Smart lipid nanoparticles based on molecular tweezers for synergistic cancer treatment

Prof. **Jeanne Leblond Chain**

Gene Delivery Laboratory, Faculty of Pharmacy, University of Montréal,
PO Box 6128, Downtown station Montréal, H4A 3J7, Canada

Although several products have reached the market, cancer nanotherapeutics are faced with crucial delivery issues. Nanomedicines should be stable upon fabrication and administration, especially in the blood circulation, but have to release their payload within the cancer cells. Stimulus-responsive systems, also called smart systems, exhibit such a dynamic behaviour. This was achieved by the design and synthesis of a series of switchable lipids, able to change conformation upon protonation at endosomal pH values, leading to the disruption of the lipid bilayer and thus to the fast release of the nucleic acids into the cytosol. This system has shown its ability to delivery drugs and genes *in vitro* and *in vivo*, with similar efficiency than commercial transfection agents and lower toxicity. Among other applications, cancer chemoresistance has been tackled through surviving downregulation. Indeed, oncogene surviving is upregulated in many cancers and results in apoptosis inhibition, cell mitosis stimulation and DNA reparation. Therefore, survivin silencing through small-interfering RNA (siRNA) technology has emerged as a powerful approach in cancer therapy to overcome chemoresistance. In our study, we used switchable liposomes to deliver survivin-targeted siRNA in different cancer cell lines and we further evaluated its synergistic impact with anticancer drugs on a retinoblastoma cancer model.

Biosketch. Prof. Jeanne Leblond Chain joined the Faculty of Pharmacy in 2011 and is now associate professor. Equipped with an engineer degree in organic chemistry, she got her PhD. at Faculty of Pharmacy at University Paris V in France where she developed new synthetic vectors for gene therapy. She joined Prof. Leroux's team in University of Montréal for postdoctoral studies in 2006. She is the director of the Gene Delivery Laboratory, which develops stimuli-responsive systems for intracellular delivery of genes and drugs. Her multidisciplinary background enables her to conduct research from the chemical design until the *in vivo* proof-of-concept. In addition, she is the director of the research axis *"Drug Formulation and Analysis"* and has co-directed the platform of biopharmacy for 5 years.