Our principal aim within research objective Number 1 was to address the role of long-chain polyunsaturated fatty acids (LCPUFA) in the pathogenesis of inflammation in bronchial asthma. This might be even clinically highly relevant question because enhanced n-6 to n-3 LCPUFA status may favour inflammatory processes, while an excess of n-3 LCPUFAs may lead to the increased production of anti-inflammatory eicosanoids. We aimed to investigate whether there is a difference in the LCPUFA status between asthmatic and healthy control children and to investigate the relationship between the LCPUFA status and inflammatory biomarkers.

As a first step, we summarised the theoretical bases of the of our research both in a book chapter published in a prestigious book [Lohner & Decsi, book chapter 2013] and in a journal article addressed to the Hungarian paediatric community [Lohner et al, Gyermekorvos Tovabbkepzes 2013].

As a second step, we addressed the question of the availability of n-3 LCPUFA in human milk in Hungary. This investigation was also based on the role of n-3 LCPUFA to serve as precursors of anti-inflammatory eicosanoids. We investigated fatty acid composition of human milk at three different stages of lactation (3rd day, 6th week, and 6th month) in healthy Hungarian mothers. We found that contribution of arachidonic acid to the fatty acid composition of human milk significantly decreased during lactation. The contribution of docosahexaenoic acid (DHA) significantly decreased only from colostrum to the 6th week of lactation, without further changes by 6 months. From the clinical point of view, we concluded that the contribution of DHA to the fatty acid composition of mature human milk in Hungarian mothers is still among the lowest values ever reported in the literature [Mihályi K et al, Eur J Pediatr, 2015].

As a combination of research objectives Number 1 and Number 2, we explored the association of maternal milk fatty acid composition with childhood wheezing phenotypes and asthma up to age 13 years. A new statistical approach was applied in children who participated in the Ulm Birth Cohort Study and whose mothers donated human milk at the 6th week and 6th month of lactation (n=720 and n=454 samples, respectively). Adjusted risk ratios with parent-reported wheezing phenotypes and doctor-diagnosed asthma were computed using a modified Poisson regression. We observed no straightforward evidence of associations between overall breastmilk fatty acid composition and specific wheeze phenotypes or doctor-diagnosed asthma. These findings may partly be attributable to several cohort-specific factors associated with breastfeeding and breastmilk collection. Further studies could improve on ours by analysing samples of breastmilk and formula and by including all children for whom these are exclusively or together the major source of fatty acids in the first months of life [Logan et al, Allergy 2017].

Within research objective Number 2, we addressed the question of the relationship of fatty acid desaturase (FADS)-2 and in atopic dermatitis (AD) patients. We determined in a Hungarian cohort of healthy volunteers (n = 20) and AD patients (n = 20) triglyceride-, sterol- and phospholipid-bound fatty acids in the plasma, mRNA expression of FADS2 and stearoyl-coenzyme A desaturase 1 in peripheral blood mononuclear cells and FADS2 concentrations in plasma. We observed higher levels of monounsaturated fatty acids, 16:1 versus 16:0 ratios in phospholipids, triglycerides and sterol esters in patients compared to healthy subjects. In addition higher levels of the FADS2-derived n-6 PUFAs γ-linolenic acid and dihomo-γ-linolenic acid were observed in patients as well as lower levels of n-3 PUFAs. We concluded that the increased expression of FADS2 in PBMCs, as a representative tissue accessible from

human blood of AD patients, might be responsible for higher levels of FADS2-derived n-6 PUFAs and lower n-3 PUFA levels in patients [Mihály et al, Skin Pharmacol Physiol 2014;27(5):242-8.]

Within research objective Number 3, we studied the role of LCPUFA status in children suffering in parallel from two diseases with immunological pathomechanisms, diabetes mellitus (DM) and celiac disease (CD). Fatty acid composition of plasma samples of children with untreated CD only (n=20) and with pre-existing DM (CDDM, n=8) were compared to those of healthy controls (n=21). Significantly decreased docosapentaenoic (C22:5n-3), docosahexaenoic (C22:6n-3), n-3 PUFA and n-3 LCPUFA values were found in CDDM group compared to controls and celiac patients. When compared to healthy controls, significant difference was found in plasma FAs of children with newly diagnosed CD only. In summary, children with CDDM showed marked signs of reduced availability of n-3 PUFA and n-3 LCPUFA in circulating lipids [Tárnok et al, J Pediatr Gastroenterol Nutr 2015].

