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A high-molecular weight fraction derived from birch pollen extracts is capable of inducing dendritic cell activation and Th2 polarization independently of Bet v 1

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Background: Over 400 million people worldwide suffer from allergic rhinitis. Birch pollen allergy is characterized by a T helper cell type 2 (Th2) immune response directed against Bet v 1 resulting in IgE-mediated allergic symptoms. However, the main driver of allergic sensitisation contained within the pollen matrix remains elusive. The identification and characterisation of the driver of sensitization is of utmost importance in understanding the underlying molecular mechanism in the disease's development. The aim of this project was to reduce the complexity of the birch pollen matrix in order to track down the inducer of sensitization.

Methods: Birch pollen extract (BPE) was fractionated via size exclusion chromatography; thereof derived fractions were pooled in order to obtain 3 main fractions with a distinct protein profile (F1, F2 and F3). Murine bone marrow-derived as well as human monocyte-derived dendritic cells were stimulated for 24 hours with either the 3 fractions or the untreated BPE, and the expression of maturation markers and the secretion of cytokines were investigated. In

an IL-4 reporter mouse model the fractions were investigated regarding their Th2-polarizing potential.

Results: The fraction F1 mostly reflected the capacity of BPE to induce the up-regulation of maturation markers such as CD40, CD80 and CD86 in both, the human and murine model. Stimulation with the other fractions hardly resulted in the up-regulation of activation markers. F1 was also the only fraction to induce IL-4⁺ CD4⁺ T cells *in vivo*.

Conclusions: We managed to identify a non-Bet v 1-containing high-molecular weight fraction (F1) as the major immunostimulatory fraction resembling the activity of the untreated extract regarding the potential to induce DC activation and Th2 polarization. In future, it is necessary to pinpoint the molecular nature of the compounds contained in F1 in order to identify the pollen-intrinsic driver of allergic sensitization.