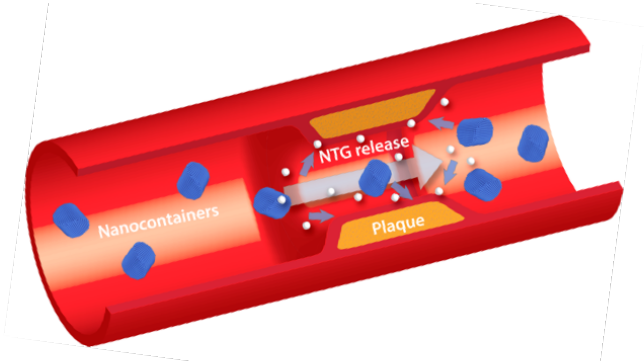
University of Basel

Department of Biomedical Engineering

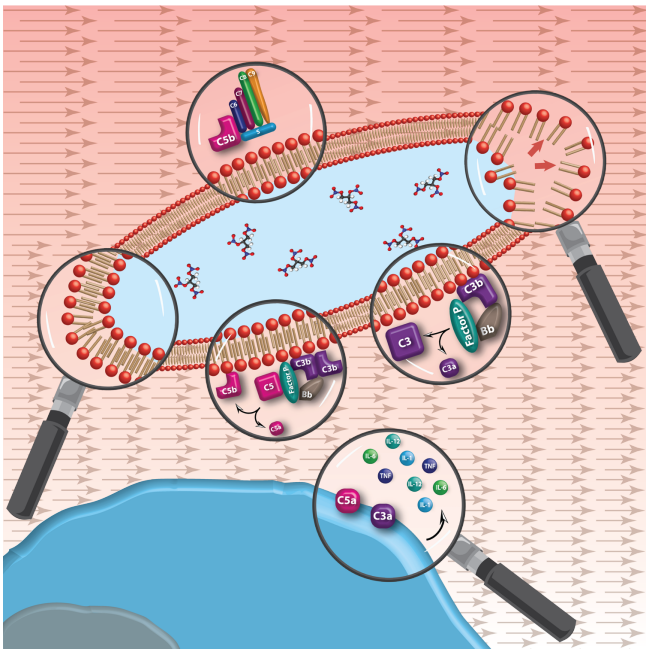
Mechano-responsive nanometre-size liposomes



Schematic representation of nitroglycerin (NTG) release from mechano-responsive liposomes about 100 nm in diameter owing to the forces in blood flow at constriction.

PhD-Thesis by Sofiya Matviykiv at BMC.

Currently, the emergency treatment of atherosclerotic cardiovascular diseases involves the systemic administration of vasodilator drugs. This results in a widening of the entire blood vessel system that is associated with a serious drop in blood pressure. We have proposed a nanometre-size drug delivery system built out of artificial phospholipids, a.k.a. liposomes, encapsulating an established vasodilator drug for the emergency treatment of myocardial infarction (1). These nanocontainers are responsive to the forces at vessel constrictions.



Schematic representation of nitroglycerin-loaded Rad-PC-Rad liposome that circulates in the vascular system. At atherosclerotic constrictions, the significantly increased wall-shear stress permits the cargo release. These liposomes barely demonstrate immune reactions *in vitro* in terms of complement system activation and cytokines production.

Physicochemical characterization of a series of mechano-responsive liposomes including size, shape and thermal stability within the clinically relevant temperature range was performed by means of dynamic light scattering, transmission electron microscopy and small-angle neutron scattering. The study has shown that the originally proposed Pad-PC-Pad liposomes become unstable above 37 °C, whereas Rad-PC-Rad are an appropriate alternative even for elevated body temperatures (2). To improve the clinical translation of this drug delivery platform, we have investigated *in vitro* immunocompatibility of liposomes (3). To evaluate the risk of hypersensitivity reaction, we detected the concentrations of activated complement proteins and cytokines using enzyme linked immunosorbent assay and flow cytometry. Within the restricted number of individuals both the Pad-PC-Pad and Rad-PC-Rad liposomal formulations exhibited low-to-moderate levels of complement proteins compared to the FDA-approved liposomal drugs. Overall, results indicate that Rad-PC-Rad liposomes are promising mechano-responsive nanocontainers suggesting them for future *in vivo* experiments. A related start-up company, Acthera Therapeutics AG, has been founded in September 2019.

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Funding:

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

BMC Biomaterials Science Center

University of Basel

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References:

(1) T. Saxer, A. Zumbuehl, B. Müller: *The use of shear stress for targeted drug delivery*, Cardiovascular Research **99** (2013) 328-333.

(2) S. Matviykiv, et al.: *Small-angle neutron scattering study of temperature-induced structural changes in liposomes*, Langmuir **35** (2019) 11210-11216.

(3) S. Matviykiv, et al.: *Immunocompatibility of Rad-PC-Rad liposomes in vitro, based on human complement activation and cytokine release*, Precision Nanomedicine **1** (2018) 45-67.