The Joint Irish Nutrigenomics Organisation Symposium

BUILDING A NATIONAL NUTRITION AND GENETICS DATABASE

Exploring the diet – genes – health and ageing link

30th May 2012

Radisson Blu Royal Hotel, Golden Lane, Dublin

Programme

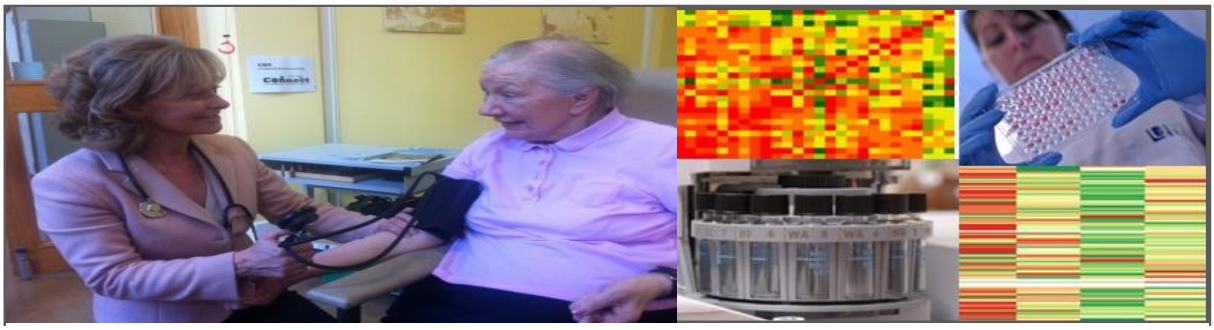
Foreword

Back in 2006, a group of researchers from around Ireland met together to discuss further initiatives in the area of food and health in Ireland.

At that time momentum was gathering in the area of Nutrigenomics, an approach that assesses the impact of nutrition on the full scale of metabolism, from the level of the gene (genomics), through to messenger RNA (transcriptomics), proteins (proteomics) and metabolites (metabolomics). It was envisaged that the integration of these state-of-the-art technologies with more traditional dietary, lifestyle and biochemistry information would allow an assessment of what is called the Nutritional phenotype, and so the concept of the National Nutritional Phenotype Database was born, a database that would integrate nutrition and genetics information on a large scale from the Irish population. Following a successful outcome to a joint research call from the Department of Agriculture, Food and the Marine and the Health Research Board under the Food Institutional Research Measure (FIRM) this concept can be brought to fruition. The completion of this database will allow Ireland to compete at the highest level in the arena of Nutrigenomics.

I sincerely hope that you enjoy this short symposium.

Prof. Mike Gibney
Project coordinator



WHERE PUBLIC HEALTH MEETS INNOVATION: Dr. Miriam Casey from the Bone Unit at St James's Hospital with a TUDA participant (left) Innovative technologies lie at the core of the JINGO project (right)

Programme

9.00 am **Registration**

9.30 am **Welcome**
Professor Sean Strain (University of Ulster)
BUILDING A RESEARCH TELESCOPE
Professor Mike Gibney (University College Dublin)

Insights from the Metabolic Challenge (MECHE) Study

9.45 am **PERSONALISING FOOD**
Dr. Miriam Ryan (University College Dublin)
DO FATS FUEL THE FIRE?
Professor Helen Roche (University College Dublin)
FITNESS AND THE METABOLIC PROFILE
Dr. Lorraine Brennan (University College Dublin)

Findings from the National Adult Nutrition Survey (NANS)

10.40 am **EPIGENETICS: HOW DOES OUR DIET DECORATE OUR GENES?**
Dr. Eileen Gibney (University College Dublin)

11.00 am **Refreshments**

Studies from the Trinity-Ulster Department of Agriculture (TUDA) project

11.15 am **B-VITAMINS IN OUR AGEING CITIZENS: IS THE BALANCE RIGHT?**
Dr. Anne Molloy (Trinity College Dublin)

VITAMIN D AND BRAINPOWER
Dr. Conal Cunningham (St James's Hospital, Dublin)

NUTRITION AND BONE HEALTH IN OLDER IRISH PEOPLE
Prof. Helene Mc Nulty (University of Ulster)

12.15 pm **Public Discussion**

1 pm **Close of Symposium**
Complimentary lunch

The JINGO Project

The Joint Irish Nutrigenomics Organisation (JINGO) is a consortium led by Prof. Mike Gibney and colleagues at University College Dublin in partnership with researchers from University College Cork, Trinity College Dublin and the University of Ulster at Coleraine. The 5-year project is funded under the National Development Plan 2007-2013 as part of the Irish Department of Agriculture, Food and the Marine's Food Institutional Research Measure (FIRM) and by the Northern Ireland Department for Employment and Learning.

