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Designer Peptides at the Oil/Water Interface

Two surface-active designer peptides DAMP4 and AM1 have been combined to form a new class of tailorable nano-emulsions (TNE) for delivery of protein antigens to dendritic cells in vivo [1, 2]. DAMP4 is a designed 4-helix bundle, MW 11.1 kDa, consisting of 4 repeat units of PSMKQLADS-LHQLARQ-VSRLEHAD, AM1 corresponds to one of the repeat alpha-helices. The new approach utilizes the surface-active peptide AM1 to stabilize oil-in-water nanoscale emulsions, followed by the spontaneous integration of the larger peptide DAMP4 which unfolds onto the emulsion surface. The small size of AM1 enables it to rapidly populate the interface providing initial stabilisation of the emulsion, allowing the larger DAMP4 time to diffuse to the interface. Because DAMP4 can be conveniently linked to functional elements such as antibodies and poly-ethylene glycol (PEG), it offers a simple way to tailor nano-emulsions with controllable surface chemistry and thus functionality. Indeed, evaluation of biological function has demonstrated that the functionalised nano-emulsion can target a specific set of cells in a receptor-specific fashion [1]. This sophisticated emulsion system is inherently complicated, comprising a minimum of three components (AM1, DAMP4 and at least one functional element, e.g., antibody or PEG), it is technically challenging to determine interfacial protein/peptide structure at an oil-water interface hindering the rational design of functional nanoemulsions. This fundamental knowledge regarding interfacial molecular conformation and arrangement is crucial to design functional nano-emulsions for advanced application such as targeted drug delivery [3].

We have been addressing this knowledge gap via Neutron and X-ray scattering experiments from planar interfaces. The interfacial properties of DAMP4 and PEGylated DAMP4 was determined by X-ray reflectivity (XRR), and other techniques at the air/water interface [4]. Neutron reflectometry has taken advantage of deuteration strategies to study interfacial structure at model oil/water interfaces [5, 6] while synchrotron XRR has been applied to study the molecular arrangement at the bulk oil/water interface and the interfacial concentration of associated metal ions under conditions that are relevant to the emulsion formation and storage. This is an important first step in developing fundamental structural knowledge of this interfacial problem.

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