

ABSENCE OF TAOK3 PROTECTS FROM HOUSE DUST MITE DRIVEN ASTHMA IN MICE

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Introduction: Allergic asthma is a chronic inflammatory airway disease resulting in airway narrowing following allergic sensitization to harmless antigens such as house dust mite (HDM). Asthma is one of the most common noncommunicable diseases and places a substantial burden on the quality of life. Thousand-And-One amino acid Kinase 3 (TAOK3) is a serine/threonine protein kinase that is involved in the stress activated MAPK cascade. It's potential role in a disease model of asthma has never been elucidated. Methods: Full body Taok3 knock-out (KO) mice were generated. We sensitized intratracheally and subsequently challenged Taok3 wild-type (WT) and KO mice with HDM. We then analyzed broncho-alveolar lavage fluid (BALF) cells, mediastinal lymph node cytokine production and lung histology. We generated tissue and immune cell specific KO mice, to pinpoint the phenotype to a specific cell type. Type 2 innate lymphoid cell (ILC2s) biology was assessed by IL-33 stimulation assays. To investigate kinase function Taok3 kinase-dead mice were generated. Results: Taok3 KO mice displayed less inflammatory cells in BALF, type 2 cytokine and airway mucus production compared to WT. HDM asthma assays in specific Taok3 KO models indicate that this phenotype is intrinsic to the immune cell compartment. Furthermore, Taok3 KO ILC2s proliferate less upon IL-33 treatment compared to WT, resulting in reduced airway eosinophilia. We are currently investigating the role of a Taok3 kinase-dead mutant mouse line in the asthma phenotype. Conclusion: Ablation of Taok3 protects from HDM induced allergic asthma, possibly by limiting ILC2 proliferation. If a Taok3 kinase-dead mutant mouse strain mimics this protective phenotype (ongoing), then TAOK3 might be a promising asthma-drug target.