The project encompasses 3 separate but complimentary studies:

- **National Adult Nutrition Survey (NANS; 1500 adults 18+ yrs)**

  This is a partner FIRM-funded project led by Prof. Albert Flynn of University College Cork in collaboration with University College Dublin. Comprehensive dietary, anthropometric, health and lifestyle data as well as targeted biochemical and genomic information have been collected from adults of all ages from the general Irish population.

- **Metabolic challenge study (MECHE; 214 adults 18-60 yrs)**

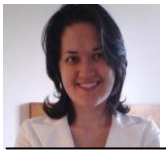
  Conducted by University College Dublin in the facilities of St Vincent's University Hospital and the UCD Institute for Sport and Health, this clinically registered trial (*clinicaltrial.gov* NCT01172951) assesses the acute metabolic response of healthy adults to the ingestion of a high fat or carbohydrate intake. Biological samples, both before and after meal intake, have been collected for biochemical and nutrigenomics analysis, as well as detailed body composition, physical fitness and function information, allowing the full complexity of the response to food intake to be assessed.

- **Trinity-Ulster Department of Agriculture Project (TUDA; 5000 adults 60+ yrs)**

  Older individuals exhibiting early signs of cognitive dysfunction, osteoporosis or cardiovascular disease are being recruited in this study conducted jointly by Trinity College Dublin and the University of Ulster at Coleraine and their affiliated clinics. Detailed medical information, biochemistry, dietary, lifestyle and genomic data are being gathered to explore diet-gene interactions across these 3 very important conditions in the elderly.

Building a research telescope
Prof. Mike Gibney, University College Dublin

Most research projects have a very defined research question as their objective. The JINGO project is somewhat different in that it sets out to construct a very comprehensive Nutritional Phenotype Database that would then be used into the future to address many challenges. The three projects within the National Nutrition Phenotype Database provide for a three dimensional analysis which integrates dietary data with phenotype data and with genomic data, the latter itself integrating genetic data with that of metabolomic data and protein profiling. Internationally, there is great interest in the National Nutrition Phenotype Database and collaborative projects have begun with groups in the EU and the US.



Personalising food
Dr. Miriam Ryan, University College Dublin

Metabolic health is driven by many factors, particularly diet. Personalised nutrition strives to tailor an individual's diet so that the composition is optimised for their particular requirements. One of the key challenges in developing tailored dietary guidelines effectively is in understanding whether the response to diet is consistent or dynamic over time, and knowing the level of variability and the factors that contribute to it is essential. The MECHE study can address this question of variability and many others by assessing the metabolic response to an oral lipid and oral glucose challenge test. An introduction to the MECHE study will be presented with some preliminary findings on the factors influencing variation in the response to dietary fat in healthy adults.

Do fats fuel the fire? Insights from metabolic challenges to highlight early markers of metabolic dysregulation
Prof. Helen Roche, University College Dublin

Nutrigenomics provides advanced approaches and tools to better understand the critical balance between health and disease. Health is based on the premise that man can respond to a metabolic response effectively – often referred to as metabolic flexibility or plasticity. In contrast, this flexibility is lost as an individual progresses through the early pre-clinical stages towards overt diet-related disease states. The metabolic challenge approach, coupled with highly detailed information arising from transcriptomic and proteomic approaches allow the possible identification of early markers indicative of health and disease. The high-density nature of the datasets arising from transcriptomic and proteomic approaches allow a network based approach to model the sets of genes, and their pathways, which often inter-connect in a very comprehensive manner to modulate metabolism. Using this gene-protein interaction network approach we can model the molecular signatures that explain several metabolic derangements that occur with a number of phenotypes such as age, increasing body weight, lean mass and insulin resistance.

