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2. **Title**

   Elucidation of molecular mechanisms accounting for cigarette smoking-related pancreatic diseases by focusing on microbiota-induced immune responses

3. **Period**

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4. **Summary**

Autoimmune pancreatitis (AIP) and IgG4-related disease (IgG4-RD) are a new disease entity characterized by infiltration of IgG4-expressing plasma cells into the affected organs and elevated serum levels of IgG4 antibody. Although AIP and IgG4-RD are attracting much attention from physicians, the immuno-pathogenesis of these disorders has been poorly understood.

Given the fact that AIP and IgG4-RD are predominantly seen in elderly men, cigarette smoking may be involved in the development of these disorders. We addressed whether cigarette smoking-induced aryl hydrocarbon receptor (AhR) activation promotes or suppresses the development of AIP. Unexpectedly, activation of AhR inhibited the development of AIP, which effect was independent of IFN-I and IL-33 production by plasmacytoid dendritic cells. Interestingly, IL-22 induced by AhR activation played a major role in the suppression of AIP as shown by the fact that neutralization of IL-22 cancelled the inhibition of AIP. These data suggest that IL-22 induced by AhR inhibits AIP and that augmentation of AhR-IL-22 axis can be a promising therapy for AIP and IgG4-RD.