



THE EARLY NUTRITION PROGRAMMING PROJECT

Project Number: FOOD-CT-2005-007036

Acronym: EARNEST

(EARly Nutrition programming - long term follow up of Efficacy and Safety Trials and integrated epidemiological, genetic, animal, consumer and economic research.)

NEWSLETTER 2 - AUTUMN 2006

EU approves first Annual Report

The first Annual report has been approved by the EU and it details the considerable progress that has been made during the project's first twelve months. Some of these achievements are described below:

Theme 1 During the first year of EARNEST, follow up examinations of the former participants of the intervention trials were initiated. The age of the subjects now ranges from 3 years to almost adulthood. In all cases the infrastructure for the studies has been, or is being, established successfully; in some studies the subjects are already being seen. In addition to the clinical studies all participants are working to harmonize their studies in terms of methodology and outcome measures with the ultimate aim of establishing a common database for the information obtained from all their studies.

Theme 2 In the same way, observational studies in theme 2 have been extended by including further subjects or, in established cohorts, by studying additional time points or further parameters.

Theme 3 Specific questions in relation to metabolic programming have been studied in small (e.g. rat, guinea pig) and large (sheep, pig) animal models with well defined dietary interventions during specified pre or postnatal periods. Using functional genomic techniques, the basis of early nutritional programming in clinically relevant model systems has begun. Excitingly, these techniques will also be applied at a later stage in the prospective adult studies, where biological samples have been saved. One of the main achievements during the first year has been the harmonisation of the study diets. This will mean immediate improvement in quality of the conclusions which can be drawn from results of these studies.

Theme 4 has made good progress in studying the consumer perceptions and understanding related to the practical implementation of new knowledge about health effects of maternal and infantile nutrition in general with specific emphasis being given to long term health effects. Identification of the most important sources of information in European countries with different cultural background, will help to promote the dissemination of EARNEST results towards the end user.

Theme 5 has started by collecting information on the prevalence of cardiovascular disease in European countries and, using modelling techniques, estimating the cost reduction by a favourable programming of the disease risk. It has already become apparent that cost reduction will occur, although only after a delay of decades. This will mean careful consideration of influencing factors over the long time period in the model.

Theme 6 EARNEST's demonstration projects in Theme 6 comprise tests of the effects of prebiotics or a biotechnologically produced breast milk lipase. Short term and long term health benefits are expected from adding these components to formula for preterm infants. As these substances are already well characterized clinical protocols for practical evaluation have been defined and the studies will start during the next year.

Theme 7 Dissemination activities have included getting a website up and running, producing a glossy brochure describing the project and organising a webcast, which allowed widespread communication about the aims of the project and the personnel involved in it.



Bert Koletzko
Project Coordinator

Early Nutrition Programming & Health Outcomes in Later Life: Obesity & Beyond

Pre-Congress Satellite Meeting of 15th ECO
Budapest, April 20-21, 2007

Joint Meeting between the Early Nutrition Programming Project and the European Academy of Nutritional Sciences

Preliminary Scientific Program

- Maternal Nutrition: Trends and Impact on Pregnancy Outcomes
- Programming of Disease I: Cardiovascular Risk
- Programming of Disease II: Obesity and Diabetes
- Mechanistic Basis of Early Life Programming
- Nutrient-Genes Interactions in Early Life Programming
- The European Childhood Obesity Trial

In addition, there will be plenary lectures, debates, poster sessions, and a young investigators' forum

www.metabolic-programming.org



www.metabolic-programming.org
email: programming@med.uni-muenchen.de

Report of the Brussels Progress Meeting- April 2006

The third meeting of the Early Nutrition Programming Project General Assembly was held in Brussels and was efficiently organised by Dr Clotilde Carlier and her team from Université Libre de Bruxelles Childrens' Hospital. We were all very impressed that Clotilde had managed to find time to fit in giving birth to a son, Charles, while she was so busy organising the conference. The group enjoyed staying close to the Grande Place and being able to nip out and sample the local beers so easily.

Professor Kolezko welcomed everybody to the meeting, now one year into the project. He drew attention to the Annual Report that would have to be submitted to the EU very soon and encouraged everybody to list their publications on the internal website. Some themes were much better at this than others.....

