EAACI Research Fellowship – Final report

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Project title: Use of *ex vivo* skin microdialysis to identify the underlying mechanisms of chronic spontaneous urticaria

Type of Fellowship: Medium Term Research Fellowship

Duration: 6 months

Location: Group of Prof. Marcus Maurer, Department of Dermatology and Allergy, Charité – Universitätsmedizin Berlin, Germany

What questions were addressed and why?
Chronic spontaneous urticaria (CSU) is a disease associated with disabling occurrence of itchy wheals and/or angioedema, which severely affects the patient's quality of life. As the exact pathogensis remains to be characterized in detail, this project aimed at developing a human *ex vivo* skin model to study the pathomechanisms underlying CSU.

What was the nature of the research?
Mast cells are believed to be major effector cells causing symptoms by releasing inflammatory mediators, including histamine, and we therefore studied mast cell activation *in situ* after injection of CSU patient serum into healthy human skin *ex vivo* (obtained with full ethical clearance from cosmetic surgeries). Histamine released from the skin-resident mast cells after injection of CSU patient serum was sampled form the excised skin specimens using microdialysis. Isolated human skin mast cells were used as a supplement to investigate the mast cell activating capacity of the CSU patient sera in a simplified setup.

What was the result?
We found that sera from CSU patients were able to activate skin mast cells *in situ* and *in vitro*. These results will be correlated with clinical and laboratory parameters obtained for the CSU patients enrolled in the study.

How will the findings impact future research?
The development of an *ex vivo* skin CSU model will allow for more elaborate studies on the disease mechanism in the future, e.g. by collection of more biomarkers such as cytokines from the skin using microdialysis. By including studies on purified skin mast cells it is possible to distinguish between biomarkers released directly from mast cells or from other cell types. This will hopefully lead to a better understanding of the disease mechanisms and thus improve treatment options for the patients.

Research course adapted from the original plan:
The excised human skin specimens were sourced from cosmetic surgeries and formed the core of each experiment. However, due to shortage of skin supplies, the project plan had to be adjusted. Therefore, only a single skin model was established; a "generic" model of CSU instead of multiple models reflecting the different CSU subtypes. Development of these models will be pursued in the future.

Personal reflection on what has been learned and how improvements can be made in the future:
The fellowship has fostered a great exchange of knowledge in both directions and thus formed the basis of a successful research stay, which has generated a lot of interesting data to be published in the near future. It has been a truly rewarding experience to join a foreign lab with another culture, other research techniques available and a different structure. Overall, there was no need for improvement, but it may be an advantage in some cases to initiate the study by conducting pilot experiments at the home institution before going abroad.

Acknowledgements
I owe the entire group lead by Prof. Marcus Maurer at Charité in Berlin an enormous 'thank you!', as they have all made my stay a very memorable and rewarding experience – for this I am extremely grateful. Furthermore, I am deeply honored to be granted with the EAACI Research Fellowship; this research stay would not have been possible without it, and I am very thankful to EAACI for the support.