Exploring Innovative Ways to Reduce the Metabolic Syndrome

Introduction
The term metabolic syndrome, previously known as syndrome X, refers to a cluster of risk factors linked to obesity and hyperinsulinaemia that increase the risk of type 2 diabetes and cardiovascular disease. There are various sets of diagnostic criteria for the metabolic syndrome. In general, metabolic syndrome is diagnosed if a patient fulfils three out of five key criteria, which include central obesity, insulin resistance, hyperglycaemia, dyslipidaemia, and hypertension. These are often accompanied by other abnormalities of vascular function and lipoprotein metabolism.

While the value of the term has been questioned, a further definition established in 2005 and presented as a global consensus statement requires that a patient has central obesity with two other factors, emphasising the importance of abdominal obesity. Different definitions make it difficult to quantify the prevalence of metabolic syndrome, but the prevalence is clearly increasing and represents a major public health problem.

Approaches to the metabolic syndrome
Insulin resistance is an important factor in the associated disturbances in both lipid and carbohydrate metabolism. Research indicates that weight loss and exercise improve insulin sensitivity, and that decreasing saturated fat rather than total fat also improves insulin sensitivity. Thus research is exploring the potential for qualitative dietary changes to provide a mechanism for reducing the adverse impact of obesity on insulin resistance and on the metabolic syndrome.

A key challenge is how to achieve qualitative dietary change. Since individuals experience difficulty in changing their dietary habits, a complimentary approach is to make qualitative changes to the food supply, to support consumers’ endeavours to improve the nutritional quality of their diet.

Role for the food industry
A key area of investigation is whether agro-production can contribute to reducing the impact of the metabolic syndrome by altering the composition of fats in basic dietary components such as meat, milk and oils in the food supply. Though there is much still to learn about the health impacts of such manipulation, the aim in relation to the metabolic syndrome is to reduce concentrations of saturated and trans fatty acids, and to increase concentrations of monounsaturated fatty acids (MUFA) and omega-3 polyunsaturated fatty acids (PUFA).

However, this raises the issue of whether such foods can be produced in sufficient scale to make a measurable difference to the composition of the diet, as this will require substantial changes in agro-production. Other issues include the obvious cost barriers resulting from small-scale production and the need for dedicated supply chains, and the impact of consumer demand for such products on market forces.

Lipgene research project
These are all areas being investigated by the Lipgene research project, which is exploring whether changes in dietary fat quality can improve insulin resistance in subjects with risk factors for the metabolic syndrome and how changes to food chain fats can be achieved. A recent workshop explored the potential for existing and new technologies to improve the nutritional composition of animal and plant foods. It also explored the cost implications of modifications to animal nutrition and of plant biotechnologies.
With natural fish stocks in decline, increasing demand for fish oils due to the aquaculture of marine fish, and dietary advice to the population to eat more fish, an alternative sustainable source of fish oils is urgently needed, for both human diets and aquaculture.

Animal foods
Since the fatty acid composition of animal foods varies in response to how the animals are fed, research is investigating ways in which milk and meat with a more favorable fatty acid profile (lower concentrations of saturated fatty acid (SFA) and higher concentrations of MUFA and PUFA) can be produced by altering the biosynthesis of ruminant lipids. A key issue, however, is to ensure that the beneficial properties of animal-derived foods are not eroded in the push for potential health gains through altered fat composition.

Manipulating the fatty acid composition of milk
Milk fat typically contains about 70-75% SFA, 20-23% MUFA and 2-5% PUFA. Understanding the complex process that determines the proportions of the fatty acids in milk has led to the identification of several nutritional approaches that can be used to manipulate the overall fatty acid composition. Studies are investigating the addition of clover silage, extruded linseed, fish oils and microalgae to animal feed to alter the lipid profile of milk.

