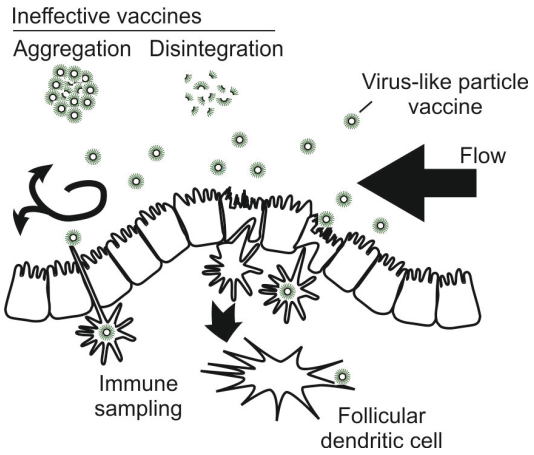
What we learnt from PEGylation of virus-like particles for vaccination

M. Radiom[1], S. Ganguillet[1], Y. Turgay[1], V. Lentsch[1], T. Keys[1], E. Causa[2], J. Kotar[2], P. Cicuta[2], R. Mezzenga[1]*, E. Slack[1]*

[1]Institute of Food, Nutrition and Health, ETH Zürich, Zürich, Switzerland, [2]Biological and Soft Systems, Cavendish Laboratory, University of Cambridge, Cambridge CB3 0HE, U.K

Virus-like particles (VLPs) have shown great potential in vaccination and drug delivery as nanocarriers of antigenic and therapeutic molecules [1]. VLPs are soft (~ 100 pN/nm) and proteinaceous colloidal particles (20–200 nm) that are susceptible to bio-mechanical and chemical stress leading to aggregation and disintegration, c.f. figure below for an example of VLP vaccines and Ref. [2]. These susceptibilities are expected to limit their application in various indications. We have very recently shown that polyethylene glycol (PEG) crosslinking of surface amine groups of a VLP assembled from *Acinetobacter* phage coat protein AP205, namely AP205 VLP, modulated the VLP's resistance to mechanical stress [3]. Building on this observation, here we present that the other stability profiles of AP205 VLP, including resistance to enzymatic degradation and pH-induced aggregation, are also modulated after PEG-crosslinking. In an *in vitro* model of human nasal tissue with motile cilia (representing mucosal administration), PEG-crosslinked as well as native AP205 VLPs were cleared via mucociliary clearance, thereby PEG-crosslinking did not make a noticeable difference. In *in vivo* mouse vaccinations, interestingly, PEG-crosslinking increased immune activation against the coat protein in addition to producing anti-PEG serum IgG. It is expected that by understanding the biophysical and immunological limits of VLPs, the VLP-based vaccine and drug delivery technology will present highly effective nanocarriers leading to reduced administration dosage and/or number of schedules.



[1] Martin Bachmann, Gary Jennings, *Nature Reviews Immunology*, **2010**, 10, 787-796.
[2] Antonius Armanious, Milad Radiom, Raffaele Mezzenga, *Current Opinion in Colloid & Interface Science*, **2023**, 66, 101703.
[3] Milad Radiom, Tim Keys, Yagmur Turgay, Ahmed Ali, Swapan Preet, Serge Chesnov, Viviane Lutz-Bueno, Emma Slack, Raffaele Mezzenga, *Journal of Colloids and Interface Science*, **2023**, 634, 963-971.