HUMAN SKIN ORGAN CULTURE MIMICKING PEMPHIGUS FOLIACEUS AND PEMPHIGUS VULGARIS

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Pemphigus foliaceus (PF) and pemphigus vulgaris (PV) are autoimmune blistering diseases with high autoantibody (IgG) levels against desmoglein 1 (DSG1) and 3 (DSG3), respectively. The etiology of these diseases is incompletely understood, and therapeutic targets are still not well established. We aimed to simulate PV and PF-like phenotypes in human skin organ culture (HSOC) using sera or IgG from PV and PF patients, respectively. The resulting phenotypes were compared to those obtained with anti-desmoglein single-chain variable fragments (anti-DSG scFv) in eight HSOCs and with *Staphylococcus aureus* exfoliative toxin (ETA) in seven HSOCs. As negative controls, we injected eight HSOCs with intravenous immunoglobulins (IVIG). Sera from five PV and five PF patients, five controls from the endemic region (EC), and five control plasma, were each individually injected in one HSOC from the same control donor. Also, we injected pooled IgG isolated from: anti-DSG1-/anti-DSG3-Ec; anti-DSG1+/anti-DSG3- active PF; without systemic treatment (WST); anti-DSG1+/anti-DSG3+ active mucocutaneous PV WST; anti-DSG1+/anti-DSG3+ EC; and anti-DSG1-/anti-DSG3- inactive PF WST (full remission), each in one of five HSOCs from the same donor. All HSOCs were cultivated for 24h. To confirm epidermal blister formation, we used hematoxylin-eosin staining. We also checked for IgG binding with immunofluorescence assays, after IgG and sera injection. As expected, the PF and PV models using ETA and anti-DSG scFv presented blisters in the granular and deep layers of the epidermis, respectively. However, patient sera did not induce blistering,

despite human IgG binding. Finally, the five HSOCs treated with IgG isolated from PF, PV, and controls, had similar blisters, although autoantibodies were not found to bind to keratinocytes in all treatments. To explain these results, further investigations with IgG from pemphigus patients and controls are necessary.