Press Release

EMBL

From fruit fly wings to heart failure. Why Not(ch)?

EMBL scientists identify key signalling pathway for heart development and healing

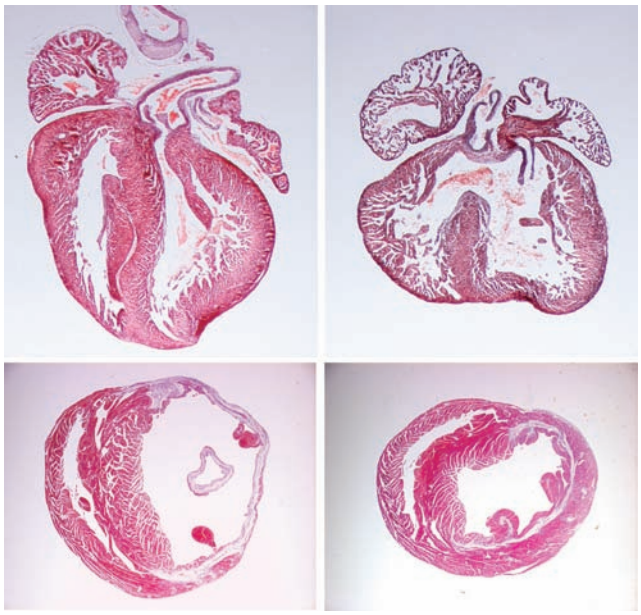
Monterotondo, 10 December 2009 - Almost a century after it was discovered in fruit flies with notches in their wings, the *Notch* signalling pathway may come to play an important role in the recovery from heart attacks. In a study published today in *Circulation Research*, scientists at the European Molecular Biology Laboratory (EMBL) in Monterotondo, Italy, are the first to prove that this signalling pathway targets heart muscle cells and thus reveal its crucial role in heart development and repair.

The *Notch* pathway is a molecular mechanism through which cells communicate with each other. Scientists in Nadia Rosenthal's group at EMBL used sophisticated genetic mouse models to uncover critical roles for this pathway in heart muscle cells. When they inactivated *Notch* specifically in the heart muscle precursor cells of early mouse embryos, the scientists discovered that the mice developed heart defects. Curiously, increasing *Notch* signalling in the heart muscle cells of older embryos had the same detrimental effect, uncovering different requirements for *Notch* as development proceeds.

"The cardiac malformations we observed are characteristic of Alagille syndrome, a human congenital disorder," said first author Paschalis Kratsios. "Therefore, our findings could help to explain the cardiac symptoms associated with Alagille syndrome and related forms of congenital heart disease."

Intriguingly, the scientists were able to improve the cardiac function and survival rate of adult mice that had suffered heart attacks by re-activating *Notch*, suggesting new therapeutic approaches to help the heart recover from damage.

"Overall, these results highlight the importance of timing and context in biological communication mechanisms" Nadia Rosenthal concludes: "Our findings also lend support to the notion that, in certain situations, redeployment of embryonic signalling pathways could prove beneficial for tissue regeneration in the adult." ●



These microscopy images demonstrate the effects of *Notch* signalling on the hearts of newborn mice (top) and of adult mice after a heart attack (bottom).
In a normal neonatal heart (top left), the two major heart chambers (ventricles) are clearly separated by tissue (septum). But when *Notch* signalling was inactivated in an embryo's heart muscle cells, the septum between the ventricles of the newborn mouse's heart was incomplete. The same defect commonly occurs in humans with congenital heart disease, often leading to circulatory distress.
In the images of adult hearts (bottom), healthy tissue is shown in red and damaged tissue in blue. Normally (bottom left), a heart attack causes extensive tissue damage to the left ventricle (right-hand cavity), but mice in which *Notch* was re-activated after the heart attack had reduced tissue damage (bottom right) and improved cardiac function.

Source Article
Kratsios, P., Catela, C., Salimova, E., Huth, M., Berno, V., Rosenthal, N., Mourkioti, F. Distinct roles for cell-autonomous *Notch* signalling in cardiomyocytes of the embryonic and adult heart. *Circulation Research*. Published online 10th December 2009.

Contact:
Sonia Furtado, EMBL Press Officer, Heidelberg, Germany, Tel.: +49 6221 387 8263, www.embl.org, sonia.furtado@embl.de

About EMBL

The European Molecular Biology Laboratory is a basic research institute funded by public research monies from 20 member states (Austria, Belgium, Croatia, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, the Netherlands, Norway, Portugal, Spain, Sweden, Switzerland and the United Kingdom) and associate member state Australia. Research at EMBL is conducted by approximately 80 independent groups covering the spectrum of molecular biology. The Laboratory has five units: the main Laboratory in Heidelberg, and Outstations in Hinxton (the European Bioinformatics Institute), Grenoble, Hamburg, and Monterotondo near Rome. The cornerstones of EMBL's mission are: to perform basic research in molecular biology; to train scientists, students and visitors at all levels; to offer vital services to scientists in the member states; to develop new instruments and methods in the life sciences and to actively engage in technology transfer activities. EMBL's International PhD Programme has a student body of about 170. The Laboratory also sponsors an active Science and Society programme. Visitors from the press and public are welcome.

About EMBL Monterotondo

The EMBL Mouse Biology Unit based in Monterotondo (Rome), is a basic research centre of excellence and innovation in mouse genetics and functional genomics, capturing new opportunities and applications of mouse genetic manipulation and becoming a hub for the international mouse research network. Alliances with other EMBL research units, neighbouring facilities in the European Mouse Mutant Archive (EMMA) and Italian national research (CNR) groups, and European academic research and clinical centres has resulted in the participation of EMBL in several EU-wide initiatives to establish an international research and knowledge database, linking information on genetics/genomics, phenotyping/physiology and biomedical features. EMBL Monterotondo currently has six research groups, with a staff of over 80 people.