

ESPE Sabbatical Leave - Theo Sas, The Netherlands – 2008 -2009

Host:

Irene Netchine associate professor and Yves Le Bouc professor
Pediatric Endocrinology Investigations
Trousseau Hospital
Avenue du Dr Arnold Netter 26
75571 Paris Cedex 12

Title of Research project was 'The role of Plasma Protein-A (PAPP-A) in pre- and postnatal growth. A study in normal and fetal growth restricted pregnancies and in children born small for gestational age (SGA) with or without Silver Russell Syndrome'.

Aim

The aim of our project was to increase our knowledge concerning the role of PAPP- A, a protease in the IGF- BP system and to what extent methylation of the 11p15 region (IGF-II gene) plays a role in intrauterine and postnatal growth in the general population of newborns. For me, as a clinical researcher, the ESPE Sabbatical Leave program was an opportunity to have the experience of working in the laboratory of a leading centre for study of various aspects of IGF biology.

Methods

In the first months of my sabbatical I have learned to perform different laboratory techniques, such as ELISA's, IRMA's, extracting and purifying DNA, performing PCR and sequencing of genes, southern blotting, bisulphiting of DNA and real time PCR.

Subsequently, together with technicians of the lab, we have performed ELISA's for measuring IGFs, BPs, and PAPP-A levels in cord blood samples from 300 [88 for PAPP-A only] mother-infant pairs which were included in the cohort EDEN study (Etude des déterminants pré et post nataux du Développement et de la santé des ENfants, Marie-Aline Charles and Jean Claude Souberbielle). In this cohort, children and their mothers have been followed from pregnancy until 1 year of age. Several auxological and laboratory measurements were obtained and are ready to use for analysis. In addition, in collaboration with Salah Azzi, researcher in the lab, I have measured the methylation index of different parts of the 11p15 region (IGF II gene) and the 6q region (ZAC gene) by using real time PCR on bisulphited DNA of cord blood of 300 newborns from the EDEN study.

Results

Preliminary data on the relationship between the degree of methylation of ZAC and auxological parameters will be presented by us as an oral presentation in the ESPE Meeting in Prague 2010 with the title 'ZAC1 (PLAG1) degree of methylation is associated with prenatal and postnatal growth parameters in a general population of children'. Interestingly, we found positive correlations between the methylation index of ZAC1 and the estimated fetal weight at 28-32 weeks of gestation, weight and subscapular skinfold at birth and one year of age. We conclude that we have demonstrated that ZAC1 methylation is weakly associated with fetal and postnatal growth.

In the next few months we will analyze the relationships between on one hand the different growth factors, PAPP-A, and the methylation status of several differential methylated regions on 11p15 region and on the other hand the auxological measurements before and after birth.

Conclusions

I have learned a lot of performing laboratory work and using molecular biological techniques trying to answer scientific questions in pediatric endocrinology. In the next few years we expect to write and publish several papers on the data which I have obtained during my Sabbatical Leave. In conclusion, I have had a very good time in Paris. I would like to thank the organisation of the Sabbatical Leave Program, the sponsor and my colleagues in Paris.

Theo Sas, June 2010