Concluding Remarks

This is again to reiterate that these last 3 days have been extremely exciting; this has been one of the most interdisciplinary and collegial meetings I have ever attended. On behalf of the organizers I am delighted with the outcome, and it is quite a challenge to try and summarize it all. Let me go through some of the concepts that we have come up with.

If we are going to take a broad overview of this, if we are going to imagine that we are going to personalize diets for infants and children, we first have to ask the questions: do we really know how children differ; are there meanings for these differences; whatever the consequences of these differences are, are they genuinely the sort of long-term outcomes that one would imagine to be genuinely worthwhile? If there are differences, are we in a position to accurately assess those, are there technologies to distinguish individuals, and then finally, can we act predictably, do we know enough nutrition to genuinely change folate?

At the meeting we tried to look at these perspectives. How do children differ? There were several presentations in which the genetic basis of variation and population is described. Bert Koletzko gave a very clear indication that very specific polymorphisms in the gene responsible for desaturating polyunsaturated fatty acids have a meaningful consequence on the level of those products and on their functional role in manipulating a variety of lipid-signaling systems, so some of the variations in people are clearly due to explicit identifiable genetic polymorphisms. But we also found that the environment has an important role. Seppo Salminen and several people illustrated, for example, that if a child is born by cesarean section the chances of it being environmentally inoculated with the appropriate bacteria are much less, and so in addition to genetics the infant’s environment alone can have a meaningful long-term processing effect on phenotype and outcome. We also heard from various people, notably Peter Gluckman at the beginning of the conference, that the environment at a specific window of time, particularly in the infant and childhood period, can imprint that individual to lifelong changes in their
ability to manage the environment in which they find themselves. Peter Gluckman emphasized that our modern environment is not something that the Darwinian process really had in mind, so we have to be aware that early imprinting can have an effect and that is another extra-genetic effect on our differences. Finally, each of us has different microflora which is established early in life and remains quite persistent through to old age, a very important aspect.

We heard from Ingegerd Adlerberth how variability can be established, again not depending on genetics. If we look at the consequences, we could now spend another 3 days on this. There were very illuminating talks on the role of variations in humans on things like immunology and immune outcomes, their ability to resist disease, on allergy and the differences between people both in genetics and imprinting on the microflora, on the development and subsequent severity of allergy. I don’t think we any of us were prepared for just how devastatingly Dennis Bier would describe the obesity epidemic. Very scary numbers in United States, and I think the rest of the world is desperately hoping that the United States has gone this way on their own but to their horror they are beginning to realize that it is not the case and clearly obesity is a diet-cost phenomenon. On the hills of the obesity epidemic there is an epidemic of metabolic diabetes and the predispositions to diabetes established earlier in life are becoming particularly discouraging. The fact that mothers who are overweight and considerably more predisposed to gestational diabetes pass along that predisposition for diabetes to their infants before they are born, is again an example of a non-genetic but a particularly discouraging aspect of the individual variation that we are forcing upon in the children.

Ching Lau talked about cancer and the variations that he is seeing in the ability to predict how patients respond to treatment. Again these differences are important and the variations due to various aspects of genetics and imprinting are the consequences. We spent actually some very interesting time on the way this should be assessed. It is very clear from all these presentations that the basic idea is to take the genetic genotype and use it as a means to distinguish, to differentiate, the population, will not happen. The complexity of genotyping is just too great for prediction, and we have seen various other ways that our genotype can vary from genetics. The fact that we are different is clear; the fact these differences are important to our lifelong health is also clear, but we also realize that we cannot use genotyping as a simple means to predict lifelong health. We have to use much more innovative and comprehensive assessment technologies to see those differences.

Hans Hofstraat talked about molecular imaging and how far along the industrialization process this has come, bringing the practice to technologies for disease. He was very enthusiastic about the opportunities to be able to bring these routes of technologies and their accuracy in position to the level that we would need to be able to understand the phenotypic variation in
terms of diet and health. Genotyping was discussed, and it is clear that these technologies are coming along very successfully.

