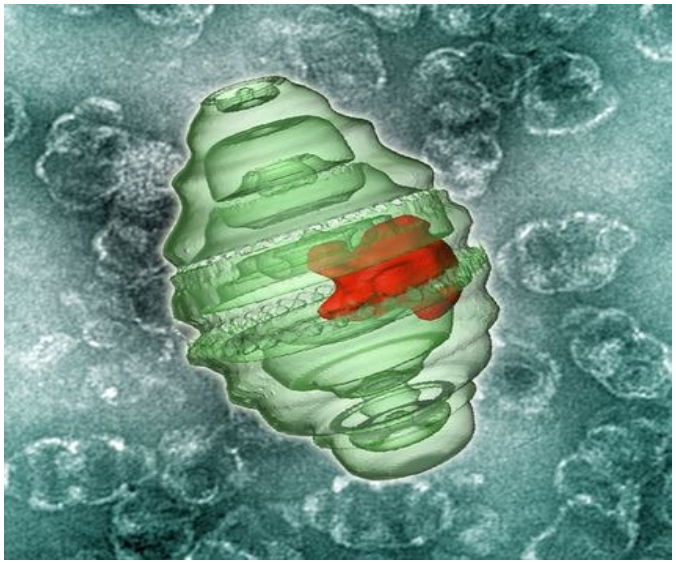
TFM offers 2026-2027

Project title: Production of Vaults: a virus-like-particle with a lock-open mechanism allowing the cargo of therapeutical as a novel drug delivery system.

Precision personalized medicine seek for next-generation biomaterials to serve as drug delivery systems with “smart” functional properties, including accurate recognition, self-organization and adaptability. Several strategies are currently inspired by the prospect of controlling the precise protein architectures as an alternative to the classic delivery systems. Among them, a particular virus like particles (VLP) named vaults represent a particularly attractive case, being about 40 nm -width-, 70 nm -length in size. Their natural function is not yet completely elucidated, although several functions related to nuclear transport, immune response, and drug multiresistance in cancer cells have been hypothesized. These nanocapsules are composed of different protein constituents and they can be produced in large quantities by expression of recombinant versions of the “major vault protein” (MVP) alone. Importantly, the vault particle represents an assembly of half-vaults. Under acidic conditions, the vaults can be reversibly opened and loaded with small molecules or biopharmaceuticals.



Microscopy image of isolated Vaults, and vault 3D reconstruction

The project consists in engineering HEK293 (human cell line) to produce engineered vaults with improved functionalities for cell tracking, quantification and specific purification. Initially, heterologous expression of MVP protein will be performed in HEK293 cells, and then purified by SEC and characterized by means of cytometry, western blot, NTA (nano-tracking analysis) and cryo-TEM. Once purified, vaults will be loaded with a small reporter molecule to assess functionality and loading capacity. Then, vaults uptake by recipient wild-type HEK293 cells will allow the assessment of vaults functionality and the potential of vaults to be used as delivery systems. Once purified, Vaults can be loaded with drugs/mRNA, by taking advantage of the dynamics of the nanoparticle (can be opened by lowering the pH).

The second part of the project consists in modifying MVP protein expression by fusing eGFP to N terminus of MVP to provide a fluorescent labelling to vaults, and StrepTag to the C-terminus (located outside the cupula structure), what will ease vaults purification, tracking and quantification. Also targeting peptides will be fused to MVP to provide specific cell targeting to direct the drug delivery to specific recipient cells.

This piece of work will be conducted in collaboration with a PhD student and Dr Ana Belén Cuenca, head of Pharmaceutical Chemistry Department, whose team will further chemically modify the produced vaults to provide with improved features.

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