glossary

Notch – a protein that can pass a signal from a neighbouring cell and change activity of genes. Notch was first discovered in 1919, as a fruit fly mutation that caused notches in the wing. Notch mutant flies also have many more neural cells than normal flies.

Stem cell - unspecialized cell that has the ability to multiply without limit, and can also give rise to specialized cell types in the body.

Embryonic stem cell - Stem cell originating from the early embryo that has the potential to make most cell types both in the body and in the laboratory.

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