Title: A human peptide protects against therapy-induced leukemia

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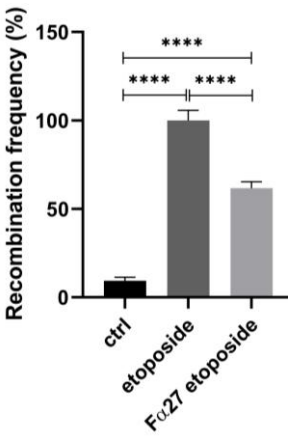
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I. Abstract

Cancer treatment with doxorubicin and etoposide increases the risk of rearrangements in the *Mixed linage leukemia or myeloid/lymphoid leukemia* (*MLL*) gene [1-3], encompassing a 7.3 kb breakpoint cluster region (*MLL*bcr) on chromosome 11 with a therapy-related 0.4 kb hotspot [2]. It was demonstrated that the mitochondrial enzyme endonuclease G (EndoG) accumulates in the nucleus after genotoxic treatment inducing replication stress where it cleaves the *MLL*bcr [4]. A GFP-based reporter plasmid mimicking *MLL*bcr rearrangements was engineered [5] and used to screen a fractionated lyophilized hemofiltrate peptide library from patients with chronic renal failure aiming at identification of a human peptide preventing *MLL*bcr rearrangements. Thus, cells were pretreated with peptides followed by etoposide or doxorubicin exposure and FACS analysis to detect GFP reconstitution. Following two rounds of chromatographic fractionation and mass spectrometric analysis, we identified a peptide that mitigates *MLL*bcr rearrangements in different cell types without affecting cell cycle or cell death (image). Immunofluorescence microscopy and chromatin immunoprecipitation revealed that the peptide inhibited nuclear EndoG accumulation and *MLL*bcr binding, whereas overall DNA damage was not influenced by the peptide. Taken together, we describe a human peptide preventing *MLL*bcr rearrangements by interfering with nuclear EndoG functions.

Image:



II. Reference:

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III. Biography:

R. Wiehe has completed her PhD 2019. She is working in the industry. L. Mattis earned a medical degree and started her career as a doctor. After his PostDoc period, B. Gole went to Slovenia to become a junior professor with his own lab.

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