

**ESPE Sabbatical Leave Programme** (Sponsored by: Eli Lilly Ltd.)

**ESPE Sabbatical Leave Programme Committee**

**Chair: Prof. Dr. Raimo Voutilainen**

**Report on Sabbatical Leave Project**

**Royal Children's Hospital**

**Paediatric Endocrinology and Diabetes Group**

**Melbourne, Australia**

**Recipient:**

Prof. Dr. Wieland Kiess

Hospital for Children and Adolescents

University of Leipzig

Liebigstr. 20a

D-04103 Leipzig, Germany

Tel. 49-341-972600, FAX 49-341-9726009,

E-Mail: [Wieland.Kiess@medizin.uni-leipzig.de](mailto:Wieland.Kiess@medizin.uni-leipzig.de)

**Time period:**

Total time period covered: Nov. 2009 til February 2010 (three months)

Time in Australia: Nov, 12, 2009 til December 23<sup>rd</sup>, 2009

Time in Germany: January til February

**Host:**

Prof. George Werther

Royal Children's Hospital

Paediatric Endocrinology and Diabetes Group

Melbourne, Australia

**Budget:**

Sum: 10 000.- Euro

**Rationale:**

After many years of clinical and scientific as well as teaching obligations at one institution, the focus of a clinician researcher tends to be mono/egocentric and restricted on one's own environment and personal customs and experience. To learn anew and start novel ideas and approaches, completely different settings and a different environment might be chosen for stimulation and recruitment of one's own personal assets. It was hypothesized that exposure to a completely different working environment would provide for new ideas to develop one's own institution further and enrich and expand one's personal (professional) work life.

**Objectives:**

- to establish a sustainable, fruitful and efficient collaboration between the Leipzig and the Melbourne group in respect to both obesity research strategies and IGF and IGF binding protein research, both basic and clinical
- to learn from managerial skills executed by leading officials of a large university hospital and research institution in an overseas country
- to get to know funding strategies and research support principles in an Anglo-American setting
- to compare established quality control and ethics and clinical practice committee settings of the two institutions

**Achievements**

A sustainable, fruitful and efficient collaboration between the Leipzig and the Melbourne group in respect to both obesity research strategies and IGF and IGF binding protein research, both basic and clinical has been established: Three joint manuscripts have come out of the sabbatical leave stay of the recipient and are being published in international peer-reviewed journals. One of the manuscripts outlines a joint biorepository project (COBRA) involving Australian, US-American and German centres. This collaborative approach has also helped the recipient to establish more firmly his role within the German obesity research network sponsored by the German Ministry of Research and Education (vice-chairman: W.K.) and will help to obtain

future funding for obesity research from the German Federal Government. The second manuscript details the development/trend of obesity prevalence in Germany over the last ten years as monitored by the Leipzig Crescnet data base. The Melbourne group contributed in fruitful discussions and helpful comments to writing the manuscript and successfully having it accepted by the Intern. J. Pediatr. Obes.. A third manuscript on the 'genetics of overgrowth' is being finalized at present and will be included in a Best Practice Clin Endocrinol Res. volume entiteld 'Genetics of Growth' and edited by the recipient. Additional manuscripts evolving from the collaboration between the two groups are planned. Most importantly, the Leipzig group has managed to elucidate the molecular defect in an Australian patient with early onset obesity, red hair but normal adrenal function as being a heterozygous POMPC mutation in the affected boy. Analysis of DNA from other members of the family is under way. In addition, the role of IGFBP-2 in a patient with lipoma due to a large deletion of the PTEN gene is being investigated.

During the stay in Melbourne, the recipient was allowed access to every ward, office and out patient clinic and research laboratory as well as was granted access to the managerial bodies including the directoral offices of the Murdoch Research Foundation, Good Friday Appeal support structure, the University of Melbourne Paediatric Department and the CEO's office of the Royal Children's Hospital. The recipient was able to learn from the managerial skills executed by the leading officials of the Royal Children's Hospital, a large university hospital and research institution in Australia. These included conversations and formal and informal meetings with the Professor of Paediatrics, the CEO of the hospital and the director of the Murdoch Research Foundation as well as with the director of the Murdoch Research Institute. In addition, luckily the RCH is building a new hospital structure on the premises: the construction of the new Royal Children's Hospital in Melbourne will cost more than 1 billion Australian dollars. It will open in 2011 and will serve the state of Victoria, Australia as the major and tertiary care children's hospital. The recipient was able to visit with the leading architect, listen to his strategic vision and concept and also tour the construction site.

The interaction with the CEO of the hospital, the director of the Murdoch Research Foundation and the members of the Good Friday Appeal group enabled the recipient

to restructure his strategy for raising grant support and volunteer support in his own institution. In fact, the ESPE Sabbatical Leave stay in Melbourne has been instrumental for founding the children's hospital's foundation `Stiftung Kinderklinik Leipzig` in Leipzig, Germany, that is presently under way. The structure and scope of this foundation follow the ones in Melbourne.

