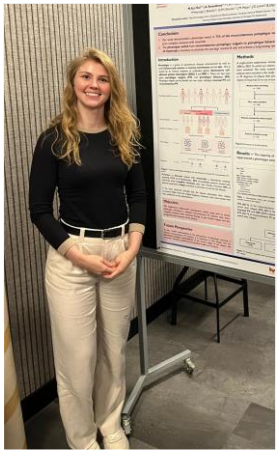
ImmunoTools *special* Award 2024



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Profiling memory B cell-derived Desmoglein 1 and 3 IgG antibodies in Pemphigus vulgaris patients

Pemphigus diseases are a group of rare autoimmune bullous diseases characterized by blistering of the skin and mucosa due to the presence of antibodies against desmosome cadherins desmoglein (DSG) 1 and/or DSG3. There are two primary phenotypes: pemphigus vulgaris (PV), distinguished by autoantibodies against DSG3, and occasionally in conjunction with DSG1, and rarer pemphigus foliaceus (PF), characterized by autoantibodies against DSG11. Acantholysis and blister formation are caused by the direct binding of DSG autoreactive antibodies, which leads to the impairment of desmosomes and the adhesion of keratinocytes in the skin and mucosa. However, the exact underlying mechanisms remain elusive2–4.

Memory B cells specific to DSG1 and DSG3 can transform into antibody-secreting cells upon re-exposure to the same antigen in vivo, ultimately contributing to the DSG1 and DSG3 antibody repertoire of a PV patient. To detect memory B cell-derived antibodies in vitro, polyclonal activation is necessary. During in vitro polyclonal activation of peripheral blood mononuclear cells (PBMCs) using interleukin-2 (IL-2) and resiquimod (R848), B cells are stimulated to secrete immunoglobulins, which accumulate in the culture supernatant. The combination of IL-2 and R848 has been utilized previously to stimulate antibody production in peripheral blood samples of PV patients5. IL-2 promotes cell survival throughout the 10-day stimulation protocol and induces T-cell mediated B-cell differentiation. R848 is a TLR7/8 agonist that activates B-, T-, and NK-cells. The objective of our study is to evaluate DSG1 and DSG3 IgG and total IgG antibody production in these samples through enzyme-linked immunosorbent assay (ELISA) to confirm the ability of patients to produce antibodies against DSG1 and DSG3 and compare the B-cell's ability to produce antibodies with that of healthy controls. By confirming the ability of memory B-cells to differentiate and become IgG-

producing plasma cells, we aim to delve deeper into our cohort to comprehend the immune mechanism of PV through subsequent analysis.

The cohort that we are analyzing is composed of approximately 40 patients with PV who have been monitored from their initial rituximab treatment, throughout their treatment process, remission, and potential relapses. This exceptional single-center cohort is highly valuable due to its longitudinal sample acquisition. With this cohort, we are able to examine patients at various stages of their illness, including active disease, remission, and relapse, which allows us to gain a deeper understanding of treatment effectiveness and disease mechanisms.

We hereby submit our application for the ImmunoTools Special Award. If it were granted it would allow us to significantly advance our research efforts aimed at exploring the pathomechanism of PV disease. Such progress would have the potential to make meaningful contributions towards enhancing current treatment protocols by potentially uncovering novel therapeutic markers, personalizing existing treatment strategies, and identifying new markers that could predict disease relapse.

References:

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