**Prof. Dr. Alexandre Detappe**

**Title:** Molecular Bottlebrush Prodrugs as Next-Generation Mono and Triplex Combination Therapies for Multiple Myeloma

**Abstract:** Current anticancer agents suffer from narrow therapeutic indexes and suboptimal therapeutic combinations stemming from mixtures of drugs with dissimilar physical properties. Nanomedicine platforms for drug delivery could address these challenges but it remains unclear whether synergistic free drug ratios translate to nanocarriers and whether nanocarriers with multiple drugs outperform mixtures of single-drug nanocarriers at the same dose. Here we report a bottlebrush prodrug (BPD) platform to answer these questions in the context of multiple myeloma (MM) therapy. We show that a bortezomib-based BPD monotherapy slows tumor progression in vivo and that mixtures of bortezomib pomalidomide and dexamethasone BPDs exhibit in vitro synergistic additive or antagonistic patterns distinct from the free drug counterparts. BPDs carrying a statistical mixture of 3 drugs in a synergistic ratio outperform the free drug combination at the same ratio and a mixture of single-drug BPDs in the same ratio. Our results address unanswered questions in the field of nanomedicine offering design principles for combination nanomedicines and strategies for improving current front-line mono- and combination therapies for MM.

**Short bio:** After a PhD in nanoscience at the University of Lyon (2016) and a postdoctoral fellowship at the Dana-Farber Cancer Institute/Harvard Medical School and at the Massachusetts Institute of Technology under the supervision of Prof. Irene Ghobrial and Prof. Peter Ghoroghchian (2016-2019) where he developed a pipeline of novel nanomaterials applied to Multiple Myeloma Dr. Detappe joined the Strasbourg Cancer Institute (ICANS) in 2019 as Professor in Medicine and group leader of the Nanotranslational laboratory. He’s laboratory is currently working on the development of novel nano-immunotherapeutic approaches in Multiple Myeloma. His laboratory is currently funded by an ERC Starting Grant since 2021.

