

Study analyses how epigenetics regulate vital functions from bacteria to humans

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After the emergence of single-celled organisms some billions of years ago, nature started experimenting with how to diversify gene function without changing the sequence of the DNA, such that the blue print remains conserved, but allows gene products to have different functions. As multicellular organisms evolved, this process of maintenance and function were provided by mechanisms which are called "epigenetics". Epigenetics allow genes to function differently by adding chemical 'tags' to DNA or to proteins that surround the DNA. Recent studies suggest that in more developed eukaryotes the changes in the protein that help DNA fold regulate how much chemical 'tag' will be attached to DNA and vice versa.

A new study published by Boston University School of Medicine researchers in the journal of *Genetics and Epigenetics*, provides a comparative analysis of the evolution of epigenetic mechanisms from prokaryotes (bacteria) to simple eukaryotes (multi-cellular) to more complex eukaryotes (humans). Bacteria evolved billions of years ago, and even at that early stage, nature started the process of allowing bacterial DNA to perform different functions without changing the order by which DNA is organized. This was achieved by adding a chemical 'tag' to one of the subunits of DNA. The group of atoms that gets attached can vary based on the organism. This simple modification is important for bacterial survival, and allows bacteria to fight infections. It is striking though that the attachment site of the 'tag' shifted to a different subunit on DNA as eukaryotes developed. Viruses also learned how to use this "tagging" process to their advantage. The virus HIV,



which causes AIDs, hides from an individual's immune system by removing a particular 'tag' from the proteins that fold DNA.

According to corresponding author Sibaji Sarkar, PhD, instructor of medicine at BUSM, it is intriguing to observe how nature shifted the site of 'tag' addition from bacteria to mammals. "The addition of 'tagging' proteins that are involved in folding DNA in eukaryotes provided another dimension," he explains.

He adds, "If we closely observe the process of regeneration in some eukaryotes including zebra fish, when a portion is cut out, it is clear that the present gene pool in the DNA provides the necessary healing process to regenerate the section of the organism. We may gain tremendous knowledge to understand how stem cells can become so many types of organs by studying this process." It appears that <u>epigenetic mechanisms</u> regulate this process. The most striking event which describes this type of multifaceted formation of organs and tissues from one cell (fertilized egg) is embryogenesis.

When mammals reproduce, the DNA sequences that are inherited cannot be altered, but from the time that the sperm fertilizes the egg, every step proceeds according to a set of rules until the tissues and organs are differentiated. Different sets of genes are used for each step of development. For example, the 'tags' in the egg are erased after fertilization and then rewritten. The proteins that rewrite this process are governed by the same proteins that fold the DNA in the mother's egg. It is reasonable, therefore, to believe that the characteristics of mom's folding proteins may dictate which type of 'tag' will take place in her offspring DNA. It is known that the epigenetic alterations of 'tagging' are regulated by environmental effects. The authors suggest that environmental factors and the mother's lifestyle will thus affect 'tagging' of the offspring DNA, which will dictate how the offspring genes will be utilized. Interestingly, epigenetic changes also take place throughout life



depending on the life style of the person.

This article includes the description of altered epigenetic changes which may lead to many types of diseases including metabolic syndrome, cardiovascular disease, autoimmune diseases, neurological disorders, aging and cancer.

The authors proposed another hypothesis which could explain how <u>cancer cells</u> increase copy numbers of tumor promoting genes and decrease or delete tumor inhibiting genes. Sarkar added, "Cancer cells possibly hijack a mechanism operative in normal cells which provides way how the methyl tagged DNA will be untagged by cutting the DNA at the site of tag and repairing it. It is an interesting idea which needs to be tested."

The epigenetic process of 'tagging' that is utilized by living organisms from bacteria to humans is a gold mine for understanding the normal functions of cells and determining where, when, and how these steps deviate from normal behavior to cause disease conditions, a <u>process</u> which is still not well understood.

Provided by Boston University Medical Center

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