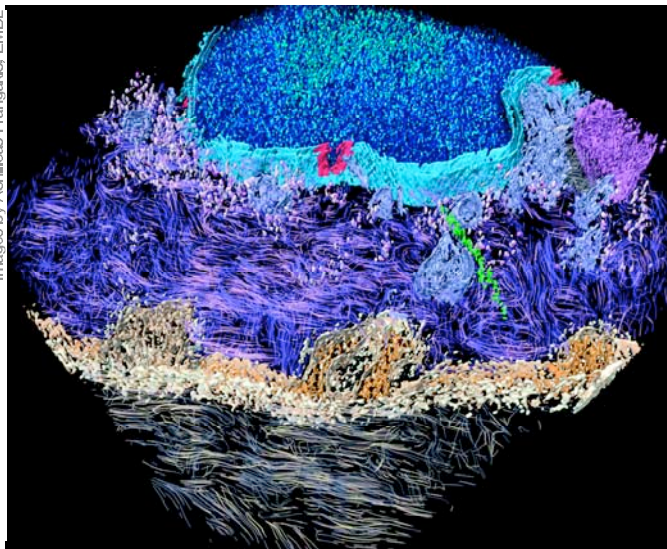


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The closest look ever at native human tissue

A powerful microscope technique reveals the molecular organisation of skin

Images by Achilleas Frangakis, EMBL



This 3D reconstruction of a human skin cell was produced by electron tomography and shows organelles in different colours: regions of cell-cell contact (sandy brown), nucleus and nuclear envelope (blue) with pores (red), microtubules (green), mitochondria (purple), endoplasmic reticulum (steel blue).

Heidelberg, 6 December 2007 - Seeing proteins in their natural environment and interactions inside cells has been a long-standing goal. Using an advanced microscopy technique called cryo-electron tomography, researchers from the European Molecular Biology Laboratory [EMBL] have visualised proteins responsible for cell-cell contacts for the first time. In this week's issue of *Nature* they publish the first 3D image of human skin at molecular resolution and reveal the molecular Velcro-like organisation that interlinks cells.

"This is a real breakthrough in two respects," says Achilleas Frangakis, group leader at EMBL. "Never before has it been possible to look in three dimensions at a tissue so close to its native state at such a high resolution. We can now see details at the scale of a few millionths of a millimetre. In this way we have gained a new view on the interactions of molecules that underlie cell adhesion in tissues – a mechanism that has been disputed over decades."

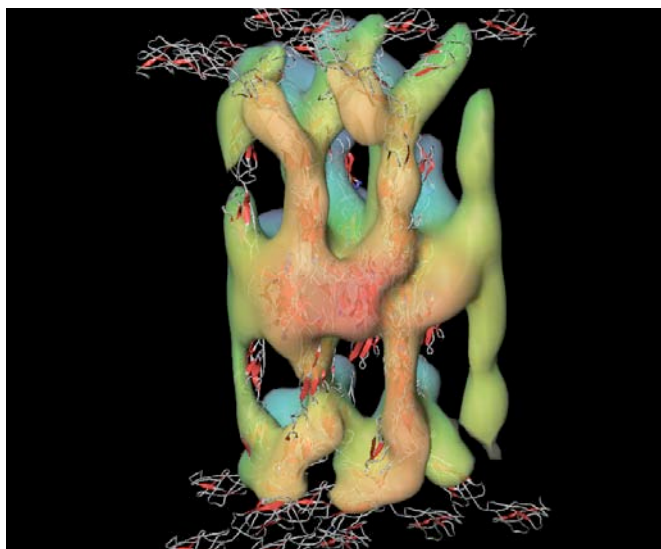
So far, the only information available about a protein's position and interactions in a cell was based on either light microscopy images at poor resolution or techniques that remove proteins from their natural context. Frangakis and his group have been developing a technique called cryo-electron tomography, with which a cell or tissue is instantly frozen in its natural state and then examined with an electron microscope. Electron microscopy normally requires tissue to be

Source Article

A. Al-Amoudi, D. Castaño Díez, M.J. Betts, A.S. Frangakis. The Molecular Architecture of Cadherins in Native Epidermal Desmosomes. *Nature*, 6 December 2007

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3D visualisation of interacting cadherin molecules in their native arrangement. Known molecular structures of cadherins (grey and red ribbons) are fit into the electron tomogram (multicolour) of the complex.

treated with chemicals or coated in metal, a procedure that disturbs the natural state of a sample. With cryo-electron tomography, images are taken of the untreated sample from different directions and assembled into an accurate 3D image by a computer.

The researchers applied this technique to observe proteins that are crucial for the integrity of tissues and organs like the skin and the heart, but also play an important role in cell proliferation. These proteins, called cadherins, are anchored in cell membranes and interact with each other to bring cells close together and interlink them tightly.

"We could see the interaction between two cadherins directly, and this revealed where the strength of human skin comes from," says Ashraf Al-Amoudi, who carried out the work in Frangakis' lab. "The trick is that each cadherin binds twice: once to a molecule from the juxtaposed cell, and once to its next-door neighbour. The system works a bit like specialised Velcro and establishes very tight contacts between cells."

The new insights into the cadherin system broadens the understanding of structural aspects of cell adhesion and shed light on other crucial processes such as cell proliferation. The technical advances achieved in cryo-electron tomography of frozen sections open up new possibilities to study more systems at native conditions with molecular resolution.

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). 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.

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