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CLEM, 1 + 1 =3

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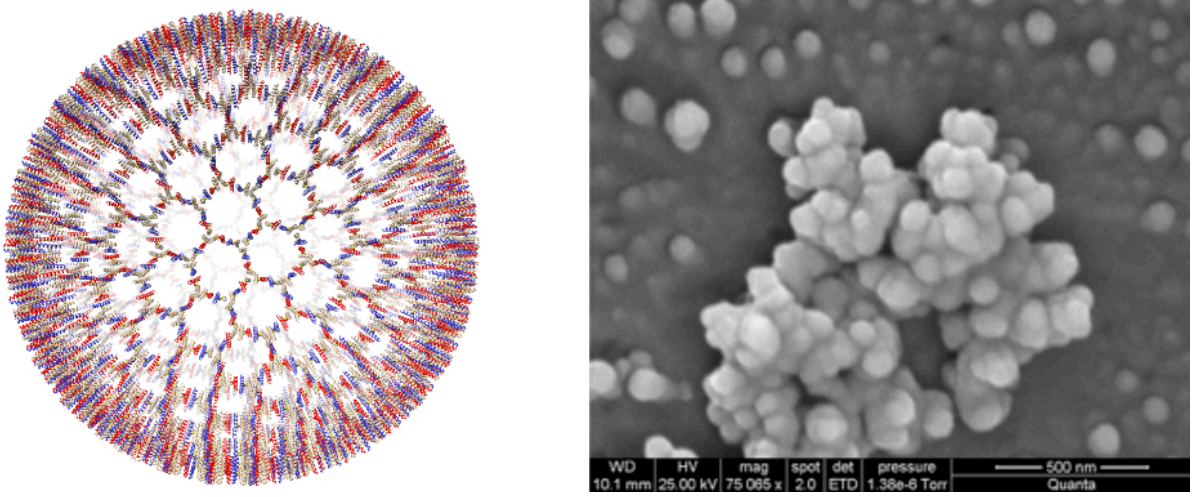
A wide variety of microscopy techniques are underpinning key discoveries in biomedical research. For instance, live-cell light microscopy can show us the dynamics of a given system. On the other hand electron microscopy (EM) gives us better resolution combined with a structural reference space. Correlative Light Electron Microscopy (CLEM) combines the strengths of both light and electron microscopy in one experiment and the sum of such an experiment should provide more data / insight than each technique alone (hence 1 + 1 = 3). There are many ways to perform a CLEM experiment and a variety of microscopy modalities can be combined [1,2]. The choice of these instruments and the experimental approach should primarily depend on the scientific question to be answered.

Any CLEM experiment can usually be divided in 3 parts; probes, processing, and analysis. I will discuss different processing techniques based on light microscopy in conjunction with Transmission Electron Microscopy (TEM), each with its own specific application and advantages and challenges.

The application of CLEM technology is not limited to pure cellular based systems. One of the aims of Synthetic Biology is to mimic and improve existing biological systems for example, in the delivery of drugs. This can be achieved by vesicles that are formed of lipids but in our case we have been using Self-Assembling peptide caGEs (SAGEs, [3], see Figure). In order to analyse how such synthetic systems are taken up, trafficked and processed in cells we can employ a large number of the techniques we use for “standard” cell biological research. Sometimes a fairly simple approach suffices to answer the question. In other cases however it requires the development of new tools and instruments to adequately do so. In this platform presentation I will highlight this approach through a number of examples.



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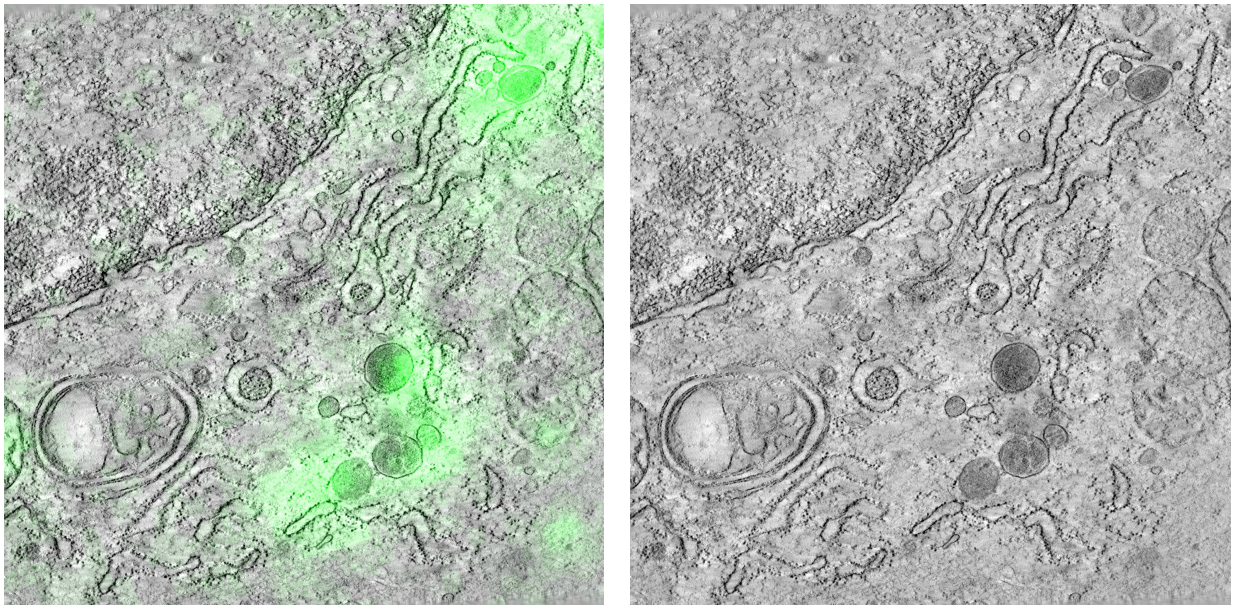

C D

Figure: SAGEs and uptake into cells.
Model of a SAGE particle (A) that can be visualised by SEM (B) as around 100nm spheres. Fluorescently tagged SAGEs are taken up into cells, where their location inside the cell can be determined using CLEM (C), as a reference only the underlying ultrastructure is shown in (D).

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