South African Swiss Allergy Study- Mechanisms of allergy development

Long-term Research Fellowship Report 2016-2017

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Allergic diseases affect approximately 1 billion people globally. In the developed countries allergic diseases are now established. However in the developing countries the allergy epidemic started later and continues to rise. First with respiratory allergies and aeroallergen sensitization and later food allergy and sensitization. Reasons for this are not known but are thought to be closely linked to environmental factors that affect immune regulation. We have focused on a single disease phenotype- Atopic Dermatitis (AD) in early childhood which is often a forerunner of the "atopic march" and early IgE sensitization. We assembled 4 groups of genetically similar communities ie. participants with AD and their healthy counterparts from urban and rural settings with the primary aim of understanding possibly different immune mechanisms of allergy initiation and persistence in different environments within a developing country, where differences in rural-urban prevalence of IgE mediated allergy have been documented and yet severe AD is seen in both settings.

We performed a cross-sectional case-control study of 160 age and sex-matched children between 12-36 months of age with moderate to severe AD by SCORAD index. IgE sensitization of common food allergens was comparable between this high risk AD cohorts of rural and urban children.

Immunologically significant differences between AD and healthy controls, and between rural and urban participants,were identified in South African children. AD patients display high levels of putative biomarkers of disease severity ie. TARC and IL- 16, as well as other allergy/ Th2 related cytokines ie. IL-13 and MCP-4. Furthermore, a subtype of AD patients producing high IL-4 levels which correlate with increase expression of pro-inflammatory markers was observed. Full transcriptomic profiling of peripheral blood mononuclear cells, using next generation sequencing techniques also revealed novel AD vs healthy and rural-urban differences. Based on these key findings we are extending our analysis to study the contribution of specific T and B cell populations through single cell next generation sequencing.

In summary, we have described novel immune mechanisms of AD initiation in South African children and we propose novel early predictive and diagnostic molecular markers of disease and targets for therapy in this population. In addition, the influence of environmental factors (i.e. rural versus urban environment) has dramatic effects on immune responses at a molecular level.

In addition to performing research at SIAF, I was also able to attend additional courses such as Fundamentals of Flow Cytometry (Module I) and Advanced Flow Cytometry (Module II) at Babraham Institute, Unversity of Cambridge, 2016, and the Combined Omics Course, Functional Genomics Centre Zurich, University of Zurich, 2017. Results from this project has been presented at several academic

events including EAACI Skin Allergy Club, GRC Food Allergy conference, EAACI Immunology Winterschool and the World Immune Regulation Meeting (WIRM).

I would like to acknowledge the support of Prof. Michael Levin and Prof. Cezmi Akdis in applying for this fellowship and thank EAACI for this generous award. I also particularly thank Prof. Cezmi Akdis for hosting me at the Swiss Institute of Allergy and Asthma Research(SIAF) and for his academic and material investment into the project. In addition, I would like to thank my SIAF colleagues and friends who freely shared their knowledge and skills and greatly supported this project. The exposure to such a robust scientific community within SIAF has been invaluable and has had a significant impact on my career and my future ambitions to combine clinical and basic research into innovative solutions for patients with atopic dermatitis.