NEWSLETTER
SUMMER 2014

Welcome
by Professor Julian Mercer

Project Co-ordinator

Group in Teveltunet

I am pleased to welcome you to the latest newsletter from the Full4Health Project Office here in Aberdeen. Remarkably, it is now 18 months since the last Full4Health Newsletter. This does not reflect a lack of activity within either the Project Office or the consortium – far from it. Rather it is the consequence of a number of events and personnel changes which by chance occurred during a period when the project was already timetabled to be very busy as it reached it's half-way point in July 2013. I will cover some of these events briefly in chronological order in order to provide a flavour of what has been going on.

After considerable input from then Full4Health Project Manager, Gabi Wagner, the Alison Douglas Summer School for Early Career Researchers (ECRs) went ahead in July 2013. Partly funded by a grant from the British Society for Neuroendocrinology (BSN), and supported by travel funds and project leaders from a number of current EU-funded projects, the structure and content of the Summer School was thrashed out at the Full4Health project meeting in Lille in March 2013. Special mention in this 'realisation' of the meeting, which was really driven by Full4Health, goes not only to Gabi, but also to the representatives of our ECRs, Linda Verhagen and John Menzies: without their energy and drive we might not have made it!

Set in a unique location and with the overall science theme of 'Hunger and Satiety', the 'Food for Thought' workshop provided an unrivalled opportunity for ECRs to work and socialise with project leaders with a broad range of scientific expertise and personal experiences. This networking and career development opportunity attracted ECR delegates from BSN, EU projects and beyond. Some of the ECRs self-financed their attendance at the Summer School, and I personally valued the confidence that they placed in us. A detailed review of the meeting is on the Full4Health website (www.full4health.eu/news/5334/). This was an event of which I think we can be truly proud.

Hard on the heels of the Summer School came the preparation of the 2nd Periodic (30 month mid-term) Report covering the period to the end of July 2013. By this time Gabi had indicated that she intended to leave Full4Health and pick-up on her active research career (inside the Arctic Circle!). This move, however, was delayed until after the submission of mid-term report and delivery of the mid-term review meeting, based on this report. The review meeting was held in Brussels in November 2013. Full4Health received a thorough but constructive review, with the generally positive comments received from the expert assessors constituting a good outcome from a long day in a European Commission meeting room.

Dinner at Gamma

At the summit

In this Issue.....

- We have two research briefs; one from Professor John-Olov Jansson in Gothenburg and the other from PhD student Nikki Cassie here in Aberdeen.
- We have also highlighted an exciting research finding from Professor Duan Chen's group in Trondheim: a new clinical application of Botox as a potential treatment for obesity will enter clinical trials in late 2014.

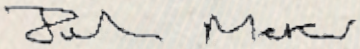
I hope that you will enjoy reading about Full4Health's latest news.

New Project Manager

At the end of 2013 we were fortunate to be able to recruit Dr Tehmina Amin to take over from Gabi, ensuring continuity in the Project Office. Many of you will have had the chance to meet Tehmina at the recent Full4Health project meeting in Trondheim, if not, then an introduction follows. Talking of Trondheim, we had an excellent scientific meeting in a spectacular location for the year 4 consortium General Assembly. We are indebted to Duan Chen and his team, and especially to Helene Johannessen, for the brilliant job they did in putting everything together for us – even the weather was superb.

ECR Mobility

One of the issues discussed in Teveltunet on the Norwegian/Swedish border was ECR mobility, and I would like to again highlight that we would be pleased to hear from any Full4Health ECR who is interested in making a study visit to the laboratory of one of the other consortium partners. This activity could be funded from the management budget held in Aberdeen. Please get in touch with the Full4Health office if you are interested in exploring this opportunity.



Hello from Full4Health's New Project Manager

My name is Tehmina Amin and I am delighted to have come on board Full4Health as Project Manager, having started in January this year.

You will all know by now that my predecessor, Gabi Wagner, left Full4Health at the end of 2013 for a return to a research career in Tromso, Norway. I would like to thank her for leaving Full4Health in such good order and wish her the best for the future.

I am a bioscientist of more than 25 years' experience, starting out in the field of Microbiology, and completing my PhD in Biochemistry at the University of Kent in 1996. After a couple of short postdoctoral positions, I decided that although research itself was not the focus I wanted in my career, I wanted to remain connected to science, but be able to redirect my significant transferrable skills. At that time, the field of science-related project management had yet to take off, but I persevered, looking for science-related jobs and got my first opportunity in a small biotech company, learning the new skills required for business development. I then progressed to variety of posts in academia, enabling me to build up a wealth of project management experience. My last position was as Research Manager for a large, academic, multidisciplinary musculoskeletal research group. I am now really pleased to be taking on the challenge of guiding Full4Health through its important final stages and to realise the dissemination of the project.

