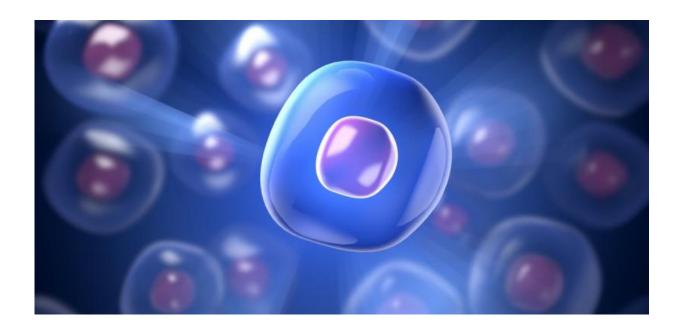


Ending a century of intrigue around 'membraneless' cell compartments

June 13 2016, by Stuart Gillespie, Oxford Science Blog



Credit: Oxford Science Blog

We've been able to see them for over a hundred years, but only now are scientists beginning to get to the bottom of what's happening inside membraneless organelles – compartments within cells that really do have no boundaries.

Most people will be broadly familiar with cellular structures such as the nucleus or mitochondria. These compartments, or organelles, are bounded by biological membranes to separate them from the rest of the



cell. But, as the name suggests, the droplets of liquid protein known as membraneless organelles have no such physical border, making them an intriguing subject for scientists keen to make use of the advanced fluorescence microscopy techniques that have opened up their inner workings in the past five years.

And now, an Oxford University-led study published in the journal *Nature Chemistry* has shed new light on the phenomenon, demonstrating that even stable structures such as the DNA double helix can be altered, or 'melted', inside these droplets. That's in addition to their ability to separate molecules such as proteins that reside within the organelles.

The work also has huge commercial potential, with Oxford's technology transfer company having filed a patent on a technique that could lead to a revolutionary platform for purifying biomolecules in life sciences research.

First author Dr Timothy Nott of Oxford's Department of Chemistry says: 'The premise of our work has been trying to understand how cells are internally compartmentalised. Broadly speaking, there are two ways of creating compartments in cells: one using membranes, which produces things like the nucleus or mitochondria, and another without membranes.

'These membraneless organelles were first observed at the turn of the last century, when experiments involving sea urchin eggs being "squashed" produced globules of liquid that fused together and behaved like an emulsion.

'In the past five years, scientists have realised that advanced fluorescence microscopy techniques can be used to carry out rapid <u>live cell imaging</u> with the aim of interrogating the physical behaviour of these droplets in cells. So only recently have we developed the toolkit necessary to analyse



what's going on.'

While there are different classes of membraneless organelles within cells, they all share the common feature of this lack of a delimiting boundary. As well as being tiny and spherical, they also have the viscosity of honey and have been likened to globules of oil in vinegar.

Dr Nott says: 'These unusual properties make membraneless organelles difficult to study. You can't just purify them from within the cell and expect them to behave the same way on the outside.

'What we've been doing is trying to reconstitute them in the lab, controlling when and how they form and performing a wide range of experiments on them.'

The team has been able to identify the main protein components of membraneless organelles – they are made up of long protein chains that 'behave like spaghetti' – which can then be targeted and purified in the lab.

Professor Andrew Baldwin, group leader in Oxford's Department of Chemistry, adds: 'Francis Crick used to say that if you want to study function, study structure. But what we find with membraneless organelles is that while they don't really have a structure, they have plenty of functions.'

Oxford University's technology transfer company is keen to hear from parties interested in developing this innovative technology (enquires@innovation.ox.ac.uk).

More information: Timothy J. Nott et al. Membraneless organelles can melt nucleic acid duplexes and act as biomolecular filters, *Nature Chemistry* (2016). DOI: 10.1038/nchem.2519



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