As suggested at the last progress meeting, much more of the time was taken up with cross theme sessions devoted to the topics that each theme is addressing from their different perspectives. One of the major strengths of the project is the opportunity for bringing together researchers who are addressing the consequences of Early Nutrition Programming using different experimental approaches and promoting interaction and collaboration between them. These cross-theme sessions helped to further these aims. There were sessions on Obesity; Neurology and Psychology; Cardiovascular diseases and updates on the studies being carried out in the Gambia and Belarus. The session on Cardiovascular Diseases for example, ranged from a detailed discussion of the possible critical windows of developmental plasticity and programming mechanisms in rat models of human hypertension to a discussion of how many deaths from cardiovascular diseases could potentially be prevented if all infant formulas were supplemented with long chain PUFA through reductions in blood pressure in later life.



Dr Susan Ozanne giving a tribute to Prof Nick Hales



Members of the Earnest consortium at the Brussels meeting

The project involves people from 16 European countries with all the various cultural and language differences which would be expected but surprisingly one of the main cultural differences is that between those doing work on animals and those whose work is in people. Animal work, particularly work on small animals like rats and mice, proceeds much more quickly than studies in people and produces results and publications more rapidly. Scientific questions can be addressed directly rather than through observational studies which see what happens to people over time. Those working with people find it hard sometimes to understand how animal models of human disease apply to people. To address these areas of potential misunderstanding, a workshop on the validity of the animal models used in the project has been proposed.

The first afternoon was devoted to individual theme meetings and useful discussions on the nitty gritty aspects of ensuring that studies are comparable and how data would be shared. A guided poster session and a session on some recent results were held to help disseminate the findings coming out of the different themes. The EU contact for the project, Isabelle de Froidmont-Görtz, spoke about the forthcoming Framework 7 research programme and gave more details about the review procedure. Professor Wim Saris, from the Diogenes project, spoke about his experiences of managing another large integrated project. Dr Susan Ozanne gave a warm and moving tribute to her long term mentor and colleague and one of the first authors in the field of early nutrition programming, Professor Nick Hales, who died last year.

Two training workshops were held directly after the meeting. These were on Anthropometry, led by Professor Chumlea from the World Health Organisation, for those involved in studies measuring growth in children; and on Media Training. The Media Training workshop was led by project partners, Rhonda Smith and Marc Catchpole. Their special invitee was BBC health journalist Geoff Watts and, together, they helped eight young scientists from across the project to understand the mind of the media.

External Advisory Board Meeting

The External Advisory Board exists to provide periodic external review and critical stimulation for the project. The members are asked to assess the feasibility and the scientific validity of the project's objectives and to provide advice as appropriate. The Board had its first meeting at The Brussels meeting in April 2006. The members of the Board, with their specific area of expertise are:

Prof. Marjo-Riitta Jarvelin (Chair, epidemiology, public health, paediatrics)
Dr. Alfredo Martinez (nutrition, molecular biology, genetics),
Prof. Dr. Daniel Ramon (biotechnology, plant science),
Prof. John Mathers (nutrition, genetics),
Dr. Pilar Rodriguez-Iglesias (nutrition, food safety),
Prof. Raanan Shamir (perinatal and infant feeding),
Prof. Torger Borresen (food technology),
Prof. Wim Saris (medicine, nutrition).



Members of the External Advisory Board. From l-r: Alfredo Martinez, Raanan Shamir, Wim Saris, Torger Borresen, John Mathers, Marjo-Riitta Jarvelin, Daniel Ramon

Theme Leaders gave presentations to the Board about the different aspects of the project and the Board agreed that the scientific targets of the project were clearly presented and generally feasible. There was a lively discussion with constructive criticism as well as further suggestions for scientific and analytical strategies. The Board was particularly impressed by the training, exploitation and dissemination plans and activities as well as about the extent of the scientific areas and tasks covered by EARNEST. However, it felt that the ambitious nature of the project might raise difficulties in meeting some of its targets and some might prove to be somewhat challenging. Their ability to identify potential problems was felt to be very helpful.

The Board will meet once a year and agreed that they would develop their terms of reference. It was encouraging that the members were keen to be more involved in the details of the projects and expressed an interest in attending the scientific part of the assembly meetings as well.

'More Time Please!' - A Report of Media Training Workshop, Brussels, April 2006

'More Time Please!' that was the conclusion of the eight members of the Early Nutrition Programming Project who took part in the Media Training Workshop held in conjunction with the Brussels General Assembly meeting.

"This is such an important topic - we need to devote more time and training to it," said one delegate.

