**„Role of lipid mediators in regulating human granulocyte function associated with neuronal pruritic responses in bullous pemphigoid “**

*Ein Antrag im Rahmen des Potentialbereichs Pathomechanismen der zellulären Differenzierung und Kommunikation bei selteneren Erkrankungen: Chancen zur Regeneration*

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**Zusammenfassung des Projekts**

Increasing evidence suggests that lipid mediators such as lysophosphatidic acid (LPA) regulate itch. Since pruritus plays a major role in bullous pemphigoid we hypothesize that lipid mediators crucially govern the symptoms associated with this autoimmune disease. Basophils and eosinophils are dynamically recruited to the skin in bullous pemphigoid and are known to be major sources of pruritic mediators, such as IL-31. Our aims are therefore to address whether LPA and other lipid mediators affect the activation and pro-pruritic responses of these granulocytes. Human primary basophils and eosinophils will be isolated from buffy coat blood and purified by Ficoll-density centrifugation followed by immunomagnetic cell sorting. Lipid mediator receptor expressions will be assessed by qRT-PCR, Western blotting and immunofluorescence microscopy. The release of inflammatory and pruritic mediators from basophils and eosinophils following stimulation with LPA and other lipid mediators (e.g. sphingosine-1-phosphate; S1P) will be determined by ELISA (cytokines, eicosanoids) and spectrofluorometric autoanalysis (histamine). Furthermore, we wish to address whether lipid mediators have chemotactic effects on these cells. Additionally, we wish to observe whether activated basophils and eosinophils affect sensory nerve ending branching using *ex vivo* culture of mouse dorsal root ganglia (DRG). Finally, we will characterize the presence of lipid mediators in serum and blister fluids of bullous pemphigoid patients using high-performance thin-layer chromatography (HPTLC). Our preliminary data shows that LPA induces histamine release from human basophils, suggesting that lipid mediators regulate human granulocyte function. Confirming a role of lipid mediators in directing basophil and eosinophil responses, especially with respect to stimulating sensory nerves, will facilitate potential targeting of lipid mediators as a new therapeutic approach for bullous pemphigoid and other pruritic diseases.