Press Release

EMBL

Embargoed until Wednesday, 30 September 2009, 18:00 BST

Putting the squeeze on sperm DNA

EMBL scientists discover a new way to read the histone code by studying streamlined sperm

Heidelberg/Grenoble, 1 October 2009 – In the quest for speed, olympic swimmers shave themselves or squeeze into high-tech super-suits. In the body, sperm are the only cells that swim and, as speed is crucial to fertility, have developed their own ways to become exceptionally streamlined. Scientists at the European Molecular Biology Laboratory (EMBL) in Heidelberg and Grenoble, the Institut de Biologie Structurale (IBS) and the Institut Albert Bonniot, both also in Grenoble, have been studying the secrets of speedy sperm. Their work, published today in *Nature*, shows how a protein only found in developing sperm cells, Brdt, directs tight re-packaging of sperm DNA.

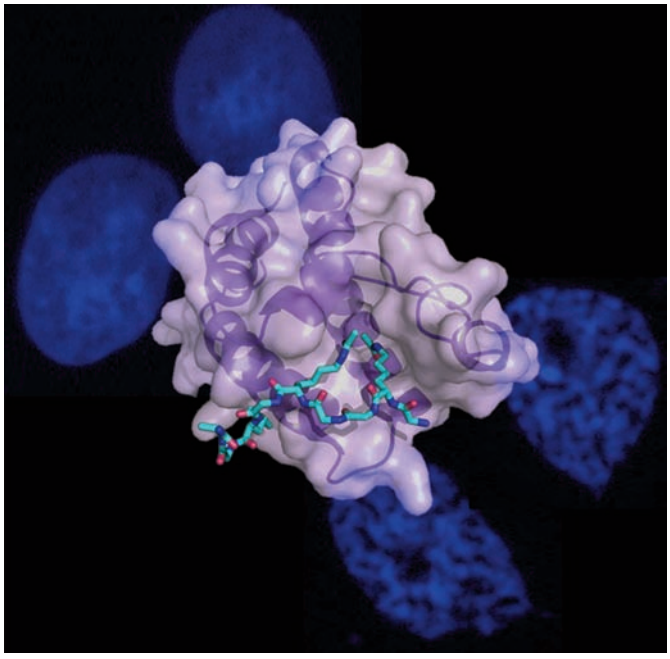
Because it is such a long and unwieldy molecule, our DNA is packaged for convenience into a complex structure called chromatin: long DNA strands are wound around proteins called histones. In sperm, however, this package has become even more compact, reducing the size of the sperm head and making it more hydrodynamic.

The nature of chromatin – how open or compact it is – is intricately regulated. Histones are marked with different chemical tags, often several per histone, that act as a code to direct changes in chromatin structure. Different proteins bind to the tags, the combination of which deciphers the code.

Until now, scientists thought that these proteins bind using one or more modular 'domains', with each domain docking to just one tag. However, this new study reports the discovery of an extra level of sophistication. The researchers studied histone binding of a protein called Brdt, finding that it binds most strongly to a histone with *two* of a particular tag (in this case, acetyl groups) – and, contrary to expectations, uses just one protein domain to do so. "We were very surprised," explains Christoph Müller of EMBL. "We looked at the structure and saw that the domain forms a pocket, binding both tags at once."

"In sperm, just before the DNA starts to hypercompact, these tags are added throughout the chromatin in a huge wave," explains Saadi Khochbin of the Institut Albert Bonniot. "If Brdt is absent, the extra compaction doesn't take place, and the sperm head would be less streamlined. Male mice lacking Brdt are infertile."

So is the special way that Brdt binds to histone tags important for its unique compacting ability? "We're not sure, but we can speculate," says Christoph Müller. "One idea is that histones acquire tags sequentially, and only compact when fully tagged. Brdt binds to the last two tags in this sequence, making Brdt-binding the very last step in the process – the final signal for hypercompaction to begin."



In the centre, a structural model determined by X-ray crystallography shows how the two tags (attached to a short section of the histone protein – all in cyan) fit neatly into the Brdt pocket (purple). In the background image, hypercompaction by Brdt causes relatively diffuse chromatin (stained blue inside the nuclei of two cells on the top left) to compact and clump together (two on the bottom right).

"We re-examined the structures of other chromatin-associate proteins and saw that this tag-binding mechanism is likely to be used by them, too, furthering our understanding of how the histone code is read," adds Carlo Petosa of the IBS.

The researchers believe their work will shed light on potential problems in sperm development and are now looking at the role this protein plays in human male infertility. ●

Source Article

Morinière, J., Rousseaux, S., Steuerwald, U., Soler-López, M., Curtet, S., Vitte, A-L., Govin, J., Gaucher, J., Sadoul, K., Hart, D.J., Krijgsveld, J., Khochbin, S., Müller, C.W. & Petosa, C. Cooperative binding of two acetylation marks on a histone tail by a single bromodomain. *Nature*, 1 October 2009

Contact:

Lena Raditsch, Head of Communications, Heidelberg, Germany, Tel: +49 6221 387 125, 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 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 the IBS

The Institut de Biologie Structurale Jean-Pierre Ebel (IBS) is a French research institute jointly operated by the Atomic Energy Commission (CEA), the National Center for Scientific Research (CNRS), and the University Joseph Fourier in Grenoble. The IBS hosts 12 independent groups (230 staff) performing interdisciplinary research at the interface of biology, physics and chemistry. In 2002 the IBS, EMBL and two other European institutes (the European Synchrotron Radiation Facility and the Institut Laue-Langevin) formed the Partnership for Structural Biology, whose primary objective is to study the structure and function of proteins and other biomolecules, particularly those involved in human disease.

About the Albert Bonniot Institute

The Albert Bonniot Institute is a research centre jointly operated by the French National Institute of Health and Medical Research (INSERM) and the University Joseph Fourier in Grenoble. The institute was created in 1999 and currently hosts 14 research teams (180 staff). Research at the institute revolves around the understanding of basic mechanisms that govern cell and tissue differentiation and their pathological malfunctioning, especially in an oncogenic setting.