For example, supplements of plant oils or oilseeds in the animal feed have been shown to reduce the short and medium chain SFA, while increasing 18:1 MUFA. However, feeding fish oil with the aim of increasing very long chain (VLC) omega-3 PUFA is less successful, as there is a low transfer efficiency of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) from the diet into milk. This is because of extensive biodehydrogenation in the rumen and subsequent transport in lipid fractions that are poorly utilised by the mammary gland. However, a case study using extruded linseed shows enrichment with C18:2 omega-3. As the costs to the farmer are higher, there is inevitably a price premium for the milk produced.

Manipulating the fatty acid composition of meat
Meat fats from ruminant animals typically contain about 45-53% SFA, 45-50% MUFA and very small amounts of PUFA. Efforts to manipulate the fatty acid composition include using oil supplements rich in PUFA, high forage based diets, or fresh grass. In poultry and pig dietary sources of VLC omega-3 PUFA have been used but can result in reduced shelf-life and off-tastes in the end product. Hence, one of the key challenges is to identify novel sources of VLC omega-3 PUFA.

The Challenge to produce plant sources of VLC omega-3 PUFA
With natural fish stocks in decline, increasing demand for fish oils due to the aquaculture of marine fish, and dietary advice to the population to eat more fish, an alternative sustainable source of fish oils is urgently needed, for both human diets and aquaculture. The key hope is transgenic plants, engineered to produce fish oils.

The aims of Lipgene are to develop a sustainable source of omega-3 VLC PUFA and reconstitute the synthesis of omega-3 VLC PUFA in linseed using plant biotechnology. The advantages of developing such a source of omega-3 VLC PUFA include the healthy overall fatty acid profile of PUFA rich vegetable oils, acceptable sensory properties, and lower production costs.

Early studies at Rothampsted Research in Harpenden, have shown that it is possible to make long chain PUFAs in transgenic plants. These studies require a detailed understanding of plant lipid biochemistry in order to optimise the outcomes, and hence there is more research work to do in this area.

Currently, a key approach to increasing VLC omega-3 intake is to fortify foods such as margarines, infant milks, bakery products, milks and milk drinks. However, this presents difficulties, as fish oils are highly prone to oxidation, which has a detrimental effect on flavour and reduces shelf-life. Adding antioxidants is inconsistent with consumers’ current desire for minimal additives. Hence research work is also investigating the oxidation mechanisms in omega-3 enriched foods such as fish-oil enriched mayonnaise and milk, yogurt and fitness bars in order to develop strategies to prevent oxidation. For example, having a low pH and the presence of iron from egg yolk are two factors contributing to oxidation in mayonnaise. This can be reduced by using ethylenediaminetetraacetic acid (EDTA) or by choosing another emulsifier with a lower iron content than egg yolk.

Economic analyses
While producing basic foods with favourable fatty acid profiles sounds like an obvious way forward, there are many issues to address in order to leverage the potential health benefits of this strategy. Such foods demand a higher price due to increased production costs, and because dedicated supply chains are needed to keep them separate from standard commodities. In addition, smaller production volumes provide no opportunity to exploit economies of scale. In a recent presentation (http://www.nutrition.org.uk/home.asp?siteId=43&sectionId=1251&subSectionId=1205&subSectionId=326&parentSection=301&which=3), Economist, James Fry estimates that the total supply costs for milk, meat or eggs with ‘healthier’ nutrient profiles are 10-60% more than their conventional counterparts, of which the greatest factor is the inability to exploit economies of scale. This leads to another issue, the consumers’ willingness to pay a higher price as this ultimately determines the size of the market.

If nutritionally manipulated foods can be shown to benefit health, this presents various policy options to maximise the benefits. For example, balancing the costs of measures to increase consumer demand for such foods, resulting in increased volumes and lower production costs, against the potential to benefit health outcomes and offset costs associated with obesity, is being explored as part of the Lipgene project. The cost savings in potential reductions in obesity can only be calculated once the other areas of research in the project have been completed. So it is a question of ‘watch this space’.