Non-spherical polymersomes and the (new) RNA world

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What do nanomedicine, the recent RNA revolution and the origin of life have to do with each other? Quite a lot! The origin of life remains as one of the biggest, if not the biggest unsolved challenges in Science. In pre-biotic chemistry, significant emphasis has been of late on synthetic cells or "protocells", where the aim is to de novo design of a system that displays all the hallmarks of life: metabolism, reproduction, and compartmentalisation.[1] Compartmentalisation is the separation of a (proto)cell or organelle from its outer environment, which typically is thought of as happening via a lipid bilayer membrane. We entered this field focusing on using polymersomes, as they are more chemically and kinetically inert than liposomes. Importantly, polymersomes are also very useful in drug delivery giving us a two-fold motivation for exploring innovative ideas in generating functional polymersomes through the combination of supramolecular and bioconjugation chemistry strategies.

Using this approach we have to date developed polymersomes mimicking key functions of biology ranging from asymmetry in shape (non-spherical polymersomes),[2-3] incorporation of biological components and generating / compartmentalising chemical energy.[4] We have also demonstrated that these polymersomes are an excellent platform for drug delivery in nanomedicine, as exemplified in our work on peptide-functionalized polymersomes targeting medullablastoma as an illustrate example.[8-9]

More recently we moved from looking at polymersomes as organelle mimicks to studying RNA-peptide aggregates as mimicks of biologically occurring RNA-protein based membraneless organelles – often referred also to as condensates or liquid-liquid phase separated droplets (Figure 1).[10] This takes us also back to the pre-biotic question of the RNA world and how RNA and peptides may have co-evolved into the ribosomes. And as in our earlier work, this does is also highly relevant to delivery challenges, in this case with regards to RNA therapeutics, where despite the success of lipid nanoparticles in the current mRNA vaccines, much remains to be done to improve RNA delivery system. To tackle that and other important challenges in RNA science, technology and therapeutics, we at UNSW have to come together to establish the UNSW RNA Institute which I will also briefly introduce here as well.

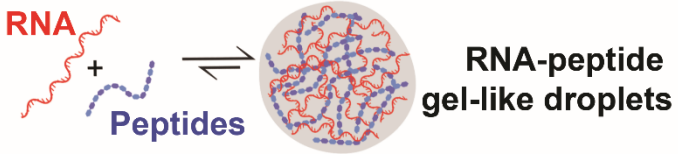

Figure 1: RNA-peptide liquid-liquid phase separated droplets.

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