TWIN2PIPSA
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On-site visit
Ciências/ULisboa
30 Apr 2024

Sophie Jackson, PhD

University of Cambridge, UK

Venue: Auditorium FCiências.ID – C1 Building

11:00 ***Self-assembly of Therapeutic Peptides***

Many therapeutic peptides self-assemble into amyloid fibrils or, in a few cases, microcrystalline states. In the case of amyloid fibrils, this is viewed as an undesirable process that can lead to the peptide having reduced efficacy, decreased shelf-life and increased issues with immunogenicity. Recent work in the Jackson's Lab on amyloid fibril formation by the therapeutic peptide GLP-1 (glucagon-like peptide 1) will be discussed. This will include the effect of net charge and pH; the presence, role and characterisation of off-pathway oligomers on aggregation propensity; and the effect of C-terminal amidation and lipidation. In addition, results from computational energy landscape approaches to gain structural information on the monomeric peptide will be reviewed. The other case study is Teverelix, which is a synthetic decapeptide comprising of L- and D-amino acids and unnatural amino acid side chains. It is used in the treatment of prostate cancer and remarkably its TFA salt (but not its acetate salt) forms a microcrystalline suspension at high concentrations which can be given directly to patients. At lower peptide concentrations it forms amyloid fibrils. Recent biophysical studies on its self-assembly pathway will also be discussed.

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