Endogenous Galectin-1 in a Murine Model of Paw Edema: Emerging Notion of a Galectin-9 Pro-resolving Effect

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The anti-inflammatory properties of Galectin-1 (Gal-1) in acute inflammation are well established but the role of endogenous Gal-1 has been poorly investigated. To address this, we performed the self-resolving carrageenan (CG)-induced paw edema model in wild-type (WT) and Gal-1\textsuperscript{-/-} mice.

Upon sub-plantar injection of 1\% CG, Gal-1\textsuperscript{-/-} mice displayed a similar first phase of edema (\leq 24 h) to WT mice, however a much less pronounced second phase (48-96 h) was evident in this genotype. This reduced inflammation was associated with lower paw expression of inflammatory genes (e.g. IL-1\beta) and cell infiltrates in Gal-1\textsuperscript{-/-} mice. Analysis of galectin protein and mRNA expression revealed high expression of Gal-1 in WT paws during resolution (\geq 48h), with some degree of expression of Gal-9. In Gal-1\textsuperscript{-/-} mice, Gal-9 protein expression, mainly in recruited immune cells, was remarkably high. Administration of recombinant Gal-1 to WT mice completely ablated the first phase of edema but was ineffective when administered therapeutically at the 24h time-point. Conversely Gal-9 administration did not alter the first phase of edema but significantly reduced the second phase when administered therapeutically. This suggests both of these proteins have anti-inflammatory actions in this model albeit at different phases of the inflammatory response.

Collectively, these data indicate that the absence of endogenous Gal-1 results in an abrogated response during the second phase of the edema reaction. One possible explanation could be increased levels of Gal-9 in these animals resulting in induction of cell death, alleviation of edema and promotion of resolution.