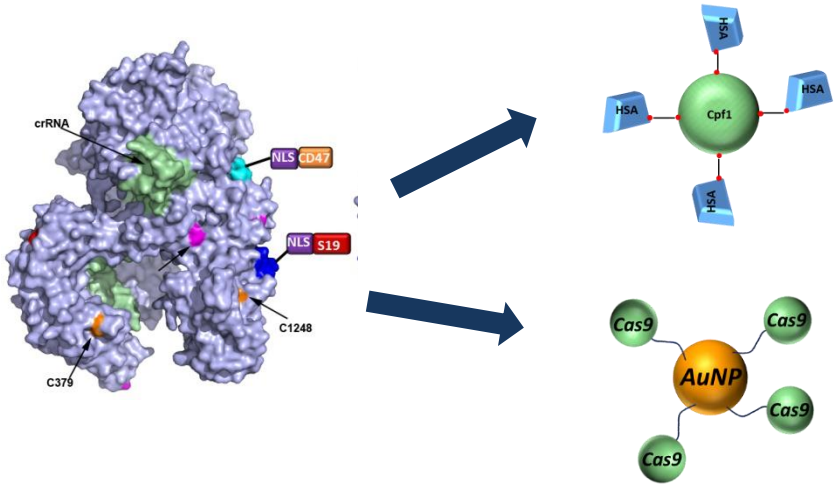
**Protein engineering of cas9 to improve its delivery in gene editing therapies**

There are high hopes in CRISPR/Cas9 as gene editing tool for the treatment of multiple genetic diseases. However, despite the significant advances, and the impressive progress made in the last years, much work needs to be done to obtain a safe therapeutic system based on CRISPR/Cas9. A key limitation of CRISPR/Cas system is the difficulty of a systemic delivery, and the risk associated with off-target effects due to non-specific binding to non-target DNAs. Due to all these limitations, the use of CRISPR/Cas9 for the treatment of diseases is reduced, and the only clinical trial using CRISPR is based on the ex-vivo modification of T-cells for immune cell therapy. Therefore, studies aiming to overcome these limitations are vital to increase the possibilities of using CRISPR-based technologies in vivo. In this sense, our aim is to prepare new CRISPR/Cas-based gene editing strategies with improved delivery and HDR efficiency. Specifically, we plan to use protein engineering strategies to modify Cas9 with small peptides able to improve its delivery. Furthermore, new Cys residues will be included at Cas external surface, which will permit its subsequent conjugation to Gold Nanoparticles (AuNPs) or Albumin Based Nanostructures (ABN).

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