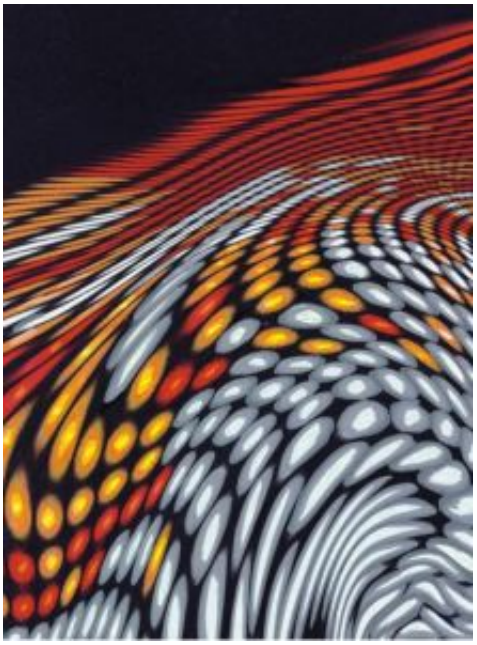
Latent memory of cells comes to life

May 17 2007



Artistic impression of nucleosomes interaction. Credit: Mette Høst, CMOL, Niels Bohr Institute, University of Copenhagen

New Danish research has examined the mechanisms behind latent cell memory, which can come to life and cause previously non-existent capacities suddenly to appear. Special yeast cells for example, can abruptly change from being of a single sex to hermaphrodite.

Researchers from the Niels Bohr Institute at the University of Copenhagen have used mathematical models and computer simulations to examine fundamental mechanisms of cell memory. The research is an

interdisciplinary cooperation between molecular biologists and physicists and has just been published in the prestigious scientific journal CELL where it is featured on the cover page (article by Dodd *et al.*, 18 May issue).

Dormant capacities

Our genetic material - DNA – is a blueprint for how we look and are. This genetic material is very stable and it is faithfully transmitted to our descendants. Once in a while though, a change occurs to the DNA, either large or small. Such changes are at the origin of the immense and varied animal and plant life on earth. Constructive changes in the DNA, that is, changes creating new functions, normally arise by a slow and gradual process that involves natural selection operating over many generations.

Sometimes however, dramatic and very sudden changes are observed in one individual in the absence of any kind of change to the DNA. This happens in fact in all of us as our body develops: cells with identical genetic information adopt very different fates, forming tissues that have apparently very little in common with each other, such as skin, brain, or bones. Mechanisms at the origin of this so-called cellular differentiation are those for which researchers at the University of Copenhagen have a possible clarification.

”The explanation for the sudden changes is that it is not the DNA itself that is altered - it is its immediate surroundings that change and thereby cause a cell to activate some of its dormant capacities” says Kim Sneppen, professor in Biophysics at the Niels Bohr Institute, University of Copenhagen.

The environment controls the DNA

The DNA coils itself around protein complexes called nucleosomes. Importantly, nucleosomes can carry various chemical modifications that either allow, or prevent, the expression of the DNA wrapped around them. Every time a cell divides into new cells, its double-stranded DNA splits into two single strands, which then each produce a new double-strand.

Nucleosomes though are not duplicated like the DNA-strands. Rather, they are distributed between the two new DNA double strands and the empty spaces are filled by new nucleosomes. Cell division is therefore an opportunity for changes in the nucleosomal composition of a specific DNA region. Changes can also happen during the lifetime of a cell due to chemical reactions allowing interconversions between the different nucleosome types. The effect of these changes can be that a latent capacity that was dormant comes to life, or, conversely, that a previously active capacity shuts down.

Same inheritance – different traits

In the practical experiment molecular biologists used a mutant of a yeast cell which was bi-stable, in that it could become either of a single sex or hermaphrodite. The experiment showed that a spontaneous change occurred in the yeast cells about every 2000 cell-generations. By building a mathematical model based on positive feedback from the microscopic state of the nucleosomes, the research group could simulate the experimental results and in this way gained insight into the mechanisms by which living cells with identical DNA can achieve extreme differentiation.

The research at the ‘Models of Life’ Basic Research Center at the Niels Bohr Institute has shown that communication between nucleosomes and positive feedback are likely to constitute fundamental memory mechanisms in individual cells. The mechanism gives both stability and

openness to new influences which the cell could need to change state. Nature has a partner which controls the cells latent memory.

Source: University of Copenhagen