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Title: Attempt at elucidating the role of Galectin-3 in CD8T cell biology during viral infection using nanobodies

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Abstract:

CD8+ T cell-mediated immunity plays a pivotal role in the control of most intracellular infections. CD8+ T cells exclusively exert their antiviral effect through close cellular interaction with the relevant virus-infected targets. The highly orchestrated response of anti-viral CD8+ T cells involves their activation, proliferation and their subsequent migration at the infected tissue sites. The interface between the circulating CD8+ T cells and vascular endothelium along with extravascular chemokine gradients constitutes a major gatekeeper in regulating this CD8+ T cell migration while the extravasation process involves complex interactions between adhesion molecules and their ligands present either on the T cell surface and vascular endothelium. This physical interaction is assisted via chemokines and their receptors which cause conformational changes in the integrins to increase their affinity for their ligands which is a prerequisite for firm adhesion and transmigration. We investigated the role of carbohydrate recognition domain (CRD) of extracellular and surface sugar-binding protein, galectin-3 in CD8+ T cell migration during viral infection using in-house produced CRD-specific nanobodies (VHH). We show the critical role of the CRD in effecting the migration of activated CD8+T cells to the site of infection. This can be corroborated with the previous observation that Galectin-3 through its CRD webs a reversible interaction with glycoconjugate ligands which advance CD8+T to roll along the endothelial surface and thus creates the basis for firm adhesion and transmigration. Further to advance our understanding of various cellular functions of different domains of Gal-3, we further created a lentiviral mediated system for the production of intracellular nanobodies (intrabodies). A graphical abstract depicting the same is presented in Figure 1. 10

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