SCIENTIFIC SEMINAR

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Radboudumc

Immune cells have a sweet tooth: new insights into galectin regulation of dendritic cell activity

Glycans and their interacting proteins galectins pose another levels of cellular organisation, shaping immune cell function. Galectin-9, a tandem-repeat type of galectin, is critical in regulating T and B cell-mediated immunity although its role in governing dendritic cell (DC) function remains largely unexplored.

We have identified galectin-9 to be required for cytokine secretion, migration and phagocytosis in DCs. Migration assays identified galectin-9 to be a novel regulator of both chemokine-induced and basal 3D migration in DCs, which was accompanied by a significant drop in DC infiltration. Concomitantly, in vivo adoptive transfer experiments confirmed the importance of galectin-9 during DC migration to lymph nodes. In addition, unbiased pathway enrichment analysis performed on genes differentially expressed between wild type and galectin-9-depleted DCs identified galectin-9 to positively correlate with DC-mediated T cell activation and proliferation and to suppress immunosuppressive DC programmes. Concomitantly, DCs lacking galectin-9 expanded 2-fold more T regulatory cells (Tregs) compared to wild type DCs, suggesting that the loss of galectin-9 on human DCs induces immunosuppressing programs. Notably, DC migration was rescued by treating galectin-9-depleted DCs with exogenous galectin-9 protein (rGal-9). Interestingly, addition of rGal-9 was also sufficient to restore the migratory capacity of immunosuppressed DCs and to enhance DC-mediated induction of cytotoxic T cells after being co-cultured with patient-derived tumour organoids.

In summary, we identified galectin-9 as a novel modulator of DC function, essential in inducing intracellular signalling cascades that enable DC migration and T cell activation. Our work shows that loss of galectin-9 impairs DC migration and tumour infiltration, leading to a deficient initiation of immune responses.

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EXCELENCIA SEVERO OCHOA

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Atrio 800
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