We also investigated PUFA and trans isomeric fatty acid status in schizophrenia patients. We found no difference in phospholipid n-3 fatty acid status between the two groups, while the values of 22:5n-6 were significantly higher in patients with schizophrenia than in controls. In triacylglycerols, values of docosatrienoic acid (20:3n-3) and docosapentaenoic acid (20:5n-3) were significantly higher in schizophrenia patients than in controls. In smoking schizophrenia patients significant negative correlations were detected between Wechsler adult full-scale intelligence quotients and values of total trans fatty acids in PL lipids, whereas no such correlation was seen either in non-smoking schizophrenia patients, or in healthy controls. Data obtained in the present study indicated that in smoking schizophrenia patients high dietary exposure to trans fatty acids is associated with lower intelligence quotients [Lohner et al, Psychiatry Res 2014].

Because LCPUFA status is associated with risk of cardiovascular diseases in adulthood, we also evaluated associations between DHA and AA levels in the umbilical cord and blood pressure and anthropometrics at 9 years. Higher AA levels at birth were associated with lower diastolic blood pressure at age 9. This observation suggests that the effect of LCPUFAs at early age is different from that in adults (Seggers et al, Early Hum Dev 100: 55-9, 2016, IF: 0.89).

Within research objective Nr. 2, we also continued follow-up investigations in children participating, as fetuses and neonates, in previous investigations. Because the associations between neonatal LCPUFA status and long-term developmental outcome are debated, we investigated the relationship between fatty acid status at birth and neurodevelopment at 9 years. We primarily studied the correlation between DHA and AA with the complex form of minor neurological dysfunction (cMND). We conclude that higher umbilical DHA levels in boys are associated with better neurological development at 9 years, whereas AA status at birth was not associated with neurodevelopment at 9 years. [de Jong et al, Early Hum Dev, 2015].

Within special research objective Nr.1 we analysed the role of trans isomeric fatty acids in influencing the availability of LCPUFA in healthy subjects. The conclusions were reported in the most prestigious journal of nutritional sciences [Decsi & Boehm, Am J Clin Nutr 2013]. We concluded that both arachidonic acid (AA) and DHA correlated significantly inversely to 18-carbon trans ismoeric fatty acids (TFAs) but not to 16-carbon TFAs, and at the sixth month of lactation AA correlated significantly inversely to 18-carbon TFAs but not to 16-carbon TFAs. Consequently, TFA and especially 16-carbon TFA TFA exposure may be a confounding

parameter in studies that investigate the relation between fetal fatty acid supply and intrauterine growth.

Also within special research objective Nr. 1, our aims were to systematically review observational studies investigating LCPUFA status from different blood compartments in overweight or obese subjects and to assess the relationship between LCPUFA profile and obesity. The meta-analysis showed significant differences in the LCPUFA composition of total plasma lipids, plasma phospholipids and plasma cholesteryl esters between overweight or obese subjects and controls. Dihomo-γ-linolenic acid (DGLA) values were significantly higher in overweight or obese subjects compared with controls in all the investigated biomarkers. The results of this meta-analysis confirmed that LCPUFA profile was altered in obesity and suggested that the differences observed in desaturase activities might be responsible for the disturbed LCPUFA metabolism in obesity. [Fekete et al, Obes Rev, 2015.].

In special research objective Nr. 2 we systematically compared fatty acid composition of plasma lipid classes in males and females. We found significantly lower contribution of both arachidonic acid and docosahexaenoic acid in plasma phospholipids in men than in women. This finding indicates that gender distribution should be regarded as significant potential confounding factor in every study assessing data on fatty acid composition of biological samples [Lohner et al, Ann Nutr Metab 2013].