CRC 1449
Dynamic Hydrogels at Biointerfaces

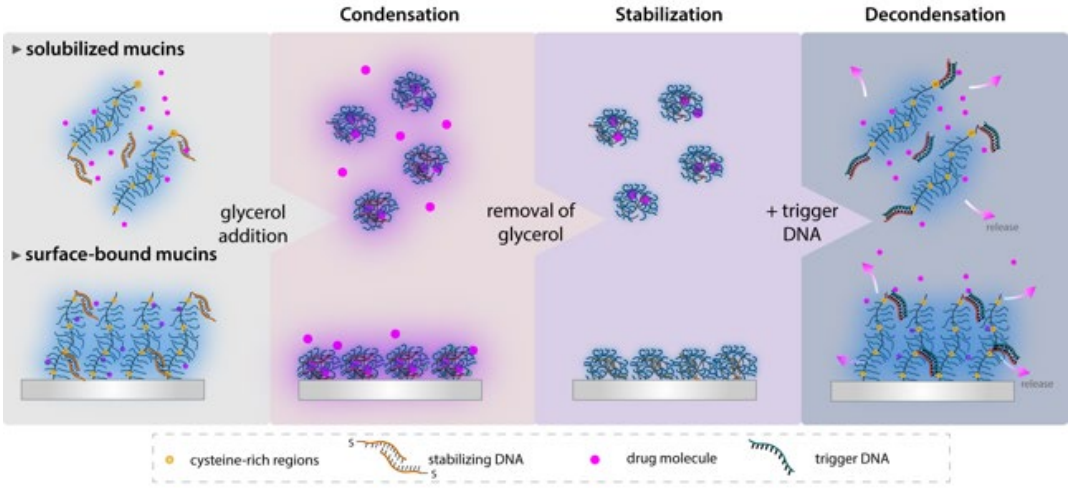
Freie Universität Berlin

CRC Colloquium: Thursday, June 24

DNA meets mucin: Alterations in mucin configuration and their applications in drug delivery

Prof. Dr. Oliver Lieleg, Department of Mechanical Engineering,
Technische Universität München

One hallmark of mucins is their ability to bind a broad range of other objects by engaging in a combination of electrostatic and hydrophobic interactions. Indeed, when we purify mucins from the porcine gastric mucosa, we typically find many molecular contaminations including mucin-associated DNA molecules [1]. Whereas the role of mucin-associated DNA remains unclear, I will discuss here how the conjugation of synthetic DNA strands to mucin glycoproteins enables control over the mucin configuration: we can generate condensed, mucin-based nanoparticles and surface coatings, into which drug molecules can be stably loaded. Stabilization of those drug reservoirs is achieved by intramolecular cross-links established by self-complementary DNA sequences that are conjugated to the mucin glycoproteins [2,3]. When exposed to suitable trigger DNA strands with higher binding affinities, strand displacement occurs; as a consequence, the condensed configuration of the mucin-based drug carriers is reverted and their payload is released. By designing the stabilizing DNA sequences such that cellular miRNA strands can act as trigger molecules inducing mucin de-condensation, we achieve cell-specific release of drugs from mucin nanoparticles in selected cancer cells.



[1] M. Marczynski, K. Jiang, M. Blakeley, V. Srivastava, F. Vilaplana, T. Crouzier, and O. Lieleg, *Structural alterations of mucins are associated with losses in functionality,* Biomacromolecules, 22 (4), 1600-1613 (2021)

[2] C. Kimna, B. Winkeljann, J. Song, and O. Lieleg, *Smart biopolymer-based multi-layers enable consecutive drug release events on demand*, Advanced Materials Interfaces. 7 (19) 2000735 (2020)

[3] C. Kimna, T.M. Lutz, H. Yan, J. Song, T. Crouzier, and O. Lieleg, *DNA Strands Trigger the Intracellular Release of Drugs from Mucin-Based Nanocarriers*, ACS Nano, 15(2), 2350-2362 (2020)