[O21]

A high fat soy oil diet enhances allergic symptoms while fish oil prevents allergic sensitization to cow's milk protein in mice via induction of regulatory T-cells

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Introduction: The increased intake of n-6 over n-3 polyunsaturated fatty acids (PUFA) may impact allergic outcome. Aim was to determine the effect of dietary lipid composition on food allergy.

Methods: Mice received a low or high fat soy oil or high fat fish oil diet before and during oral sensitization with whey. Allergic parameters were assessed. Besides serum transfer experiments, splenocytes of whey-sensitized donor mice fed high fat soy or fish oil were adoptively transferred to control diet fed recipients prior to whey sensitization.

Results: The acute allergic skin response was increased in mice fed high compared to low soy fat while serum immunoglobulins were unaltered. However, in high soy fat fed naïve recipients passively sensitized with hyperimmune serum the acute skin response was enhanced compared to low soy fat. This indicates that high soy fat enhanced the effector response. Furthermore, in sham mice fed high soy fat splenic Th1- and Th2-cell frequency was enhanced. By contrast, the skin response and whey-IgE and -IgG1 levels were reduced in the fish oil group rich in long chain (LC) n-3 PUFA compared to mice fed high soy fat. Serum transfer confirmed the humoral response to be suppressed. Furthermore, in fish oil fed naïve recipients passively sensitized with hyperimmune serum the acute skin response was diminished compared to high soy fat. In addition, fish oil reduced the percentage of Th1- and Th2- cells in sham mice while enhancing FoxP3 + regulatory T-cell (Treg) in spleen and intestine. Splenocytes of fish oil fed whey sensitized donors transferred tolerance to recipients while depletion of Treg prevented this.

Conclusion: A high fat vegetable soy oil diet rich in n-6 PUFA enhances the severity of the allergic effector response in cow's milk allergic mice. Partial substitution with n-3 LCPUFA largely prevents allergic sensitization and Treg contribute to this.

Keywords: Oral tolerance; Food allergy; Dietary intervention; Mouse model

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[O22]

Alteration of mouse microbiome composition affects immunity against RSV

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Background and objective: Early bacterial colonization is necessary for the development and maturation of neonatal immunity. Inadequate innate or adaptive responses of the neonatal immune system might contribute to RSV induced disease severity. To investigate if intestinal microbial composition affects host RSV induced immune responses, we altered the gut microbiome in a mouse model for primary RSV infection and in a FI-RSV induced vaccination model for enhanced disease.

Materials and methods: Microbiome composition was altered in C57BL/6 mice using either a 7 wk dietary intervention with specific prebiotic oligosaccharides (*scGOS/lcFOS/pAOS*) or a 4 wk broad spectrum antibiotic treatment during the FI-RSV vaccination. Fecal taxonomic composition and lung RSV specific immune responses were determined.

Results: During primary RSV infection, specific prebiotic intervention increased the number of IFN-γ producing CD4 + T cells 8 days post infection compared to control diet. Moreover, in the FI-RSV model, dietary intervention decreased lung total cell influx, eosinophilia and the number of IL-4, -5 and -13 producing CD4 + T cells. Lower microbial diversity induced by broad spectrum antibiotics during FI-RSV vaccination correlated with decreased numbers of IFN-γ producing CD4 + and CD8 + T cells 6 days after viral challenge.

Conclusions: Specific modulation of the microbial composition and diversity via pre- or antibiotics correlate with different host immunity response against RSV and suggests that optimizing the early microbial implementation may have an impact on the susceptibility to RSV induced disease.

Keywords: Microbiome; Respiratory infection; Immune; Modulation

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[O23]

Metabolomics approach for the study of the cholesterol lowering effect in with glucose and cholesterol lowering effects of berberine from *Coptis chinensis* in the livers of Sprague Dawley rats

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Berberine, an isoquinoline alkaloid of the protoberberine type, is derived from the root, rhizome, and stem bark of many plant species such as *Coptis chinensis* Franch and is commonly used in traditional Chinese medicine. In this study, we present an integrated strategy to deconvolute the metabolic signatures associated with the cholesterol lowering effects of berberine in the livers of Sprague Dawley rats. The rats were dosed with berberine (50 mg/kg) and urine, liver and kidney samples were collected. Metabolites such as fatty acids, cholesterol, glucose and others in tissues samples such as liver and kidney were analysed by gas chromatography/mass spectrometry (GC/MS). The urinary metabolites were analysed using targeted profiling with liquid chromatography tandem mass spectrometry (LC/MS) and non-targeted profiling with proton nuclear magnetic resonance (^{1}H NMR). The administration of berberine resulted in a reduction of glucose, maltose, fatty acids (saturated and unsaturated) and cholesterol in the rat liver samples. However, the glucose reduction, lipid and cholesterol lowering effects of berberine in the livers of rats were not observed in the kidney samples collected. The analysis of urinary metabolic profiles on different days showed that to initiate the cholesterol reduction in the rat livers, a high rate of carbohydrate usage was found to be an early event (day 2). The results suggested that the animals utilized alternative energy sources by altering the synthesis of amino acids, fatty acids and other elements. Concurrently, changes in the level of glutamine and nucleotide metabolism for the treated animals on day 2 suggested a shift in the transmission of ATP and synthesis of nucleic acids. Finally, our results demonstrated that the combination of LC/MS and ^{1}H NMR provided a unique metabolic profile associated with the cholesterol lowering effect of berberine in rat livers.

