'X-shape' not true picture of chromosome structure, new imaging technique reveals

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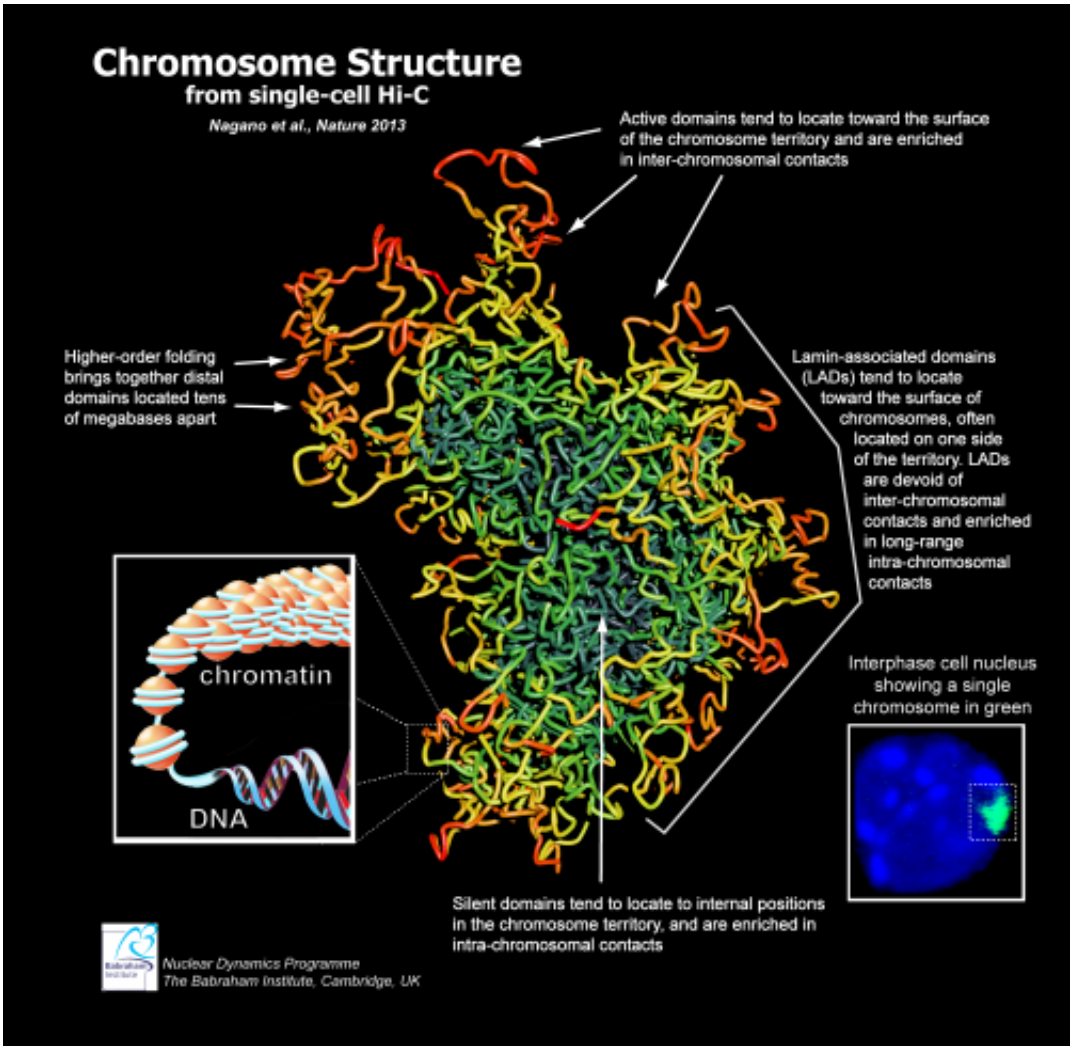

This is the chromosome structure from single-cell Hi-C. Credit: Dr. Peret Fraser, Babraham Institute

A new method for visualising chromosomes is painting a truer picture of their shape, which is rarely like the X-shaped blob of DNA most of us are familiar with.

Scientists at the BBSRC-funded Babraham Institute, working with the University of Cambridge and the Weizmann Institute, have produced beautiful 3D models that more accurately show their complex shape and the way DNA within them folds up.

The X-shape, often used to describe chromosomes, is only a snapshot of their complexity.

Dr Peter Fraser of the Babraham Institute explains: "The image of a chromosome, an X-shaped blob of DNA, is familiar to many but this microscopic portrait of a chromosome actually shows a structure that occurs only transiently in cells – at a point when they are just about to divide."

"The vast majority of cells in an organism have finished dividing and their chromosomes don't look anything like the X-shape. Chromosomes in these cells exist in a very different form and so far it has been impossible to create accurate pictures of their structure."

Peter's team has developed a new method to visualise their shape. It involves creating thousands of molecular measurements of chromosomes in single cells, using the latest DNA sequencing technology. By combining these tiny measurements, using powerful computers, they have created a three-dimensional portrait of chromosomes for the first time. This new technology has been made possible thanks to funding from the Biotechnology and Biological Sciences Research Council (BBSRC), Medical Research Council (MRC) and the Wellcome Trust.

Dr Fraser added: "These unique images not only show us the structure of

the chromosome, but also the path of the DNA in it, allowing us to map specific genes and other important features. Using these 3D models, we have begun to unravel the basic principles of chromosome structure and its role in how our genome functions."

This latest research, published in *Nature*, puts DNA into its proper context in a cell, conveying the beauty and complexity of the mammalian genome in a far more effective way than volumes of text previously have. In doing so it shows that the structure of these chromosomes, and the way the DNA within them folds up, are intimately linked to when and how much genes are expressed, which has direct consequences for health, ageing and disease.

Douglas Kell, BBSRC Chief Executive, said: "Until now, our understanding of chromosome structure has been limited to rather fuzzy pictures, alongside diagrams of the all too familiar X-shape seen before cell division. These truer pictures help us to understand more about what chromosomes look like in the majority of cells in our bodies. The intricate folds help to unravel how chromosomes interact and how genome functions are controlled."

More information: 'Single cell Hi-C reveals cell-to-cell variability in chromosome structure' DOI: 10.1038/nature12593

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