Fitness and the metabolic profile

Dr. Lorraine Brennan, University College Dublin

A current limitation in the applicability of genome-wide-association-studies in the development of personalised nutrition is the lack of incorporation of gene x environmental interactions. Environmental factors such as diet, exercise, smoking, alcohol intake all play a key role in determining the phenotype. To date we are limited in our knowledge of the impact of exercise on the metabolic profile. The present talk will focus on the relationship between fitness level and the metabolic profile. Through use of the MECHE cohort we demonstrate that increased levels of certain amino acids are present in biofluids from subjects with a lower fitness level. Moreover, we link this characteristic metabolic profile with a distinct phenotype expanding our knowledge of the impact of the important environmental factor, exercise, on the phenotype.

Epigenetics: how does our diet decorate our genes?

Dr. Eileen Gibney, University College Dublin

Epigenetics has traditionally been defined as 'the study of heritable alterations in gene expression that are not caused by changes in DNA sequence'. Epigenetic processes that stably alter gene expression patterns are thought to include cytosine methylation, post-translational modifications of histone proteins and remodelling of chromatin and RNA-based mechanisms. Within the context of food and health there is considerable interest in how diet can modify the methylome (genomic-wide DNA methylation patterns), particularly how dietary factors that influence one-carbon metabolism, may influence the availability of methyl groups, and if in fact consumption or lack of consumption of a particular nutrient causes a positive or negative changes in overall or gene specific epigenetic or 'methylome' status. The vitamin folate is the primary carrier of one-carbon units destined to form the methyl groups on S-adenosylmethionine that are donated in methyltransferase reactions. As an initial study examining interactions between diet and epigenetic status, we examined the methylation status of DNA samples from selected individuals of the NANS cohort, who are at low (n=35) and high (n=31) ends of distribution for both circulating folate levels (RBC and plasma) and calculated folate intakes, thus capturing biochemically confirmed extremes of folate intakes. DNA from these subjects underwent full methylation analysis using Illumina Infinium Methylation arrays (human methylation 27 bead chip), which quantitatively interrogates 27,578 CpG loci covering more than 14,000 genes at single-nucleotide resolution. Initial findings suggest that even at the extremes of such dietary intake, there is little effect on either global or gene specific methylation patterns, with no significant differences seen in global methylation status and a maximum locus specific difference of 15% seen between the high and low groups. Such findings suggest that within this healthy population, the influence of diet, in terms of folate intake, on the status of the methylome is minimal. This study was funded in part by the UCD College of Life Sciences Strategic Research Fund, awarded for the development of Epigenetic work within UCD.

B vitamins in our ageing citizens: Is the balance right?
Dr. Anne Molloy, Trinity College Dublin

The rationale for collecting data on a cohort of older citizens within the JINGO project is to determine how age acts as a metabolic challenge and how nutrient status and genetic make-up can modulate the metabolic stress imposed by the ageing process, specifically where this stress leads to cognitive dysfunction, bone disease and hypertension. TUDA is a cross-sectional cohort of over 5,000 free-living elderly subjects age 60 years or more, recruited from out-patient clinical settings in Dublin and Ulster between 2008 and 2012, with full written consent to carry out molecular and genetic research. It consists of three sub-cohorts of 1,500-2,000 subjects in which one group has clinically verified mild cognitive impairment, the second has DXA-verified mildly impaired bone mineral density (BMD) and the third has hypertension. Data collected from this cohort include detailed clinical, anthropometric, medicinal, nutritional, lifestyle and blood chemistry information plus limited genetic polymorphism data; all participants have undergone sophisticated cognitive function, bone function and cardiovascular function tests at recruitment and 60% also have muscle function and bone density measurements including DXA analysis. All medical data are derived from a comprehensive questionnaire completed during a 90 min interview plus three separate test questionnaires of cognitive function [MMSE, FAB, RBANS]. Each of the three elements represents a continuum of disease progression from early involvement to moderate disease status. Overlapping of these disease conditions exist across the three sub-cohorts and controls for any one condition are found within the total cohort. Thus the TUDA cohort will allow the National Nutrition Phenotype Database to be explored across three very important conditions of the elderly. In addition, the ethical approval obtained for this cohort allows for future contact with participants, thereby facilitating longitudinal and prospective studies and making the TUDA cohort an extremely valuable resource for future research in ageing.

