Nanomaterials for lymphatic delivery of vaccines and immunotherapies

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The lymphatic system consists of lymphatic vessels, lymph nodes and lymphoid tissues that have traditionally been assigned roles in immune control, lipid transport and fluid balance[1-5]. More recently, the lymphatics have been found to regulate tissue repair and organogenesis, and to influence the progression of pathologies ranging from cancers to autoimmune, infectious and cardio-metabolic diseases[1-3]. Importantly, immune cells within the lymphatics are the target for vaccines and immunotherapies to treat these conditions[1,4,5]. Directed delivery of vaccines and immunotherapies to lymphatics can thus enhance efficacy and reduce off-target effects[1,4,5]. Specific delivery to lymph is typically achieved via administration of nanomaterials, macromolecules or molecules that associate *in situ* with endogenous proteins or lipoproteins that traffic from injection sites (e.g. intradermal (ID), intramuscular (IM), intraperitoneal (IP), subcutaneous (SC)) via the lymphatics due to their large size and inability to cross the blood capillary endothelium[1,4]. The lymphatic capillaries, by contrast, have open button-like junctions that enable the entry of such large molecules and particles[1,4]. In this presentation I will highlight the optimal properties for nanomaterials and molecules to traffic from injection sites to lymphatic vessels and lymph nodes. In particular, I will focus on recent work from our lab exploring how lipid-conjugated materials can associate with endogenous lipoprotein and protein trafficking pathways into lymph, including the best design of such materials to increase lymphatic uptake. I will also reveal recent insights into the trafficking of nanomaterials within lymph nodes and the ideal properties to achieve delivery and release within specific immune cell niches in lymph nodes. Finally, I will demonstrate how consideration of the lymphatic distribution of nanomaterials can significantly improve vaccine and immunotherapy efficacy.

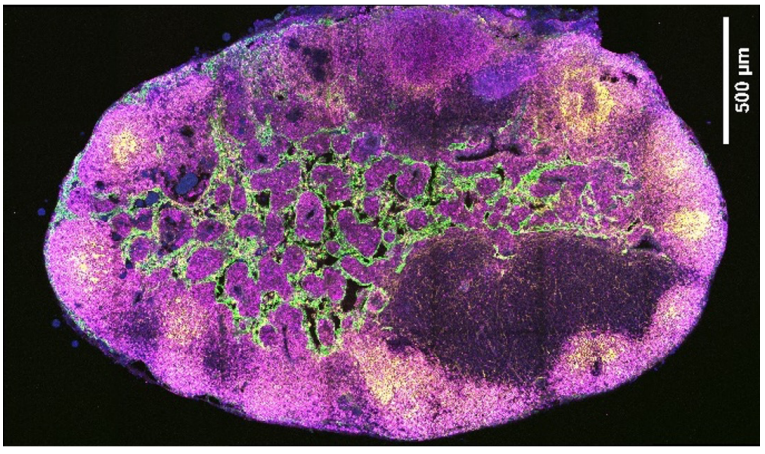

Figure 1: Representative confocal image showing B cell depleting immunotherapy (Cy5-αCD20) (yellow) distribution in a joint-draining lymph node relative to cell nuclei (blue), B220+ B cells (pink) and LYVE-1+ lymphatic endothelial cells (green) at 4 hours after intra-articular injection in a mouse with collagen induced arthritis.

References:

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[4] Abdallah, M; et al. *Journal of Controlled Release* **2020**, 327, 117-128.
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