BRIGHAM AND WOMEN'S HOSPITAL

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Channing Methods Meeting

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The role of vitamin D in autism: a network study

Analyzing population-based omics profiles requires summarizing multidimensional data. Correlation networks (CN) have been used for this purpose, but they do not account for the individual variability across the samples of a population. This limitation makes them unsuitable for linking a patient's omics profile to its phenotype or disease status. Here I present an alternative strategy to connect molecular patterns of single individuals with their associated phenotypic traits. This approach is based on LIONESS, a method to reverse-engineer sample-specific networks starting from an aggregate population network. I apply LIONESS to the metabolomic profiles of 381 children from the VDAART population study to investigate the neurodevelopmental role of vitamin D in autism spectrum disorder (ASD). I show that vitamin D is involved in a collection of metabolic pathways, including tryptophan metabolism, lipid metabolism, and unsaturated fatty acid metabolism. Changes in these metabolic interactions lead to different disease outcomes, wherein ASD comorbidities emerge. Closer analysis of the tryptophan pathway highlights the kynurenine subpathway as playing a key role in the neuroprotective effect of vitamin D. Interestingly, these findings were not evident from bulk co-expression analysis. In summary, our study sheds light on the functional impact of vitamin D in ASD etiology and opens new paths for the clinical implementation of vitamin D in autism treatment.

Bio: Dr. De Marzio received a BSc and MSc in astroparticle physics and a Ph.D. in Statistical Physics with a thesis on the dynamical properties of complex metastable fluids. Following her graduate studies, she was a postdoctoral fellow at M.I.T. in the group of Bin Zhang, where she investigated the 3D structure of the genome through a combination of Molecular Dynamics Simulations and theoretical models. Currently, Dr. De Marzio is a postdoctoral fellow at the Channing Division of Network Medicine at Brigham and Women's Hospital and Harvard Medical School. Her current interests lie at the intersection between computational genomics, network science, and biomechanics. Her overarching goal is to develop integrative multi-omics frameworks to understand the molecular mechanisms underlying complex diseases including asthma, COPD, and autism.