Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

459 Neuronal Regulation of Asthma

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RATIONALE: Type 2 (T2) cytokines like IL-4 and IL-13, key drivers of asthma pathogenesis, critically depend on downstream Janus kinase 1 (JAK1) signaling in tissues. However, surprisingly, little is known about the mechanisms by which JAK1 contributes to lung inflammation. Thus, we sought to use both JAK1 gain- and loss-of-function approaches in vivo to examine the cell-specific contributions of JAK1 in asthma.

METHODS: We employed an established model of T2 asthma in which mice were treated with intranasal *Alternaria alternata*. To test the role of JAK1 signaling *in vivo* we generated novel human JAK1 gain-of-function mutant (hJAK1GOF) mice. We also employed $JAK1^{flox}$ mice to delete JAK1 in a lineage-specific manner. Finally, we used resiniferatoxin (RTX) to perform chemical denervation of lung-innervating neurons.

RESULTS: While hJAK1GOF in the hematopoietic compartment enhanced asthma-like lung inflammation, surprisingly, insertion of hJAK1GOF into the stroma was protective. These findings provoked the hypothesis that sensory neurons, through JAK1 activation, may suppress lung inflammation. Consistent with this, chemical denervation and conditional deletion of JAK1 in lung-innervating neurons exacerbated asthma-like pathology.

CONCLUSIONS: JAK1 signaling in lung-innervating neurons resulting suppresses T2 lung inflammation.

460 Clinical characteristics of subjects with lack of seroconversion following COVID-19 vaccination

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RATIONALE: Vaccine non-response during the COVID-19 pandemic has considerable individual as well as societal risks. We queried the Mayo Clinic COVID-19 database to investigate the clinical characteristics of subjects with lack of seroconversion after SARS-CoV-2 vaccination.

METHODS: Demographic and clinical data were collected from 805 subjects who had a validated antibody assay against the SARS-CoV-2 spike protein at least 14 days after completion of their COVID-19 vaccination. Clinical characteristics from patients with a negative (<0.4 U/ml) antibody response were assessed and summarized.

RESULTS: A total of 183/805 (23%) subjects had lack of seroconversion after SARS-CoV-2 vaccination. Therapy with immunosuppressive drugs were noted in 93 (51%) of subjects with the majority (n=83/93, 89%) receiving ongoing immunosuppressive therapy at time of vaccination. Among 80 (44%) patients with an immunodeficiency, 32 (40%) had a primary immunodeficiency. Cancer (n=128, 70%), B-cell depletion therapy (n=90/115, 78%), and immunosuppressant steroid usage (n=71/93 on immunosuppressants, 76%) appeared to be the other common characteristics for vaccine non-response. Most cancer patients (n=87/110 where known, 79%) were not in remission. Among the 128 patients with cancer, the most common type was hematological (n=116, 91%), with leukemia (n=82/116, 71%), lymphoma (n=23/116, 20%) and paraproteinemias (n=10/116, 9%) accounting for majority of cancer cases.

CONCLUSIONS: Primary immunodeficiency along with active malignancy and ongoing immunosuppression with steroids and/or B-cell depletion therapy appeared to be the most common characteristics for those who failed to seroconvert following COVID-19 vaccination.

461 Differential induction of trained innate immunity following early-life immunization with aluminum adjuvant results in preferential priming of Th2-biased immune responses

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RATIONALE: While aluminum adjuvant-based vaccines are commonly administered to neonates, their immune effects specific to early life are not well understood. The immature infant immune system is Th2-biased and dependent on environmental cues to mature towards Th1/Th2 balance. Thus, the induction of strong Th2 immunity with alum vaccines in early life may perturb this balance, leading to predisposition towards development of Th2 immunity to subsequent allergen exposure.

METHODS: Mice were immunized with the hepatitis B-alum vaccine (HB) as neonates (1wk), infants (3wks) or adults (>8wks). Mice were subsequently exposed to ovalbumin intranasally weekly. The ovalbumin-specific cellular immune response was characterized, and mice were challenged with ovalbumin to determine induction of allergic reactivity.

RESULTS: Immune responses to HB-alum vaccine were more strongly Th2 polarized when given earlier in life. Th2 skewing was not limited to HB, as neonates that were immunized were more likely to develop Th2 immunity upon subsequent exposure to unadjuvanted ovalbumin. This also correlated with allergic reactivity, suggesting that early-life alum immunization may increase the likelihood of sensitization. Interestingly, adult mice that were immunized with HB-alum generated ovalbumin-specific responses more consistent with tolerance.

CONCLUSIONS: Immunization with alum in early life predisposes towards induction of Th2-biased immunity to subsequent allergen exposure likely through induction of trained immunity that prolongs the Th2 bias of the infant immune system. Because vaccines are crucial elements of health in infancy, furthering our understanding of early-life immunization will be critical moving forward in the design of vaccines for infants to reduce bystander immune events triggered by alum immunization.