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EDITOR'S FOCUS

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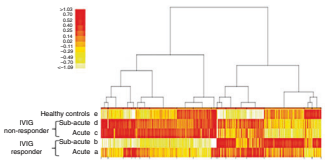
EARLY CAREER INVESTIGATOR

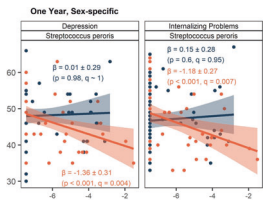
Congratulations to Olga Romantsik, the Early Career Investigator for August 2022. Dr. Romantsik completed her medical studies at Tartu University in Estonia, followed by a fellowship in neonatology at Genoa University Hospital. She credits several mentors who were pivotal in her career development, including Heili Varendi and David Ley. Dr. Romantsik's Ph.D project focused on the pathophysiological mechanisms of intraventricular hemorrhage (IVH) and potential treatment strategies. She has written several Cochrane reviews, which she believes help clinicians to make the best treatment decisions for patients. Currently a consultant in neonatology at Skåne University Hospital in Sweden, Dr. Romantsik expresses her gratitude to all her mentors and especially "the tiny patients and their families." In a paper in this issue, she and colleagues show that severe IVH alters white and gray matter development. See pages 343 and 403

KAWASAKI DISEASE



In a large population-based study in Japan ($N = 36,885$), Takeuchi et al. demonstrated for the first time that preterm infants are at high risk for Kawasaki disease (KD). The findings also suggested that exclusively breastfeeding might prevent KD among such infants. Ito et al., commenting on the paper, propose that breastfeeding may induce long-term epigenetic modifications in the immune system. Similarly, Verd et al. suggest that breastfeeding may modulate other multi-inflammatory syndromes such as COVID-19 and that an infant's feeding history is important in risk assessment of children during COVID-19. Zhao and Chen found a potential role in for long noncoding RNAs (lncRNAs) in KD, such as inhibition by SOCS2-AS1 of miR-324-5p, providing new insights into treatment of the disease. Okabe et al. found that the gene expression profile of monocytes of patients with KD identified KD-specific molecules—G0/G1 switch gene 2 (G0S2) and the lncRNA HSD11B1-AS1—associated with inflammation of innate immunity in KD. These lncRNAs may be novel key targets for the diagnosis of patients with KD. Finally, a Family Reflections piece conveys the urgent need for accurate diagnostic and prognostic testing and details the necessary research directions. See pages 557, 347, 340, 388, 378, 602

INFANT AND EARLY CHILDHOOD MICROBIOMES ASSOCIATE WITH NEUROBEHAVIOR

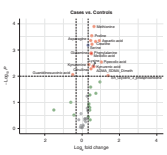


Laue et al. examined early-life microbiome and neurobehavior, including sex-specific associations. They found that infant and early-childhood microbiomes are associated with neurobehavior, including anxiety, depression, hyperactivity, and social behaviors. Gut microbiome diversity and taxa were explored at 6 weeks and 1 and 2 years, and the Behavioral Assessment System for Children (BASC-2) was completed at 3 years for 260 children. Scores for Better Internalizing Problems among boys were associated with higher diversity at 6 weeks. *Bifidobacterium* in the microbiome at 6 weeks was associated with better Adaptive Skills scores. Thus, gender-specific differences in behavior were associated with early-life microbiomes. See page 580

PEAK DOSE INTENSITY A RISK FACTOR FOR L-ASPARAGINASE ASSOCIATED PANCREATITIS

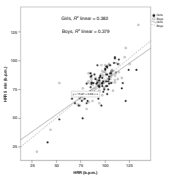
Asparaginase-associated pancreatitis (AAP) is life-threatening and may be associated with asparagine depletion resulting in reduced protein synthesis in organs with high protein turnover, such as the liver and pancreas. Chen et al. studied 353 children with acute lymphoblastic leukemia treated with L-asparaginase (L-asp) in Taiwan, of whom 14 developed AAP. The study confirmed older age and asparaginase exposure as risk factors for AAP. The finding that AAP correlated more strongly with peak dose intensity than with the cumulative dose of L-asp has implications for treatment modification and reduced toxicity. (Photo: Pornpak Khunatorn/Getty). See pages 459 and 341

BLOOD METABOLITES MAY PREDICT OUTCOME IN NEONATAL ENCEPHALOPATHY



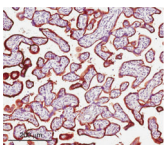
Friedes et al. used plasma metabolites from the first day of life to predict 2-year neurodevelopmental outcomes in babies with neonatal encephalopathy (NE). Infants with NE (45 versus 30 controls) underwent LC/MS/MS metabolomic profiling covering >366 metabolic pathways. Histidine and C6 sugar amine were significantly associated with cognitive, motor, and language scores, and betaine with cognitive and motor Bayley-III composite scores. Adding histidine, C6 sugar amine, and betaine to a Sarnat score-based clinical regression model improved the model's performance for Bayley-III cognitive, motor, and language scores. Discovery of metabolic pathway supplementations and/or rescue mechanisms may lead to useful adjuncts to therapeutic hypothermia for NE. See page 466

NORMAL VALUES FOR AUTONOMIC CARDIAC FUNCTION



Latorre-Román et al. compiled autonomic cardiac function reference values at rest, during maximal exercise, and in the recovery period in 512 children aged 7 to 11 years. Aerobic performance and peak heart rate were negatively correlated with body mass index and cardiometabolic risk. Over 90% of children were within the normal range for resting heart rate, with boys demonstrating lower values than girls. See page 526

HEPCIDIN'S ROLE IN PLACENTAL IRON EFFLUX



Hepcidin has a direct impact on iron transport across the human placenta. McDonald et al. found that hepcidin treatment of trophoblastic cells reduced export of iron and expression of ferroportin and transferrin receptor. Ferroportin and ferritin gene expression was lowest in placentas from small-for-gestational-age newborns. This study demonstrated the role of hepcidin in iron efflux from human trophoblasts and has important implications for understanding iron metabolism in pregnancy. See pages 396 and 605

ACKNOWLEDGEMENTS

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