The recipient was able to compare established quality control and ethics and clinical practice committee settings of the two institutions, the RCH and the Hospital for Children and Adolescents in Leipzig. Structure, function and outcome measures of these institutions are quite similar. A longitudinal assessment and comparison with historical data on treatment success rate, quality of care and happiness of customers/families with sick children had already been established before the visit to Australia. The work and views of both the Clinical Ethic Committee and the Research Ethics Committee at the two institutions is quite similar.

The recipient visited the hospital's outpatient clinics and wards as well as routine and research labs. In addition, facilities like theatre, schools for kids, the media centre and other amenities for the in-patients could be scrutinized. It became clear that charity for the RCH plays an important role in Australia but is almost not existing in Germany. The general paediatric wards and also specialist services were heavily loaded with patient care and similar problems and day-to-day problem solutions were apparent.

The paediatric diabetes and paediatric endocrinology group received the recipient extremely cordially and in a very open, normal and hearty fashion. Integration into daily routines was complete: this included participation in out-patient clinics (diabetes, obesity), specialist seminars and case conferences (skeletal health, diabetes), journal clubs and informal discussions on cases and research projects. The members of the group also became true friends and offered access to the treasures of both the city of Melbourne and the state of Victoria.

The obesity research group of the department, in particular, Dr. Matt Sabin, who also became a good friend, shared many ongoing and planned activities including their setup of a biorepository and their conducting an ambulatory obesity counseling and

treatment program. Dr. Fergus Cameron had the insight to draw our attention to a case of early onset obesity who later was diagnosed by the Leipzig group to carry a heterozygous POMC mutation. It is unclear whether or not POMC heterozygosity contributes to the development of obesity. Hence, this patient and his family might become quite instrumental to elucidate the role of POMC in obesity and appetite control in more detail. Prof. Melissa Wake presented her department of community paediatrics. Upon his return, the recipient has started to plan for the establishment of a similar institution albeit at a much lower level and to a much smaller dimension in Leipzig since community paediatrics is not strong in Germany.

### **Presentations and meeting participation:**

During the stay in Australia the recipient delivered four formal presentations: he gave one plenary talk at the official APEC conference in Coolumb, Queensland, on the genetics of childhood obesity. In addition he delivered one Grand Round presentation to the staff of the Royal Children's Hospital in Melbourne on obesity in childhood and adolescence. In the formal meetings of the Victoria Obesity group, he presented an overview on obesity research and research strategies in Germany. Finally, the recipient gave a talk on the work of the Leipzig group on human IGF-I receptor mutations in the research seminar series of the Melbourne Pediatric Endocrinology and Diabetes Group. During the stay in Melbourne, he also participated actively in other Grand Rounds and research seminars, for example in an international seminar on the genetics of overweight, delivered by Steve O'Rahilly, Cambridge, and secondly in a research seminar on epigenetics again delivered by colleagues from the UK.

### **City life and country fare**

The recipient was able to tour the country, in particular Wilson's Promontory National Park, Mornington Peninsula, The Grampians National Park and The Great Ocean Road on free days. He was also able to enjoy Melbourne's museums, theatres and concert halls during the evenings. Again, Prof. Werther and his family were wonderful hosts and the recipient is truly and very much grateful to them for having enabled this memorable, outstanding and most valuable stay in Australia.

## **Publications:**

Sabin M, Wake M, Clemens S, Saffery R, G. Werther, W. Kiess, Z. McCallum, M. Campbell, N. Crimmins, J. Woo, G. Leong, O. Ukoumunne. New directions in childhood obesity research: how a comprehensive biorepository will allow better predictions for outcome. BMC (submitted) (2010)

Sabin M, Werther M, Kiess W. Genetics of overgrowth syndromes. In: Best Practice and Research in Clinical Endocrinology, Elsevier Publ. Vol. Genetics of growth, ed. by W. Kiess, R. Pfaeffle 2010 (in press)

Blüher S., Meigen C, Gausche R, Keller E, Pfäffle R, Sabin M, Werther G, Odeh R, Kiess W. Age-specific changes in obesity prevalence in German children over a 10 year period. Int. J. Pediatr Obes. (in press) (2010)

## **Future projects and collaborations:**

**(1) Case of a boy with monogenetic obesity syndrome**

**(2) Biorepository**

**(3) International collaboration, Australian Ped. Endo Group and ESPE**

## **Acknowledgement**

The recipient wishes to thank ESPE and in particular the ESPE Sabbatical Leave Programme Committee for having supported this short term sabbatical leave which was instrumental for the further professional development of the recipient and the future for his institution. The recipient is extremely grateful to Prof. George Werther and his wife Mary for their friendship, hospitality, great sense of humour and willingness to take up with their visitor ! He also wishes to thank the staff at RCH, Melbourne, in particular the paedocrinology and diabetes group for all their support, kindness and lots of interaction.