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Synthetic cells capture and reveal hidden messages of the immune system

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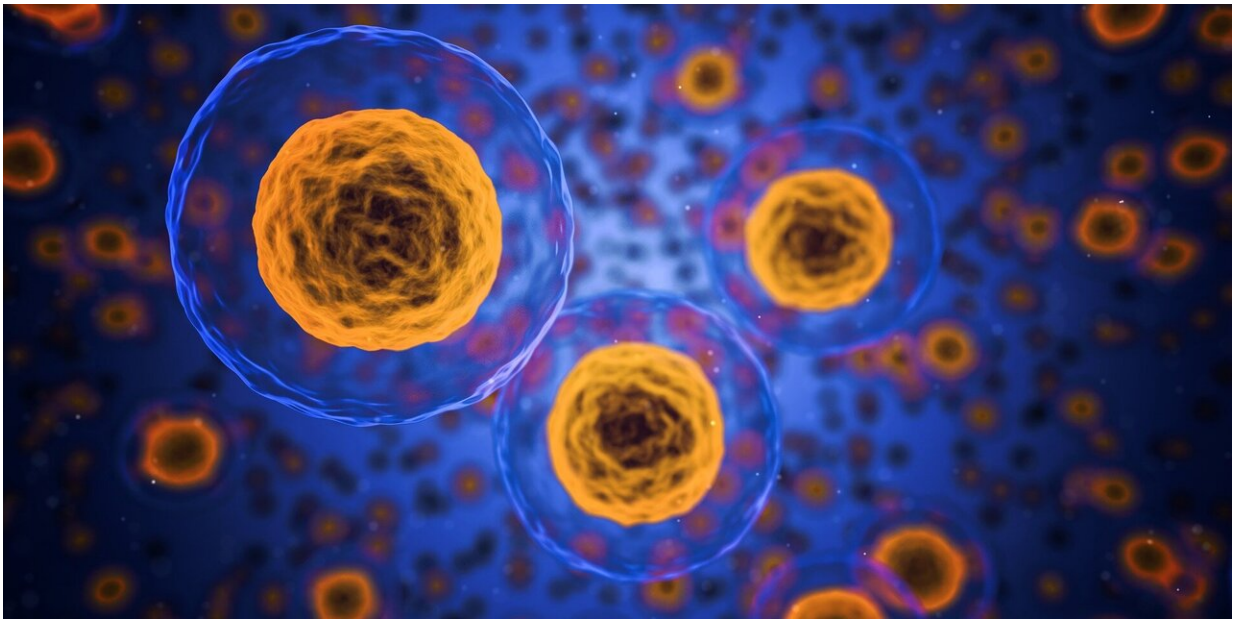

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When immune cells detect harmful pathogens or cancer, they mobilise and coordinate a competent defence response. To do this effectively immune cells must communicate in a way that is tailored to the pathogenic insult. Consequently, the body's response to various health challenges depends on successful coordination among the cells of the immune system.

Key players of the immune system include helper T cells and antigen presenting cells, such as dendritic cells and the antibody-producing B cells. T cells communicate with antigen presenting cells through short-lived contacts called immune synapses. These contacts are highly specialised endowing cells with the appropriate platform for exchanging information in a timely and efficient manner. Key messages are dispatched across the immune synapse via nanometer size vesicles referred to as synaptic ectosomes.

Research led by Prof. Mike Dustin's group of the Kennedy Institute of Rheumatology at the University of Oxford has tracked the movement of ectosomes and unravelled their contents. As described in their research findings, published in eLIFE, the team developed a three dimensional synthetic cell and successfully intercepted and deciphered the messages contained in helper T cell derived ectosomes. Employing super resolution microscopy, called dSTORM, this work found that these T cell synaptic ectosomes have size scales of a millionth of a meter but despite their reduced size they can package enough information to orchestrate the response of dendritic cells. In addition, cell free ectosomes and their synthetically engineered versions result in dendritic cell maturation, an essential process for the establishment of adequate immune responses.

dSTORM experiments further highlighted how both antigen recognition and effector functions can coalesce in single ectosomes implying that help mediated by T cells is highly targeted. Finally, by employing mass spectrometry and CRISPR-Cas9 gene editing technology, the team further elucidated key molecular machinery, known as ESCRT proteins, responsible for the dispatch of ectosomes from helper T cells.

"This research revealed that the formation and composition of these ectosomes depends on direct molecular interactions at the immune synapse and has profound implications on understanding cell-to-cell

communication" co-lead author of the study Dr. David Saliba said. Harnessing this new knowledge is important for the development of future therapies that can help shape the immune response to specific diseases.

More information: David G Saliba et al, Composition and structure of synaptic ectosomes exporting antigen receptor linked to functional CD40 ligand from helper T cells, *eLife* (2019). DOI: 10.7554/eLife.47528

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