Encapsulin Protein Nanocages for Targeted Drug Delivery

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Usually, drugs are distributed through the whole body and can cause side effects. Therefore, the drug efficiency is reduced at the site of interest. Targeting drugs to the pathologic site is then crucial and it requires a specific carrier, such as nanoparticles. Among the variety of nanoparticles developed for drug delivery, protein cages are good candidates due to their well-defined monodisperse shape, hollow structure and their biocompatibility.[1,2]

In our group we are working with homo-multimeric protein nanocages called encapsulin and that evolved in some bacteria and archaea by providing advantageous compartmentalization of certain processes. Currently, they are being studied for applications as drug delivery platform, nanoreactor and imaging agent for their convenient modification and production. We specifically study the encapsulin found in the bacteria *Thermotoga maritima* (Tm) and aims to modify it for targeted drug delivery. Tm encapsulin is composed of 60 monomers that self-assemble into a 24 nm particle according to the icosahedral T=1 symmetry (Figure 1). [3]

This encapsulin has the advantages to be easily engineered, easy to produce and it is not taken up un-specifically by cells. The surface has been successfully engineered genetically to insert at different positions, specific targeting peptides for key pathogenic cell types in liver diseases i.e. macrophages and hepatic stellate cells[4] or brain endothelial cells. [5,7] With the intention to deliver drugs to or across these cells, we are now working on actively openable nanocages by inserting light sensitive amino acids or cleavable peptide sequence in the encapsulin protein sequence to disrupt the cages in response to irradiation or specific enzymes respectively (Figure 2).

I will also present the progress on targeting a cytokine with anti-fibrotic effect to LX2 liver cells, the optimization for using the nanocages as transporter to cross the blood brain barrier and the investigation of the immunogenicity of the different cage variants.

References

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Figures

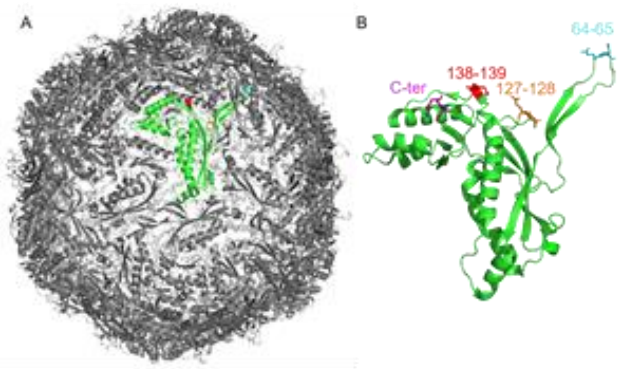

Figure 1. Model of Tm encapsulin with outside loops of interest highlighted. A is the cage with a single monomer in green. B is a monomer with the engineerable position in different colors.

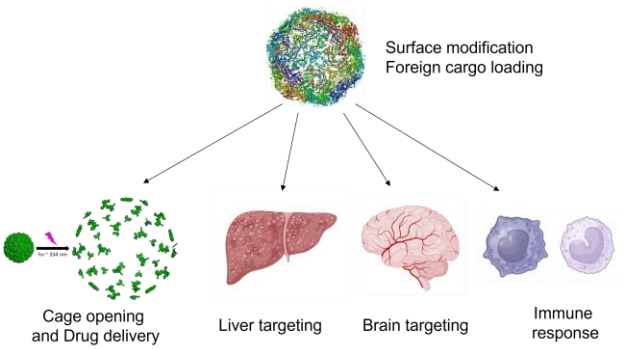

Figure 2. Different targeting drug delivery project using encapsulin nanocages.