I also wear another hat – I spend half my time on Full4Health and the other half as Managing Editor for Journal of Neuroendocrinology, an online journal of which Julian is the Editor-in-Chief. The 2 jobs blend together very well and may, on occasion, have useful crossover potential.

After having spent the last 6 months familiarising myself with the project and e-mailing you all incessantly, it was a real pleasure to finally meet many of you at our 3rd Project Consortium Meeting in Trondheim, Norway in June. The meeting was a tremendous success and judging by the many comments received, was enjoyed by all who attended. I would like to thank the local team of Duan Chen and his group, particularly Helene Johannessen, who organised the venue and meeting so fantastically well. We were in a beautiful part of the Norwegian mountains and it was great to have some time to enjoy it, with walks and swimming, when we were not working. All the work packages were represented with some excellent talks, but we all know that some of the best discussions are had when time is taken out for social activities.

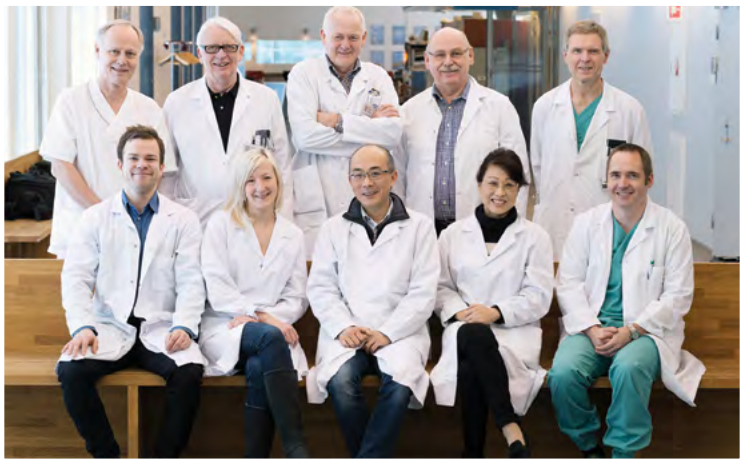
It was really encouraging to see that when we were finally discussing the potential dissemination of the project, that many of you had thought hard about this and tried to embody your work in a lay-friendly nutshell. We will capitalise on this as we now move to take Full4Health to its final stages. In the coming months, we will be hoping to reengage with EU policy makers, looking to publish special issues of F4H work in appropriate journals and making sure that the outcomes of the very important work that has been achieved in this project are communicated as widely as possible.

I wish you all every success in the final 18 months of the project.

Botox: from cosmetic use to obesity treatment

Professor Duan Chen

Department of Cancer Research and Molecular Medicine, Norwegian University of Science and Technology, Trondheim, Norway



Professor Duan Chen's research team
Photo by Geir Mogen/NTNU

Since the 1990s, Botox has become well known to the public as a means of cosmetic enhancement. Current work being undertaken by the Full4Health partner in Trondheim, Norway, is investigating a different application of Botox which may have potential as a new treatment for obesity.

During the past two decades, the number of obese individuals has increased rapidly, leading to a global obesity epidemic. Lifestyle modification through diet and physical activity has beneficial effects but these do not usually last for long, as lifestyle changes are difficult to maintain long-term. Potential weight loss drugs have also failed to provide a reliable solution to date, with effect sizes being rather limited and with a number of products which have reached the clinic having to be withdrawn due to unacceptable side-effects. So far, only weight-loss surgeries (such as gastric bypass and sleeve gastrectomy) have been shown to have long-term therapeutic effects. However, the surgery is expensive and poses significant re-operation and mortality risk. Considering the large number of obese patients, the high surgery-related cost and risk of complications, development of new minimally invasive procedures is urgently needed.

