Title: The α-gal syndrome – Investigating immune reactions to tick bites leading to inflammation and allergic sensitization

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The α-Gal syndrome (AGS) is an emerging form of food allergy characterized by delayed hypersensitivity reactions to mammalian meat products. These are mediated by IgE antibodies against the carbohydrate galactose-α-1,3-galactose (α-Gal), most likely following sensitization through tick bites. However, why immune responses after tick exposure diverge between tolerance, inflammation, and allergy remains poorly understood.

To address this knowledge gap, a longitudinal cohort of individuals with documented tick bites has been initiated to unravel distinct immune patterns associated with the development of α-Gal antibodies. Participants are followed over time for antibody responses, cellular activation, and exposure to tick-borne pathogens, alongside a characterization of the corresponding tick. Participant demographics demonstrate a well-balanced cohort in terms of population diversity and geographic distribution. Preliminary data from the current cohort confirm results from our previous study, showing that α-Gal sensitization, based on serum IgE measurement, is detectable in the general population in Luxembourg, and appears more frequent in individuals with repeated tick exposures[1]. An initial screening of the ticks revealed carriage of the common pathogen *Borrelia burgdorferi* sensu lato in 24% of ticks. Importantly, immune cell assays revealed detectable responses to both α-Gal and tick-derived extracts in sensitized individuals, allowing early conclusions that their activation and cell subset patterns might differ from those seen in non-sensitized participants.

Peripheral immune responses shortly after a tick bite may provide predictive markers, distinguishing protective defense against ticks from inflammatory responses leading to allergic sensitization. Identifying such signatures would offer new perspectives for the prevention and management of AGS.

References

1) Chakrapani N, Swiontek K, Hübschen JM, et al. Recurrent tick bites induce high IgG1 antibody responses to α-Gal in sensitized and non-sensitized forestry employees in Luxembourg. Clin Transl Allergy. 2024;14(10):e12396. doi:10.1002/clt2.12396

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