*Jason Chieh* talked about the nutrigenomic concept and that there are some very important things that genotyping actually can tell you. Selected genotypic analysis for, as *Dennis Bier* pointed out, susceptibility to methylation and improvement of neural tube defects by folate represents a very obvious opportunity. It is not that we would ignore genotyping, we just can’t use it as a sole basis.

*Rob Waterland* talked about methylation and in fact not only is he able to understand mechanistically the effect of the environment on DNA methylation, he showed that it is increasingly possible to measure this to actually assess in individuals what their early history of life did to their methylation on their own individual DNA, an astonishing advance in methodology. Expression profiling is already being brought to practice in diagnostics for cancer; it is clear that this is a very attractive assessment technology for a variety of health aspects ultimately including nutrition.

*Gerry Berry* talked about the potential of metabolic profiling using practical examples for a variety of diseases such as PKU. *Piero Rinaldo* also talked about the fact that blood spot analyses, which seems to be a very simple basic technology, are going to be a platform that will serve many of the things that we imagine, and which exist today. Ironically many of the issues that are limiting it are not scientific at all, they are related to the politics of moving forward. And we saw in the meeting that there is a great deal of ongoing debate on how much faster we can move this.

Can we act on these differences, this is sort of the good news in the bad news. This is where nutrition as a science should be delivering the actionable science on which we base the future of diet recommendations for individuals and we have to be honest, this is an area where we need some significant work. *Bo Lönnerdal* talked about proteins and the ability to understand, for example, simple variations in the amount of protein to be delivered even as simply as the phase of infant formula, early infancy, different protein level than later, a very straightforward and as you pointed out a very actionable and potentially important improvement.

Oligosaccharides, *Seppo Salminen* talked about probiotics, the ability to deliver bacteria. This is such a fascinating and growing field that there is little question that in the next few years we will see very individualized probiotics as a concept for particular individuals at risk, etc. *Bert Koletzko* again talked about lipids, the ability to recognize people who need a different lipid profile and then the ability to deliver them. Finally *Bo Lönnerdal* talked about micronutrients and treatment with for example iron, that some individuals in a population are significantly enriched, that their health is improved by the exact same amount of iron added to their diet, but that another group in that population could suffer deleterious consequences. So even something so simple, which we think of as being so straightforward, as iron supplementation
genuinely and in certain populations needs an individualized approach. So what do we need to do? It is pretty clear that we need to push methodologies that are associated with getting quantitatively accurate end points in association with diet and health, but this is an important limitation, there is no question. The trials that should be done need to incorporate the kind of methods and mechanisms capable of seeing the texture of the population. If large trials are being conducted we need to know not just how the average mean population responds, but also how the population on an individual level responds. We also have to recognize the importance of accuracy and specificity of ingredients; simply measuring probiotics without knowing for example the genome, oligosaccharides, is not enough. Feeding simple polymers and not knowing what their actual structures and functions are, we need to be much better there.

Finally the industry, it would be very good to see the industry explore methods and to actually begin to consider how to deliver personalized foods to the population. What is the business model that will make this a success? If it costs more money than it delivers, it is not going to work. We have to continue to support multidisciplinary research. Ching Lau showed us that capabilities are available; we want to bring those together and that is going to require recruiting scientists from the many disciplines that nutrition has.

We have moved very much forward in our oligosaccharide program; we would never have thought about milk and nutrition before. We brought Carlito Lebrilla and David Mills, who had not thought about the microbiology of oligosaccharides, a world class analytical chemist and a world class microbiologist together, and they are now working on a very well-defined program. I think Dennis Bier’s picture of all those walking sticks racing around Finland is proof positive that we clearly need more workshops in the northern countries. On behalf of the organizers, I am delighted that you could come and we will see you hopefully at another workshop.

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