Where's the Starting Point? Researchers try to unravel the mystery of DNA Replication During Cell Division

Cells divide so that an organism can grow, wounds can heal or cells with a limited lifetime, such as blood cells, can be renewed. However, before a cell starts to divide it must first replicate its entire genetic makeup (i.e., its DNA). This basic biological principle holds true for yeast, bacteria, viruses, and animals, and, thus, also for humans.

The cell must ensure that the entire genetic material – in humans three billion nucleotides – is replicated without loss, thus preventing the genome from becoming unstable and causing malformations or diseases such as cancer. But how and where does DNA replication start?

"For the last 20 years, researchers have tried to identify such starting points or origins in the DNA of mammals. But we cannot find them", says Dr. Manfred Gossen, research group leader at the Max Delbrück Center for Molecular Medicine (MDC) Berlin-Buch, Germany. Shedding light onto this "blackbox", as he says, is one of the scientists in his laboratory, Dr. Anand Ranjan (now at the National Institutes of Health, NIH the USA) who has just authored a paper in the *Proceedings of the National Ascademy of Sciences* (PNAS) (Vol.103, No. 13, pp.4864-4869, 2006).

In yeast, researchers know the origin of DNA replication. A complex made up of several proteins binds to certain regions of the DNA, depending on the presence of the molecule ATP (adenosine triphosphate), best known as nature's energy store. This DNA-binding process of the protein complex initiates DNA replication in yeast.

In humans, replication of the 46 chromosomes (which contain the complete DNA sequence) starts at thousands of different sites, which are not known in detail. What is clear is that replication must be carried out in a very precise and synchronized way to ensure the stability of the genome. ATP also plays a role in this process in humans by managing the formation of the protein complex (similar to the one in yeast) and, thereby, and ensuring its stability as shown by Drs. Ranjan and Gossen. However, unlike in yeast, in human cells, ATP acts ahead of the protein complex' s binding to the DNA origins. Moreover, in studying DNA replication in humans, researchers still do not know where within the DNA molecule replication begins. However, the new findings of Drs. Ranjan and Gossen will facilitate the analysis of those mechanisms which regulate human DNA replication.

Source: Max Delbrueck Centre for Molecular Medicine