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Early findings in the development of an enzymatically triggered nanoformulation

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In order to spare healthy cells and decrease adverse effects, innovative concepts of tumor targeting aim at bringing the cytotoxic payload most selectively to tumor cells is needed. One concept is to use enzymes overexpressed in the surrounding of proliferating cells, like the gelatinase matrix-metalloproteinase 9 (MMP-9), as a trigger for drug release. Our aim is to synthesize and characterize self-assembling nano-formulations consisting of an MMP9-labile peptide coupled to an anti-cancer drug. By use of bio-conjugate chemistry an amphiphilic molecule containing paclitaxel and an MMP9-labile peptide was synthesized to form nanoparticles. To identify a tumor entity as a target for our novel nano-formulation we quantified expression of MMP-9 in a commercially available tissue collection by multiplex real-time PCR. Several tumor entities showed significantly increased expression comparing normal to malignant tissue. Immunohistochemistry and database analysis suggested brain tumors, particularly glioblastoma multiforme, as a tumor entity where MMP-9 could be used to trigger drug release. Established brain cancer cell lines were characterized for MMP-9 expression and activity. LN-18 and U87-MG cells were selected for *in vitro* characterization of the synthesized nano-formulation. In preparation of *in vivo* xenograft studies LN-18 and U87-MG cells were stably transfected with mKate2 and characterized for expression. Taken together, we verified overexpression of MMP9 in glioblastoma multiforme. Commonly used brain cancer cell lines were characterized prior to *in vitro* studies on MMP9 triggered drug release, and preparations for *in vivo* xenograft studies have been finished. Further studies are needed to fully characterize the nano-formulation and understand its effects *in vivo*.

Biography

Daniel Ehrsam has done his graduation in Pharmaceutical Sciences from the University of Basel in 2014. He did his master's research work on brain ischemia pathways under supervision of Dr. Margaret Weiss at Texas Tech Health Science Center. He has worked at the Swiss Tropical and Public Health Institute on helminth drug development. In 2015, he joined the research group of professor Dr. Henriette E Meyer zu Schwabedissen for his PhD studies. His research is focused on the development of an enzyme based targeted drug delivery system.

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