The cohort is unique in its collaboration with Northern Ireland and has received additional funding from the DEL Cross Border R&D Funding Programme: “Strengthening the All-Island Research Base. This also draws on the academic strengths of the UU and TCD partners who have had collaborative research programmes for many years studying links between status of folate, vitamin B12 and related nutrients and risk of chronic disease in the elderly. Recruitment for the TUDA cohort ends on 31st May 2012 and data collation is well underway. Some important nutritional questions are now being addressed in a preliminary way. This talk will give an overview of the cohort and present preliminary data on current topical research issues in relation to B vitamin status.

Vitamin D and brainpower
Dr. Conal Cunningham, St. James’s Hospital Dublin

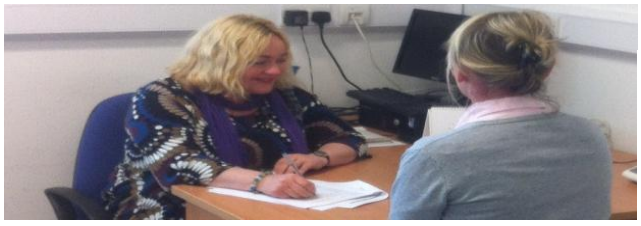
A link between vitamin D, muscle and bone disease has been long established. More recently however investigations have focused on links between vitamin D and the Central Nervous System. One of the strengths of the TUDA study is the detailed cognitive and mood assessments the patients underwent. The TUDA study has examined in detail, associations between vitamin D and both cognitive function and mood. Preliminary analyses have found some interesting results. The literature surrounding vitamin D and cognition and the preliminary findings of the TUDA study will be discussed.

Nutrition and Bone Health in Older Irish People

Prof. Helene Mc Nulty, University of Ulster

One major focus within the TUDA cohort study is the investigation of osteoporosis, an age-related, crippling bone disease that impacts adversely on the economy and on the lives of many people in Ireland. Osteoporosis is characterised by low bone mineral density (BMD), increased bone fragility and susceptibility to fractures. We aim to determine the range of nutritional, environmental and genetic factors involved in the development of osteoporosis and thus identify strategies to help maintain bone health as people age. When complete, our valuable resource will provide a detailed picture of the factors involved from a total of 3500 older people, including patients being recruited at the bone clinic in St James' Hospital Dublin, as well as participants of a similar age with generally healthier bone status (controls). Data will include not only BMD measurements (from DXA scans), but the related clinical, nutritional, lifestyle, biochemical and genetic factors. Among the nutritional factors, there is a particular focus on vitamin D, well recognised to play an important protective role against osteoporosis. Another area for investigation, not widely researched to date, focuses on the emerging scientific evidence that low B vitamin status may be linked with an increased risk of osteoporotic fracture. The extensive vitamin information available within the TUDA resource will enable a robust investigation of these nutrients and identify their potential protective roles in bone health.

Preliminary findings from 2000 individuals who were not recruited on the basis of having existing bone disease, show an overall prevalence of osteoporosis of 18%; with a greater prevalence in females (25%) compared to males (10%). Vitamin D deficiency (detected in 16%), or insufficiency (in 42%) was linked with a significantly increased risk of osteoporosis. We also find some early evidence that folate and vitamin B2 are positively associated with bone health, particularly in women. These early results highlight the need to prevent vitamin D deficiency in older people (e.g. through fortified foods, given the very limited ability in Ireland to synthesise vitamin D through the skin), and also add to the emerging evidence that folate and related B-vitamins may play protective roles against osteoporosis. These early findings will be fully explored when data from the complete TUDA cohort (including those with more advanced bone disease) are available for analysis. The roles of gene-nutrient interactions in bone disease will also be investigated, along with the potential for optimising bone health by improving vitamin status in genetically at-risk people. This exciting aspect is already showing interesting findings in relation to preventing high blood pressure as people age. Thus, the potential role of personalised nutrition in disease prevention will be a main focus of our research activities within the TUDA study cohort.



Questionnaire based work is integral to the NANS and TUDA study. Pictured here: Dr. Geraldine Horigan, University of Ulster

NOTES :

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Department of Agriculture, Food and the Marine
An Roinn Talmhaíochta, Bia agus Mara

HRB Health Research Board

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AN ROINN SLÁINTE AGUS LEANAÍ

Department for Employment and Learning
www.delni.gov.uk

If interested in finding out more about the project or to discuss collaboration please contact:

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Further information can also be found at
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