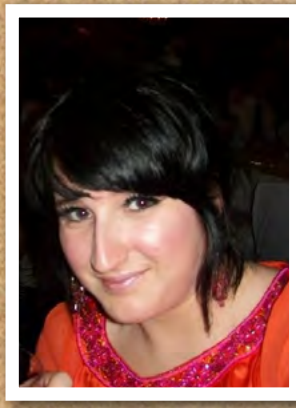
Supported by the EC research programme Full4Health, the group in Trondheim, led by Professor Duan Chen, has recently performed preclinical trials using Botox in laboratory animals. They injected Botox into the stomach wall in high fat diet-induced-obese rats, and found that Botox injection reduced food intake and body weight by 30% compared to saline injection over a course of 4 weeks. They have also used Botox injection as a "rescue method" in obese rats that underwent sleeve gastrectomy surgery but either failed to lose body weight or regained body weight after surgery. Interestingly, Botox injection worked as well in this latter group of rats: 25% weight loss. These promising results suggest that this simple therapy could potentially be a new minimally invasive treatment for obesity.

The mechanism of Botox action has been well studied. It blocks the release of the neurotransmitter acetylcholine from the nerve terminals. The stomach wall is rich in these nerves (e.g. vagus nerve) that play various physiological roles in communication between the stomach and the brain (the so-called "gut-brain axis"), and in the control of gastric emptying. The Trondheim group has found that Botox injection did not delay gastric emptying, and did not cause any pathological changes in the stomach. Currently, the research group is investigating the possible involvement of the gut-brain axis.

Botox injection has been and is still used in patients with achalasia to relax the spastic lower oesophageal sphincter. So, it can be easily injected through gastroscopy and requires the patient to stay in hospital for only a few hours. The promising results generated by Professor Chen's team have led to initiation of a Phase II clinical trial at St. Olav's Hospital, Trondheim, Norway. Obese patients have been recruited and the clinical trial will start during late 2014. Both scientists and clinicians are hoping that this simple procedure can become an effective method for treating obese patients with very little risk and significantly lower cost in comparison to any obesity surgery currently used. Given the size of the global obesity problem we face, this may prove to be an important clinical development.

Meet the Early Stage Researcher - Nikki Cassie

Obesity and Metabolic Health, Rowett Institute of Nutrition and Health, Aberdeen



I am a PhD student in the Obesity and Metabolic Health theme at the Rowett Institute of Nutrition and Health, University of Aberdeen, Scotland, under the supervision of Dr Perry Barrett and Professor Julian Mercer. We are researching gut-brain interactions in the regulation of hunger and satiety. Our aim is to investigate the impact of food structure and macronutrient content on the activation of neurones in the primary afferent areas of the brain responsible for receiving signals of GI origin.
More research is needed into how food components promote satiation and satiety.
The prospect of discoveries contributing to reduce food intake, thereby alleviating the problems of over-consumption such as obesity, and reducing pressures on food resources, is very exciting.

Gut Feeling

What is the problem this research is addressing?

When we feel hungry we eat, but what makes us stop eating and does it matter if the food we eat is a substantial dinner, or a milkshake, even if the calorie content is the same?
The current obesity epidemic comes with major consequences for health and the economy and is the leading cause of preventable premature death worldwide. In the absence of efficacious drug treatments and with surgical interventions currently being inappropriate for the majority of the overweight population, focus remains on diet and lifestyle strategies. It is widely recognised, however, that attempts at weight management through reducing the amount of calories consumed, while often effective in the short term, are generally not a long term solution as participants return to their previous habitual dietary intake, in terms of both quantity and composition. This has led to more interest in the concept of weight control by reducing appetite and energy intake, through manipulating the satiation and satiety properties of the food we consume. Such dietary manipulation could be viewed not just as treatment for obesity but also potentially as a preventative measure.

What research are you undertaking in Full4Health?

This research is investigating whether different macronutrients, and the form in which they are presented, may affect the satiation and satiety properties of ingested food. Diets high in fat, protein or carbohydrate will be presented as a solid meal, or exactly the same diet will be presented in a liquid form. In order to minimise variability, diets are based on a defined commercial diet but vary in the content of fat or protein at the expense of the carbohydrate component.
Food intake, body weight and body composition of rats fed high protein, high fat or high carbohydrate diets in either solid or liquid formulation are being recorded.
The potential of macronutrients and food structure to influence satiety is being assessed using induction of *c-fos* - a marker for neuronal activation. *c-fos* is being assessed in the hindbrain and in the hypothalamus, two key areas of the brain involved in regulating food intake. Furthermore the repertoire of hindbrain genes involved in satiation/satiety processes is not known. To this end we are seeking to use laser capture microdissection coupled with high throughput sequencing to identify gene expression changes in the hindbrain following ingestion of a meal.

What is already known about the topic?

