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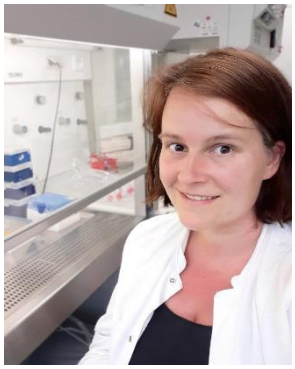
Title: DNA repair protein LEDGF necessary for proteasomal degradation of signalling molecules



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Abstract

DNA repair protein LEDGF necessary for proteasomal degradation of signalling molecules: Lens epithelium derived growth factor (LEDGF), is known to be overexpressed in different solid cancers and cancer cell lines but is also involved in acquired immunodeficiency syndrome (AIDS) and diverse inflammatory diseases. Due to its chromatin-binding ability, it acts as a transcriptional coactivator, promoting anti-apoptotic pathways leading to increased tumor aggressiveness and chemotherapy resistance. The role of LEDGF in DNA-damage repair (DDR) is still largely unknown particularly regarding the link with the ubiquitin system.

Thus, different LEDGF model cell lines were generated, a knock-out of LEDGF as well as a re-expression of LEDGF/p75 using CRISPR/Cas9 technology.

As expected, LEDGF-deficient HEp-2 cells exhibited a decreased proliferation and migration, as well as an increased sensitivity towards the topoisomerase II inhibitor etoposide. Moreover, LEDGF depleted cells showed a significant reduction in the recruitment of downstream DDR-related proteins (replication protein A subunit of 32kDa), and an increased amount of DNA fragmentation. This underpins the involvement of LEDGF in homology-directed DNA repair. For the first time, the participation of LEDGF/p75 in the ubiquitin-dependent regulation of damage response signaling molecules like γH2AX and BRCA1 was shown.

Speaker Biography:

Victoria Liedtke has completed her master in biotechnology at BTU Cottbus-Senftenberg in march 2019. Since april 2019 she is a PhD student in the research goups Molecular Diagnostics and Molecular Biology. Since January 2020 she is a scholarship holder of the Friedrich Naumann Foundation for Freedom.

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