PRESS RELEASE

Strangled cells condense their DNA

9 November 2015, Mainz, Germany. *Scientists at the Institute of Molecular Biology (IMB) have been able to see, for the first time, the dramatic changes that occur in the DNA of cells that are starved of oxygen and nutrients. This starved state is typical in some of today's most common diseases, particularly heart attacks, stroke and cancer. The findings provide new insight into the damage these diseases cause and may help researchers to discover new ways of treating them.*

When a person has a heart attack or stroke, the blood supply to part of their heart or brain is blocked. This deprives affected cells there of oxygen and nutrients (a condition known as ischaemia) and can cause long-term damage, meaning that the person may never fully recover. Ina Kirmes, a PhD student in the group of Dr George Reid at IMB, investigated what happens to the DNA in cells that are cut off from their oxygen and nutrient supply.

In a healthy cell, large parts of the DNA are open and accessible. This means that genes can be easily read and translated into proteins, so that the cell can function normally. However, the researchers showed that, in ischaemia, DNA changes dramatically: it compacts into tight clusters. The genes in this clumped DNA cannot be read as easily anymore by the cell, their activity is substantially reduced and the cell effectively shuts down. If cells in a person's heart stop working properly, this part of the heart stops beating, and they will have a heart attack. Similarly, when blood supply is blocked to cells in someone's brain and their cells there are starved of oxygen and nutrients, they have a stroke.

Dr Reid is excited about the implications of this finding. "When you have a stroke, when you have a heart attack, this is likely to be what's happening to your DNA", he explains. "Now we know that this is what's going on, we can start to look at ways of preventing this compaction of DNA."

The key to this discovery was a close collaboration with Aleksander Szczurek, joint first author on this publication, who is part of the group of Prof. Christoph Cremer at IMB. They developed a new method that made it possible to see DNA inside the cell at a level of detail never achieved before. Their technique is a further development of "super-resolution light microscopy", which uses blinking dyes that bind to DNA to enable the researchers to define the location of individual molecules in cells. This novel technology has been described in a separate paper, published in *Experimental Cell Research* in September.

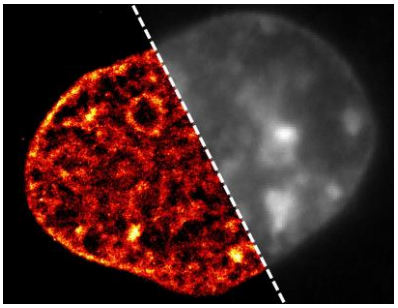
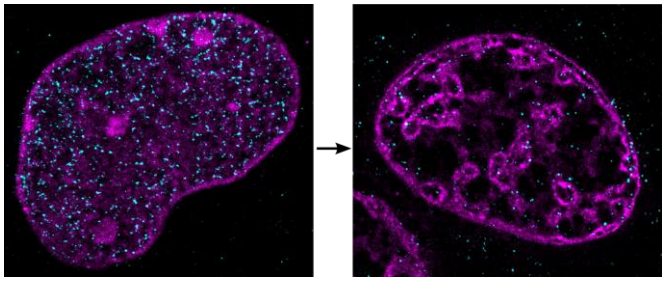


Figure 1: Novel microscopy technique reveals unprecedented detail inside cells. *Image of a cell's DNA taken with the new super-resolution microscopy technique developed at IMB shows the DNA in crisp detail (left). By contrast, a conventional microscopy image is blurry, making it impossible to see the striking changes in DNA discovered by the scientists at IMB (right). Image credit: A. Szczurek & I. Kirmes*

Figure 2: Dramatic effects of ischemia. *The new super-resolution microscopy technique developed at IMB reveals that DNA forms highly unusual, dense clusters when cells are starved of oxygen and nutrients. The images show DNA in a cell nucleus under normal (left) and ischaemic (right) conditions. Image credit: A. Szczurek & I. Kirmes*



Further details

Original references:
Kirmes I, Szczurek A, Prakash K, Charapitsa I, Heiser C, Musheev M, Schock F, Fornalczyk K, Ma D, Birk U, Christoph Cremer C, Reid G (2015). A transient ischaemic environment induces reversible compaction of chromatin. *Genome Biology*, 16, 246

Żurek-Biesiada D, Szczurek AT, Prakash K, Mohana GK, Lee HK, Roignant JY, Birk U, Dobrucki JW and Cremer C (2015). Localization microscopy of DNA *in situ* using Vybrant® DyeCycle™ Violet fluorescent probe: A new approach to study nuclear nanostructure at single molecule resolution. *Experimental Cell Research*, doi: 10.1016/j.yexcr.2015.08.020

Further information about Dr George Reid's research can be found at www.imb.de/reid.
Further information about Prof. Christoph Cremer's research can be found at www.imb.de/cremer.

About the Institute of Molecular Biology gGmbH
The Institute of Molecular Biology gGmbH (IMB) is a centre of excellence in the life sciences that was established in 2011 on the campus of Johannes Gutenberg University Mainz (JGU). Research at IMB concentrates on three cutting-edge areas: epigenetics, developmental biology, and genome stability. The institute is a prime example of a successful collaboration between public authorities and a private foundation. The Boehringer Ingelheim Foundation has dedicated EUR 100 million for a period of 10 years to cover the operating costs for research at IMB, while the state of Rhineland-Palatinate provided approximately EUR 50 million for the construction of a state-of-the-art building. For more information about IMB, please visit: www.imb.de.

About the Boehringer Ingelheim Foundation
The Boehringer Ingelheim Foundation is an independent, non-profit organization committed to the promotion of the medical, biological, chemical and pharmaceutical sciences. It was established in 1977 by Hubertus Liebrecht (1931-1991), a member of the shareholder family of the company Boehringer Ingelheim. With the PLUS 3 Perspectives Programme and the Exploration Grants, the foundation supports independent group leaders. It also endows the internationally renowned Heinrich Wieland Prize as well as awards for up-and-coming scientists. In addition, the foundation pledged to donate 100 million euros to finance the scientific running of the Institute of Molecular Biology (IMB) at Johannes Gutenberg University Mainz for ten years. In 2013, the Boehringer Ingelheim Foundation donated a further 50 million euros to Mainz University: www.boehringer-ingelheim-stiftung.de.

Press contact for further information
Dr Ralf Dahm, Director of Scientific Management
Institute of Molecular Biology gGmbH (IMB), Ackermannweg 4, 55128 Mainz, Germany
Phone: +49 (0) 6131 39 21455, Fax: +49 (0) 6131 39 21421, Email: press@imb.de