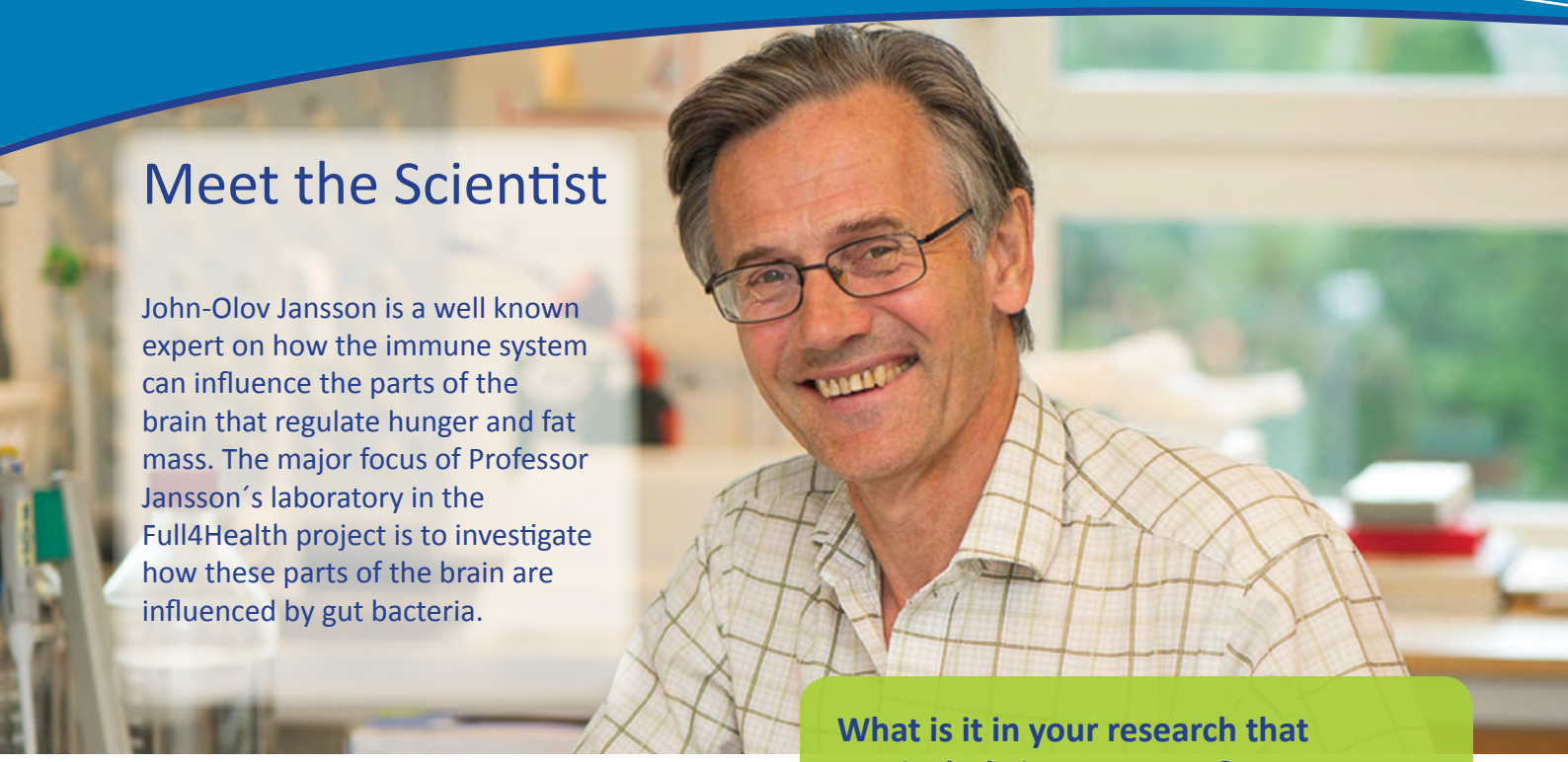
The gut is the first organ that receives food after ingestion and communicates to the brain information on the size and the composition of the meal via two types of signals. First, there is activation of vagal afferent nerve cells which respond to mechanical stimulation. This sensory mechanism provides information about the volume of food consumed. Second, peptide hormones are released from cells which line the gut following the sensing of the nutrients present in the food. These hormones, which include GLP-1, PYY and GIP, are secreted by enteroendocrine cells of the gastrointestinal tract and act either at local vagal afferent nerves connecting the gut to the hindbrain, or via their release into the bloodstream where they influence the activity of hindbrain and other areas of the brain involved in sensing food intake. Satiation and satiety signals gathered during eating are conveyed to the hindbrain and are integrated before further signalling to integrating centres in the hypothalamus and other regions of the brain.