Keywords: Cholesterol lowering; Berberine; Metabolomics

Further reading

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[O24]

Pioneer oral nutraceutical formula (PLP10) for the treatment of relapsing remitting multiple sclerosis: A randomized, double-blind, placebo-controlled proof-of-concept clinical trial

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Introduction: Multiple sclerosis (MS) treatments are products of reductionism, partially effective with no (re)myelinating/neuroprotective abilities associated with significant side-effects. We aimed to assess whether our novel interventions, formulated based on systems medicine (SM), comprising specific polyunsaturated fatty acids (PUFA) and vitamins reduce disease activity in patients with relapsing remitting (RR) MS who were either treated with disease modifying treatment (DMT) or untreated.

Methods: We contacted a 30-month randomized, double-blind, placebo-controlled, proof-of-concept clinical study at the CING. Of a total of 80 patients, 20 were randomly assigned to receive intervention A (docosahexaenoic acid (DHA)/eicosapentaenoic acid (EPA) (3:1 w/w) omega-3, linoleic acid (LA)/gamma(g)-linolenic acid (GLA) (2:1 w/w) omega-6 fatty acids, omega-3/omega-6 (1:1, w/w), other specific PUFA, monounsaturated fatty acids (MUFA), minor quantity of specific saturated fatty acids (SFA), vitamin A and vitamin E), 20 to receive g-tocopherol, intervention C, 20 to receive the combination of A and C, intervention B (PLP10) and 20 to receive placebo, as an oral solution, once daily. The primary end point was the annualized relapse rate (ARR) and the key secondary end point was the time to disability progression. ISRCTN87818535.

Results: PLP10 reduced the ARR by 70% ($p = 0.003$), in relation to the baseline ARR and the placebo increased by 46% ($p = 0.354$). For the primary end point, PLP10 reduced the ARR by 58% (95% CI 0.10–0.79, $p = 0.016$) and for the secondary end point, significantly reduced the risk of sustained progression of disability by 86% over the 2-year period (Hr, 0.11; 95% CI 0.01–0.97, $p = 0.047$) vs. placebo (Figs. 1 and 2). More patients in the PLP10 group (72%) vs. placebo group (20%) were free from new or enlarging T2-weighted lesions on brain MRI scans over the 2-year study. No adverse events were reported. Interventions A and C showed no significant efficacy.

Discussion: PLP10 treatment significantly reduced the ARR, and the risk of sustained disability progression without any adverse or significant side effects. This is the first clinical study of SM approach medical nutrient formula that holds strong promise as an effective treatment for RRMS.

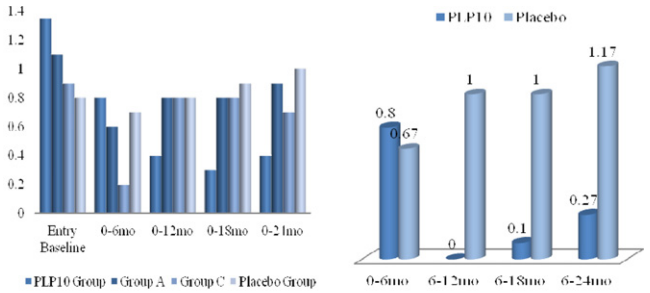

Fig. 1. Panel A demonstrates the ARR of all-time on-study patients during the 24 months pre-treatment and at different on-study time-windows per treatment-arm. Panel B demonstrates the all-time on-study population ARR between 0–6, 6–12, 6–18, and 6–24 months time windows, of PLP10 vs. placebo group.

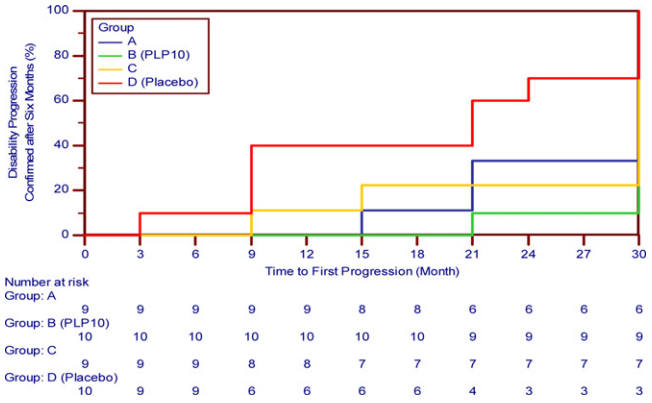

Fig. 2. Demonstrates the Kaplan–Meier plot of the time to sustained progression of disability.

Keywords: Multiple Sclerosis, Neutraceutical, Degenerative diseases, autoimmune diseases

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[O25]

Targeting gut-immune-brain triangle in neurodevelopmental disorders

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The gut-immune-brain axis has been implicated in various psychiatric disorders, including developmental disorders such as autism spectrum disorder (ASD). ASD is associated with an abnormal enteric microflora and leaky gut (Adam et al., 2011, BMC Gastroenterol; Magistris et al., 2010, J. Pediatric Gastroenterol Nutr). In addition, accumulating data indicate that the gut microbiome communicates with the central nervous system(CNS) and influences brain function and behavior (Cryan & Dinan, Nature Rev Neurosc, 2012). Interestingly, manifestation of allergic disease in early life (<12 months) is associated with differences in neurodevelopment and behaviour (Meldum et al., 2012, Early Life Dev). Many studies have identified the associations between gut immune cells, particular microbes and different allergic disease phenotypes (Russell et al., 2012, Curr Opion Gastroenterol). Furthermore, disturbed