Editorial

We are entering into a new era: as a result of outstanding progress over the last decades, the molecular nature of the interaction between nutrition, nutritional interventions and complex biochemical signalling pathways and functions have become more and more elucidated. The speed of progress is also impressive: it became highly accelerated due to new molecular techniques and the improved understanding, mainly in the field of genetics. In the present issue, we have four reports that point out new knowledge in the field of the interaction between nutrition and genetics, more commonly summarized as nutrigenetics. Different areas are discussed, such as the field of fatty acid metabolism and related health issues, the effect of nutrition and antioxidant status on disease prevention, the effect of methyl metabolism on brain development, and, lastly, a report on the molecular mechanism of epigenetic regulation with a prospective to translate this knowledge to daily life in the near future.

In the first article, Lattka et al. [1] report on the potential health benefits of polyunsaturated fatty acids (PUFA). They challenge the existing concept claiming that a sufficient supply of PUFA translates necessarily into a beneficial effect for neuronal development or prevention of allergic diseases. Research over recent years highlights that the genetic background (e.g. different polymorphisms in the fatty acid desaturase *FADS* genes) markedly determines the efficiency of how PUFAs are processed endogenously. Thus, this gene-nutrient interaction significantly modulates the effect of the exogenous supply of PUFA and, depending on the genetic back-

ground, the postulated end points are not always comparable. For example, the beneficial effect of breastfeeding on the intelligence quotient of a child clearly depends on his individual genotype with regard to PUFA metabolism. The authors develop a series of nice arguments, raising a future perspective where nutritional supplementation or strategies will be based on the individual genetic background.

In the second article, Zeisel [2] reviews exhaustively the metabolism of choline and the role of methyl-group supply on brain development. Similarly, as discussed for PUFA metabolism, clinical and experimental studies showed that the requirements of choline supply are not identical between different individuals; due to genetic advances, high-risk profiles can be identified, i.e. polymorphisms in the *PEMT* gene. This gene is regulated by sex hormones, with estrogen being a strong up-regulator of *PEMT* gene expression. However, a rather common single nucleotide polymorphism (SNP) of *PEMT* causes a loss of estrogen responsiveness, creating in premenopausal women with this particular SNP a markedly higher need for exogenous choline supply compared to the wild-type gene. To highlight the complexity of these methyl pathways, an important gene implicated in the folate metabolism is *MTHFD1* (methyltetrahydrofolate dehydrogenase 1). Certain polymorphisms lead to a decreased availability of methyltetrahydrofolate and cause an extra need for betaine (a choline metabolite) for the formation of methionine from homocysteine. To maintain a homeostatic situation, individuals with these SNP require mark-

edly higher choline and folate intake. Since choline is extremely important for neuronal development and neural tube closure, it is easily understandable from these genetic data why some persons are at a high risk for relative methyl-donor deficiency and thus have a high risk for severe pathologies. To advance rapidly, Dr. Zeisel suggests to perform appropriate studies based on genetic determinations, whereby clear data would allow one to produce individualized recommendation for supplementation. For example, this will allow one to give a precise recommendation for folate and choline supplementation to young women who wish to become pregnant.

The third article of Da Costa et al. [3] focuses on the impact of nutrigenetics on the modulation of oxidative stress. It is well established that chronic oxidative stress is implicated in the development of various chronic diseases such as cancer, cardiovascular disease and neurodegenerative diseases. Based on these studies, an optimal supply of exogenous antioxidants was postulated, such as vitamin C, E or carotenoids, to reduce disease risk. In their present work, based on rather contradictory studies, Da Costa et al. [3] demonstrate that the uptake of exogenous antioxidants is dependent on several mechanisms; different polymorphisms were reported for key enzymes in these steps, explaining why identical exogenous supply does not yield in identical effects between different individuals. In addition, a complex endogenous antioxidant system contributes to detoxify these metabolites. The authors discuss how variations in the genes coding these enzymes may impact oxidative stress and the risk of disease development, via different enzymatic antioxidant activity and levels of reactive species.

The last report of Ruemmele and Garnier-Lengliné [4] highlights the molecular mechanisms whereby nutritional modifications may impact the regulation of gene expression yielding in short-term and long-term effects. These post-genetic modifications are summarized by the term epigenetics. With the discovery of the molecular mechanisms, such as histone modification, DNA methylation, or via microRNA, it became understandable how a nutritional intervention at critical time points may cause long-term effects decades later. These molecular data allow to build a new concept of disease prevention and also provide a way of how nutritional interventions should be analyzed, i.e. in order not to overlook the long-term scale.

All four reports analyze and review the interaction between nutrition and the human genome from different standpoints but all come to a common conclusion: external nutritional modifications do not necessarily provoke the same biological effects in different individuals, especially on a long-term scale. Differences might be explained not only by individual genetic variations, but also the timing of nutritional interventions (the so-called 'window of opportunity'). There are good data to support that different time points during development in utero and early in the postnatal period constitute such windows of opportunity. These new data open an exciting and challenging future as to how nutritional interventions could be used to prevent disease development later in life.

Frank Ruemmele, Paris

References

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- 3 Da Costa LA, Badawi A, El-Sohemy A: Nutrigenetics and modulation of oxidative stress. *Ann Nutr Metab* 2012;60(suppl 3):27–36.
- 4 Ruemmele FM, Garnier-Lengliné H: Why are genetics important for nutrition? Lessons from epigenetic research. *Ann Nutr Metab* 2012;60(suppl 3):38–43.