

CHROMATIN OUTSIDE THE CELL: THE NEW PARADIGM IN BIOLOGY

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Since the discovery of the structure of DNA by Watson and Crick in 1953, "DNA inside the nucleus" has been the dominant biological paradigm which has spawned the complex science of molecular biology and genomics. Although this reductionist approach has been a commercial success, produced an enormous quantity of information and given us intricate insights into cellular functioning, it has provided little understanding of human health and disease and to that extent has been largely unproductive. This is primarily because this DNA-centric molecular approach has entirely ignored physiology. We know now that there is a huge amount of DNA in the form of extra-cellular cell-free chromatin (cfCh) that exists in the extracellular compartment of the body, including in circulation, that is derived from the billions of cells that die in the body every day. cfCh is fragmented but has extraordinary and diverse local and systemic biological functions which places cfCh in the realm of physiology. cfCh has the ability to integrate into genomes of healthy cells to damage their DNA and trigger apoptotic and inflammatory responses. DNA damage and inflammation are integral to ageing and ageing-related disorders such as cardio-vascular diseases, diabetes, stroke and neurodegenerative disorders. Cancer is another example which may be initiated and propagated via cfCh by its ability to bring about DNA damage, genomic instability and inflammation. Our recent finding that patho-physiological effects of cfCh can be abrogated by the use of appropriate cfCh inactivating agents suggests therapeutic possibilities. The above considerations lead me to propose that "DNA (chromatin) outside the cell" should now be considered the central paradigm in biology replacing the currently accepted model in which the DNA resides inside the nucleus.

Biography

Indraneel (Neel) Mittra is with Dr. Ernest Borges Chair in Translational Research, Advanced Centre for Treatment, Research & Education in Cancer, Tata Memorial Centre, Mumbai, India. Professor Mittra obtained his medical degree from University of Delhi and is a Fellow of the Royal College of Surgeons of England and holds a PhD degree from University of London. He did his post-doctoral training with Dr Renato Dulbecco, Nobel Laureate, at the Imperial Cancer Research Laboratories in London. Professor Mittra's current research interests lie in the area of biology of extracellular nucleic acids and their role in ageing, inflammation, degenerative disorders and cancer.

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