Run by the project's Communication Managers, Minerva, the eight young scientists worked through a comprehensive briefing on the ways of working with print, radio and television media.

Geoff Watts, BBC science & health journalist from the UK, provided a touch of reality through his succession of television interviews, increasingly challenging as the day went on! Participants were able to review and critique constructively their own and others interviews. Geoff also explained what journalists wanted from interviews with scientists and gave tips on how to ensure the interview is a success for the journalist and the viewer as well as the interviewee.

"The sessions on preparation were all highly rated by our participants," comments Course Leader Rhonda Smith of Minerva. "Experience of writing proactive press releases, reactive statements and giving radio interviews were also covered. Feedback stated that the course could not have been improved, but that more time would have been beneficial."

Geoff Watts told the delegates that, "Some people who work in health care continue to equate health and medical journalism with education. This is a mistake: journalism is not about health education any more than it is about political or arts education. It is about stories that interest people. Nor do reporters and broadcasters owe their first loyalty to the health care community. Their loyalty is to their readers, listeners and viewers - who will go elsewhere if they are unsatisfied."



Julia von Rosen being interviewed by Geoff Watts

"Perfect! Very clear structured material was provided and I learned a lot in a great atmosphere," said one delegate.

This learning will be put to the test as the Early Nutrition Programming Project prepares for its first scientific meeting in Budapest, April 2007, with challenging targets on media coverage. The media students will be active partners in that endeavour.

Anthropometry Workshops

In order to assess how nutrients consumed during infancy and early childhood can differentially influence the longitudinal growth patterns of infants, anthropometry and training protocols were developed. Training sessions are necessary to insure standardization of the study protocol during data collection. Three training sessions were conducted during the follow-up, in Germany, Italy and Belgium.

The sessions in Italy and Belgium were conducted by Prof Cameron Chumlea (Department of Community Health, Wright State University, Ohio, USA) who is also the lead anthropometrist of the WHO Multicentre Growth Reference Study (MGRS), the NHANES and the Fels Longitudinal Study. Training sessions employed demonstrations on how to measure children and provided comparisons between the several observers in each clinical site as they participated in the training sessions. These sessions included a presentation of the MGRS Video and demonstrations of instruments and measurement techniques performed on an independent sample of local children who were similar in age to those of the study children.

Measurements recorded by investigators from each country were compared with measurements recorded by Prof Chumlea. Reliability statistics told us that differences in values between corresponding measures by the data collection staff and Prof Chumlea are small for each measurement for each child in each session. In addition, the differences in values between corresponding measures between the data collection staff are similarly small for each child in each of the training sessions.



Dr Clotilde Carlier measures the head circumference of a child

The accuracy and reliability of the anthropometric data allow a clear understanding of the level of measurement error in the analysis and provide an interpretation of change with age in measurement values in relation to the various independent variables. The analysis of anthropometric data will allow us to assess the impact of nutrition on the growth processes in various growth parameters of the children and on their potential future health risks.



Prof Chumlea

Profile on EARNEST post docs: Sylvain Sebert

My name is Sylvain Sebert. I am working in a postdoctoral position for the EARNEST project in Michael Symonds' laboratory at the University of Nottingham. My main interest is the developmental origins of the metabolic syndrome (obesity and insulin resistance). More precisely, we tend to discriminate in large animal models between the metabolic and cellular mechanisms responsible for excessive fat deposition and impairments of glucose and lipid metabolism. I am particularly interested in the gene regulation involved in energy partitioning between lean and fat tissues and the central and peripheral regulation of appetite and food intake.

I previously did my PhD at the National Institute of Agronomic Research (INRA) in Nantes, France. During this period, I studied metabolic and physiological repercussions of diet-induced obesity during childhood in the Yucatan mini-pig model. I particularly developed some skills in nutrition physiology, regulation of gene expressions and insulin signalling.

From this background in the pathophysiology of juvenile obesity and insulin resistance, I was keen to carry on research projects related to obesity. Being particularly interested in the relationship between growth and obesity development, when I heard about the EARNEST programme, I naturally contacted Michael Symonds, the theme leader of the Animal, Cell and Molecular Studies. Luckily, he was looking for someone when I got in touch with him. That is how I joined the EARNEST programme!



