[MS5-P26] Supercharged ferritin as a cell delivery platform. Tobias Beck,[a] Matthias Kuenzle,[a] Donald Hilvert,[a]

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The delivery of proteins into cells is a challenging task and hampers the application of these biological macromolecules as therapeutic agents. However, positively supercharged proteins and nanoparticles with a positively charged surface have been reported to be taken up into living cells.[1,2] Based on these findings, we envisioned that a nanocage with a positively charged surface could be employed as a transporter to deliver cargo into cells. We used the ferritin nanocage as a scaffold since the protein is known to have high plasticity towards mutation. The Rosetta software suite [3] was employed to design several variants with an increasing number of positively charged residues on the surface (Arg, Lys). Selected mutants were produced and purified. We have shown that the variants form capsids similar in size to the wild type protein and retain the wild-type ability to load iron particles in the lumen. We are currently working on the encapsulation of protein cargo: the lumen of ferritin is decorated with negatively charged residues, thus any positively charged molecule can be packaged inside, at least in principle. Preliminary results indicate that we are able to load the supercharged ferritin capsid into a larger capsid, AaLS-13, which has a negatively charged inner surface. These capsid- inside-capsid structures represent a first step towards the design of artificial microcompartments.

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