Synaptic Ectosomes: The Neural-Like Signaling Mechanism of T Cells in the Immunological Synapse

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The immunological synapse (IS) is a dynamic supramolecular hub that regulates the adaptive immune response. At the IS, engagement of T cell receptor to agonist peptide-Major Histocompatibility Complex (pMHC) results in a coordination of bidirectional signalling events including TCR signalling, costimulation/corepression and cytokine release. In a process reminiscent of neural synaptic transmission, here we show that T cells release trans-synaptic ectosomes (SE). We develop a 3D bead Supported Lipid Bilayer to act as a synthetic proxy for antigen presentation and capture SE from single IS for further characterisation by flow cytometric and mass spectrometric analysis. This revealed that SE are important for delivery of T cell help through CD40 ligand, ICOS ligand and other signals. We couple this with Super resolution microscopy to determine the topographical nature of SE and utilise CRISPR/Cas9 system to unravel the mechanistic details for SE release to the synaptic cleft. Finally, we show that T cell purified SE and synthetic vesicles retain the capacity to induce dendritic cell maturation, cytokine production.