



MEDIA RELEASE

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Sex differences start in the womb

Disease risk in later life differs for women and men - scientists at *The Power of Programming* Conference present evidence to demonstrate this may start in the womb

Pregnancy places competing demands on a mother's physiology: on the one hand her body wants to produce a strong healthy baby but if this at the expense of her own health, she will not be able to care for the baby and it might also jeopardise her chance of having future babies. Some of the genes (the imprinted genes) that she passes on to her child therefore try and protect her own body from excessive demands from her child.

Imprinted genes inherited from the father however do not show the same restraint – their goal is to get as many resources for the fetus as possible. Evidence that this battle of the imprinted genes might be at the root of later life disease processes will be presented at the International Conference *The Power of Programming* in Munich on 6th-8th May, organised by the EC-funded Early Nutrition Programming Project (EARNEST).

Dr Miguel Constancia from the University of Cambridge said today (7th May):
“The imprinted genes derived from the father are greedy whilst those from the mother are conservative in their needs to ensure future reproductive success.

“We have found evidence that imprinted genes play important roles in the control of endocrine functions of the placenta. These placental adaptations have marked effects on nutrient delivery to the fetus, resulting in the programming of

homeostatic mechanisms with metabolic consequences extending to adulthood, for example for type 2 diabetes susceptibility.”

Other research presented at *The Power of Programming* conference discussed the evidence that some programming effects are different in male and female offspring. **Dr Rachel Dakin** from the University of Edinburgh will show how maternal obesity is associated with sex-specific programming effects in young adult mice. Female offspring of obese mothers had raised blood insulin levels, whilst male offspring did not. Male offspring did have alterations in the expression of liver genes important in lipid and glucocorticoid metabolism.

Professor Ricardo Closa Monasterolo from the University Rovira I Virgili of Tarragona presented work that suggested that infant boys and girls might have different responses to lower or higher protein diets. Females given higher protein formula milk had higher IGF-1 levels than males, whilst males showed higher C-peptide/creatinine levels compared to females.

Whether these differences in metabolic responses to the two variations in protein levels in formula milk will lead to differences in the rates of obesity, or other pathological conditions in later life, remains to be seen, but it does raise the possibility that infant formula milks might one day be specifically tailored for boys or girls.

Professor Claudine Junien (Professor of Genetics, INRA, France) an expert in this subject and a plenary speaker at The Power of Programming conference says: “For me a gene, a cell and even a sex does not think and has no intelligent design. Instead it reacts to diverse environments and situations according to what its build-up can afford, pushing in one direction or another (or several at a time). The limits to which it can go without going awry or dying have been established progressively throughout the slow and long process of evolution, with different genetic backgrounds throughout the world depending on the diversity of experiences over the ages.

We have data showing that gene expression and DNA methylation are sexually dimorphic in male and female placentae under normal/control conditions. Surprisingly, in stressful conditions, such as a high fat diet or low

calorie diet, or maternal overweight/obesity - the male and female placentae do not use the same strategies: they use different gene pathways and networks to cope with the stress.

Does this directly lead to different outcomes? It may lead to sex-dependent differences in the outcome of programming with long lasting effects. Alternatively, it may be that males climb the mountain taking the north face while females take the south face - but they ultimately reach the same peak after using these different paths.”

Professor Berthold Koletzko, the Co-ordinator of the EARNEST project said, “This is a new and exciting area of research which suggests that some of the differences in disease risk seen in men and women in later life might be explained by different responses to programming effects in early life.”

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The Power of Programming (6-8 May) Munich is a landmark international conference on the science of Early Nutrition Programming. Full details of speakers and sessions at www.metabolic-programming.org/munich2010/index.htm

Ludwig-Maximilians-Universität (LMU), Munich one of the oldest in Germany, is at the forefront of research into metabolic programming with the EC funded EARNEST project (www.metabolic-programming.org), co-ordinated by Professor Berthold Koletzko of the University Children’s hospital. The Power of Programming conference, organised by EARNEST, is bringing together leading experts from around the world to discuss the effect of nutrition and other environmental influences during early life on long term outcomes such as obesity, cardiovascular disease, and chronic lung disease, behavioural and cognitive problems.

The EARNEST Project is being carried out with financial support of the European Commission under the 6th Framework Programme for Research and Technical Development (FOOD-CT-2005-007036). It does not necessarily reflect the EC views and, in no way, anticipates future policy in this area.

EARNEST has included follow-up studies from the EU Childhood Obesity Project (CHOP) a multi-centre intervention trial in five European countries. Over 1000 infants were randomised to receive infant and follow-on formulas with lower or higher protein content for their first year and were then followed up for 2 years. A group of breast fed infants were also followed up for comparison. Study Results were published last year (Koletzko *et al.*, 2009) (Schiess *et al.*, 2009)
