Press Release

EMBL

Zeroing in on heart disease

Innovative strategy pinpoints genes underlying cardiovascular disease risk

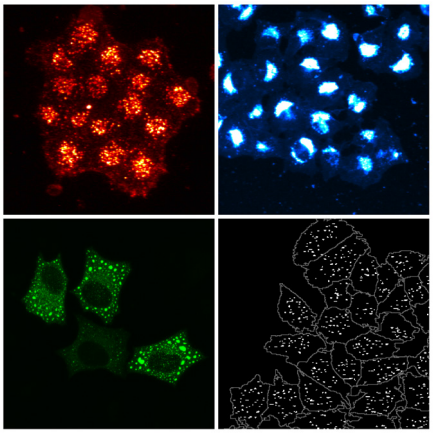
Heidelberg, 28 February 2013 – Studies screening the genome of hundreds of thousands of individuals (known as Genome-wide association studies or GWAS) have linked more than 100 regions in the genome to the risk of developing cardiovascular disease. Researchers from the European Molecular Biology Laboratory (EMBL) and the University of Heidelberg, through the joint Molecular Medicine Partnership Unit (MMPU), are taking these results one step further by pinpointing the exact genes that could have a role in the onset of the disease. Their findings are published today in the *Public Library of Science (PLoS) Genetics*.

The scientists used a technology called 'RNA interference' that can selectively decrease the level of expression of targeted genes. By observing what changes, if any, this decrease causes in cells, researchers can identify the function of the genes and, on a larger scale, objectively test the function of many genes in parallel.

Cholesterol levels in the blood are one of the main risk factors for cardiovascular disease. They are controlled by the amount of cholesterol that cells can take in - thus removing it from the blood - and metabolise. The researchers used RNA interference to test the function of each of the genes within 56 regions previously identified by GWAS as being linked with cardiovascular disease. They selectively decreased their action and measured what, if any, changes this induced in cholesterol metabolism. From this they could deduce which of the genes are most likely to be involved in the onset of the disease.

"This is the first wide–scale RNA interference study that follows up on GWAS. It has proven its potential by narrowing down a large list of candidate genes to the few with an important function that we can now focus on in future indepth studies," explains Rainer Pepperkok at EMBL, who co-led the study with Heiko Runz at the University of Heidelberg.

"In principle, our approach can be applied to any disease that has an observable effect on cells," adds Heiko Runz. "The genes identified here may further our understanding of the mechanisms leading to cardiovascular disease and allow us to improve its prediction and diagnosis." ●



Credit: Peter Blattmann/EMBL and Christian Schuberth/ University of Heidelberg

Cells stained for observation by fluorescence microscopy to discover cholesterol-regulatory genes
(top left: cholesterol (orange) uptake by cells; top right: free cholesterol (blue) in cells; bottom left: localisation of a protein (green) involved in cholesterol regulation; bottom right: automated image-analysis showing the cell outer membrane (grey) and the cholesterol (white))

Source Article
RNAi-based functional profiling of loci from blood lipid genome-wide association studies identifies genes with cholesterol-regulatory function - Peter Blattmann, Christian Schuberth, Rainer Pepperkok, and Heiko Runz – Published in *PLoS Genetics* on the 28 February, 2012 – DOI: 10.1371/journal.pgen.1003338

Contact:
Isabelle Kling, EMBL Communication Officer, Heidelberg, Germany, Tel: +49 6221 387 8355, www.embl.org, isabelle.kling@embl.de
Lena Raditsch, EMBL Head of communications, Heidelberg, Germany, Tel: +49 6221 387 8125, www.embl.org, lena.raditsch@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 85 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. Around 190 students are enrolled in EMBL's International PhD programme. Additionally, the Laboratory offers a platform for dialogue with the general public through various science communication activities such as lecture series, visitor programmes and the dissemination of scientific achievements.