Food composition is important for satiation and satiety; for example we know that diets high in protein tend to reduce the feeling of hunger, but we don't yet understand how the relationship between food composition and structure impacts on satiation and satiety, with respect to body weight and composition. Therefore more research is needed to establish the effectiveness of food in regulating hunger and appetite through gut-brain communication pathways.

What do you hope will be the major outcomes?

We hope to identify and characterise the neural and molecular mechanisms that are integrated in the brain's regulation of hunger and satiety, and the role of dietary macronutrients and food structure. The food-gut-brain axis is still not yet fully understood and by understanding the role of food structure and macronutrient content on neuronal activation and signalling in the caudal brainstem, we may be able suggest ways in which the food industry might manipulate food to increase satiation and satiety properties, identifying routes to preventing excess energy intake and providing the general public with better food choices for a healthier lifestyle.

Meet the Scientist



John-Olov Jansson is a well known expert on how the immune system can influence the parts of the brain that regulate hunger and fat mass. The major focus of Professor Jansson´s laboratory in the Full4Health project is to investigate how these parts of the brain are influenced by gut bacteria.

Tell us about yourself and your lab

Our lab at the Sahlgrenska Academy in Gothenburg is mainly working on interactions between the immune system and regulation of fat mass. We are elucidating the mechanisms behind the surprising finding that the immune system regulators, interleukin-6 (IL-6) and IL-1 suppress body fat in healthy animals without infection or inflammation. We recently obtained evidence that the well-known body fat-suppressing effect of glucagon-like peptide-1 (GLP-1) is mediated by IL-6 and IL-1 in the brain (Shirazy R *et al* Proc Natl Acad Sci USA 110:16199-16204, 2013).

What is it in your research that particularly interests you?

The concept that the gut bacteria may communicate with the brain and thereby influence our behaviour, e.g. with respect to food intake, is fascinating. Interestingly, gut bacteria also have links to immunity. Until recently, it was assumed that gut bacteria only had a role in digesting food.

Do the bugs in your gut influence the hunger responses of your brain?

Prof. John-Olov Jansson

The Sahlgrenska Academy
at The University of Gothenburg, Sweden

What is the problem that this research is addressing?

Recent research suggests that the bacteria in our gut send signals to our body that influence the amount of weight we put on. Some of these effects are likely to be exerted on the parts of the brain regulating body fat and hunger, but little is known about this at present.

What is already known about the topic?

The number of gut bacteria is 10 times higher than the number of cells in the rest of our body. Despite this, until recently, very little was known about the function of the gut bacteria, except that they help us to digest food. A few years ago, a group in the USA reported that mice with no gut bacteria are leaner. In addition, studies have demonstrated that the composition of the bacteria and other microorganisms in the gut differs between obese and lean individuals. To a large extent, the mechanisms behind these observations are still unclear.

What research are you undertaking in Full4Health?

Although little is known about how the gut bacteria talk to the rest of body to influence body fat, it is likely that they affect the parts of the brain that control hunger and susceptibility to body fat accumulation and weight gain. We are now investigating how the hypothalamus and the brainstem, two parts of the brain regulating hunger and body fat, are influenced by the presence of the gut bacteria in experimental studies. The project is a collaborative study combining the expertise of Prof. Jansson´s group regarding brain regulation of body fat, with that of a world leading expert on gut bacteria, Dr Fredrik Bäckhed. A first article presenting the results was recently published (Schéle E *et al* Endocrinology 154:3643-3651, 2013).

What do you hope will be the major outcomes?

We hope that we will discover important body fat regulators in the brain that are influenced by the gut bacteria, and that this will result in potential new targets for drugs to treat obesity. There is also a possibility that disturbances of gut bacteria could contribute to extensive loss of weight and appetite. New therapies for such diseases may also emerge from the present studies.

Contact us

Project Office:
The University of Aberdeen Rowett Institute of Nutrition and Health
Greenburn Road
AB21 9SB Aberdeen, Scotland, UK
+(44) (0)1224 43 8586
Email: full4health@abdn.ac.uk

Project Coordinator: Prof. Julian Mercer, Head of Obesity Research, j.mercer@abdn.ac.uk

Project Manager: Dr. Tehmina Amin +(44) (0)1224 43 8586, t.amin@abdn.ac.uk

Dissemination WP Manager: Dr. Sue Bird, +44 (0)1224 43 8668, sue.bird@abdn.ac.uk

www.full4health.eu

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