Inna Kruman, J Neurol Neurophysiol 2012, 3:6
http://dx.doi.org/10.4172/2155-9562.S1.002

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference on
Central Nervous System - Drug Effects & Novel Drug Development

September 5-7, 2012 DoubleTree by Hilton Philadelphia Center City, USA

Cell cycle as a part of DNA damage response in postmitotic neurons

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DNA lesions interfere with transcription and replication and if not repaired produce genomic instability resulting in cell malfunction or death and contribute to different pathologies. Virtually every organism is equipped with a special defense mechanism known as the DNA damage response (DDR) whose function is to sense genome damage and activate pathways which repair DNA damage and eliminate the irreparably damaged cells. The DDR has been investigated mainly in mitotic cells, in which the cell cycle checkpoints are a major contributor to the DDR. Not much is known about the DDR in postmitotic neurons. It is known, however, that all eukaryotic DNA repair systems operating in proliferating cells also operate in neurons and that dysfunctional DDR plays an important role in neurodegeneration and is associated with syndromes (e.g. ataxia telangiectasia) characterized by neurological abnormalities. This suggests the importance of DDR for postmitotic neurons. While the cell cycle checkpoints are part of DDR involved in DNA repair, apoptotic signaling, and cell fate decisions in mitotic cells, their contribution to the DDR of postmitotic neurons remains unclear. Nonetheless, evidence accumulates that DNA damage-initiated apoptosis of postmitotic neurons is associated with cell cycle signaling. Recently, we have demonstrated that cell cycle activation is also important for DNA repair in postmitotic neurons. The involvement of the cell cycle machinery in both DNA repair and DNA damage-initiated apoptosis in neurons suggests a potential function of cell cycle checkpoints in the DDR of postmitotic cells. This presentation will focus on the DDR of postmitotic neurons.

Biography

Dr. Kruman received her PhD in Cellular Biology from Moscow State University (Russia). She is an Associate Professor in the department of Pharmacology and Neuroscience, Texas Tech University Health Sciences Center, USA. Her research interests focus on mechanisms of apoptosis and DNA damage response in neurons. She has authored over 50 scientific publications, including articles in major peer reviewed journals such as Neuron and Journal Neuroscience, book chapters and invited reviews.

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