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AB0017 IMMUNE CHARACTERISTICS OF PERIPHERAL BLOOD IN SECONDARY SJOGREN’S SYNDROME PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Secondary Sjogren’s Syndrome (sSS) is diagnosed when symptoms of SS coexist with other systemic connective tissue disease, often secondary to rheumatoid arthritis(RA). The occurrence of SS secondary with RA will worsen the course of disease and increase the high incidence and mortality of RA. At present, the immune characteristics of peripheral blood of SS with RA are not clear.

Objectives: To observe the difference of immune characteristics in peripheral blood between sSS secondary to RA, primary Sjogren’s syndrome(SS), RA patients.

Methods: 20 sSS with RA patients, 20 pSS patients and 20 RA patients hospitalized in Shanxi medical university the second Hospital were enrolled. The percentage and absolute numbers of lymphocyte phenotypes and CD4+ T subsets in peripheral blood were examined by flow cytometry.

Results: As for the percentage and absolute number of total T, B, NK, CD4+ T, CD8+ T and the ratio of CD4+ T to CD8+ T cells, there was no significant difference between the sSS with RA, RA, and SS group. There was also no statistical difference in the percentage of CD4+ T subsets(Th1, Th2, Th17 and Treg) between the three groups. But the ratio of Th17 and Treg in sSS with RA group was increased than pSS group. About comparison of absolute number of CD4+ T subsets, there was no statistical difference among the three groups except that the Th1 cells in RA group was significantly higher than SS group.

Conclusion: Elevated Th17/Treg may be an immunological feature that differentiates sSS with RA patients from pSS patients. In addition, in general, peripheral blood of patients with RA and SS have similar immune characteristics.

REFERENCES:
Background: Current treatment approaches for autoimmune conditions comprise primarily of systemic immunosuppressants or cytokine blockade. The concentration of therapeutic molecules to the tissues that are the sites of autoimmune and inflammatory diseases is a prominent approach with the potential to induce therapeutic benefit and avert risks associated with systemic immunotherapies. Pandion Therapeutics is developing a bifunctional antibody platform that can drive localized immune modulation by combining a “tether antibody” that targets a tissue of choice and “an effector end” that activates specific regulatory immune pathways to restore immune-homeostasis.

Objectives: Here we report the engineering of a skin-tethered PD-1 agonist and a skin-tethered CD39 that inhibit T cell activation and function and deplete local ATP, respectively, modulating different arms of the immune system in a tissue specific manner.

Methods: Biophysical assays were performed to characterize Skin-tethered immune effectors for drug-like properties and in vitro and in vivo assays for target binding, cellular activity and tissue specific-localization. Moreover, these bifunctionals were tested in pathway-relevant preclinical models such as Villiglo and Contact Hypersensitivity.

Conclusion: We believe that this therapeutic approach has the potential to drive the resolution of cutaneous inflammation, providing an opportunity for developing new targeted therapies for autoimmune and inflammatory skin diseases.


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AB0020 ACPA ILLUSTRATING THE IMPACT OF IGG FAB-GLYCOSYLATION ON TRANSCPLANTAL TRANSFER OF ANTIBODIES AND THEIR BINDING TO THE NEONATAL FC-RECEPTOR (FCRN)


Background: Fc neonatal receptor (FcRn) is crucial for IgG half-life and transplacental transport. Different sites of IgG carry glycans which may affect binding to FcRn. While the effect of Fc-glycans has been investigated, the impact of Fab-glycosylation (-14% IgG) on IgG-FcRn interaction remains unclear. Anti-chromatin and protein antibodies (ACPA) of rheumatoid arthritis patients exhibit remarkably high Fab-glycosylation (~90%). This makes ACPA an ideal model to investigate how Fab-glycosylation influences IgG-FcRn interaction.

Objectives: To investigate the potential impact of IgG Fab-glycosylation on IgG transplacental transfer and interaction with FcRn.

Methods: To investigate transplacental transport of ACPA and total IgG, serum of ACPA positive RA patients (mothers) as well as of healthy mothers and their respective newborns was analyzed. IgG Fab- and Fc-glycosylation was investigated with liquid chromatography and mass-spectrometry. Furthermore, ACPA monoclonal IgG were produced and glycoengineered to acquire several variants of the same monoclonal antibody differing only in their glycosylation profile. These glycovariants were then used to investigate the impact of Fab-glycosation on the affinity of IgG for FcRn. Surface plasmon resonance (SPR) results suggested that presence of Fab-glycans slightly lowered the affinity of IgG for FcRn. However, presence of Fab-glycans did not have a significant effect on the results of FcRn affinity chromatography. Together, these results suggest that Fab-glycans may impair association of IgG with FcRn, while dissociation likely stays intact.

Conclusion: Our results suggest that Fab-glycans inhibit IgG-FcRn binding which negatively affects the transplacental transfer of Fab-glycosylated IgG. The impact of Fab-glycosylation on IgG half-life requires further investigation.

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AB0021 CHARACTERISATION OF AGE-ASSOCIATED B CELLS IN EARLY, DRUG NAIVE RHEUMATOID ARTHRITIS


Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease of unknown aetiology that affects mainly the joints. While RA is a risk factor for cardiovascular disease, its influence on age-related changes remains unclear. Here we assessed the impact of age on the B cell compartment in RA.

Objectives: To investigate whether this population differs between RA patients and age-matched early psoriatic arthritis (PsA; disease controls) and healthy donors.

Methods: Newly presenting early RA and other inflammatory arthritis patients, naive to immunomodulatory treatment, were recruited. Control subjects (both RA and PsA cases) were age-matched early disease patients. Disease activity was assessed using a customised NanoString nCounter Human Immunology v2 Panel.

Results: Transcriptionally, ABCs were present in a subset of RA naive patients with elevated expression of CD19, CD21, and CD27, as well as Ki67, CXCR3 and low levels of CXCR4 and CXCR5. These data demonstrate that ABCs have a unique, activated, transcription profile.

Conclusion: Our results indicate the presence of a unique ABC population in RA patients. Further studies are needed to investigate the role of ABCs in RA pathogenesis and to identify potential therapeutic targets.