Some recent publications by Earnest members

Lauritzen L, Halkjaer LB, Mikkelsen TB, Olsen SF, Michaelsen KF, Loland L, Bisgaard H. Fatty acid composition of human milk in atopic Danish mothers. *Am J Clin Nutr.* 2006 Jul;84(1):190-6

Fernandez-Twinn DS, Ozanne SE. Mechanisms by which poor early growth programs type-2 diabetes, obesity and the metabolic syndrome. *Physiol Behav.* 2006 Jun 30;88(3):234-43.

Andersen HS, Gambling L, Holtrop G, McArdle HJ. Maternal iron deficiency identifies critical windows for growth and cardiovascular development in the rat postimplantation embryo. *J Nutr.* 2006 May;136(5):1171-7.

Bellinger L, Sculley DV, Langley-Evans SC. Exposure to undernutrition in fetal life determines fat distribution, locomotor activity and food intake in ageing rats. *Int J Obes (Lond).* 2006 May;30(5):729-38.

Jauniaux E, Poston L, Burton GJ. Placental-related diseases of pregnancy: involvement of oxidative stress and implications in human evolution. *Hum Reprod Update.* 2006 May 8;

Knudsen VK, Hansen HS, Osterdal ML, Mikkelsen TB, Mu H, Olsen SF. Fish oil in various doses or flax oil in pregnancy and timing of spontaneous delivery: a randomised controlled trial. *BJOG.* 2006 May;113(5):536-43.

Loh G, Eberhard M, Brunner RM, Hennig U, Kuhla S, Kleessen B, Metges CC. Inulin alters the intestinal microbiota and short-chain fatty acid concentrations in growing pigs regardless of their basal diet. *J Nutr.* 2006 May;136(5):1198-202.

Rees WD, Hay SM, Cruickshank M, Reusens B, Remacle C, Antipatis C, Grant G. Maternal protein intake in the pregnant rat programs the insulin axis and body composition in the offspring. *Metabolism.* 2006 May;55(5):642-9.

Szajewska H, Horvath A, Koletzko B. Effect of n-3 long-chain polyunsaturated fatty acid supplementation of women with low-risk pregnancies on pregnancy outcomes and growth measures at birth: a meta-analysis of randomized controlled trials. *Am J Clin Nutr.* 2006 Jun;83(6):1337-44.

Torrens C, Brawley L, Anthony FW, Dance CS, Dunn R, Jackson AA, Poston L, Hanson MA. Folate supplementation during pregnancy improves offspring cardiovascular dysfunction induced by protein restriction. *Hypertension.* 2006 May;47(5):982-7.

Reviews:

Demmelmair H, von Rosen J, Koletzko B. Long-term consequences of early nutrition. *Early Hum Dev.* 2006 Aug;82(8):567-574.

Langley-Evans SC, Bellinger L, McMullen S. Animal models of programming: early life influences on appetite and feeding behaviour. *Matern Child Nutr.* 2005 Jul;1(3):142-8. Review.

Makrides M, Duley L, Olsen SF. Marine oil, and other prostaglandin precursor, supplementation for pregnancy uncomplicated by pre-eclampsia or intrauterine growth restriction. *Cochrane Database Syst Rev.* 2006 Jul 19;3:CD003402. Review.

www.metabolic-programming.org
email: programming@med.uni-muenchen.de

Relevant Meetings

2007

Early Nutrition Programming Project International Conference

Early Nutrition and Health Outcome in Later Life: Obesity and Beyond
Budapest, Hungary. 20-21st April 2007
www.metabolic-programming.org/Budapest2007

15th European Congress on Obesity
Budapest, Hungary. 22-25th April 2007
www.eco2007.org

40th ESPGHAN Annual Meeting
Barcelona, Spain. 9 -12th May, 2007
www.espghan2007.org

International Conference on Fetal Programming and Developmental Toxicity
Torshavn, Faroe Islands. 20-24th May 2007
www.pptox.dk

17th ECOG Workshop
Athens, Greece. 5-7th July 2007
www.childhoodobesity.net

10th European Nutrition Conference
Paris, France. 10-13th July 2007
www.fens2007.org

5th International Congress on Developmental Origins of Health and Disease
Perth, Australia. 6-9th November 2007
www.dohad2007.org

2008

16th European Congress on Obesity
Geneva, Switzerland. 14-17th May 2007
www.iaso.org

3rd World Congress on Pediatric Gastroenterology, Hepatology and Nutrition
Iguassu Falls, Brazil. 16-20th August 2008
www.wcpghan2008.com

