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Choline as a nutraceutical for treating neurodevelopmental disorder: Rett syndrome

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Rett Syndrome (RTT) is a postnatal neurodevelopmental disorder that primarily affects girls, with 95% of RTT cases resulting from mutations in the Methyl-Cpg-Binding Protein 2 (*MECP2*) genes. To model RTT *in vitro*, a short hairpin RNA was used to knockdown the expression of *MECP2* in primary neurons. Abnormalities in the cholinergic system have been shown to be associated with the disorder. We found choline supplementation to *MECP2*-knockdown neurons increased their soma sizes and the complexity of their dendritic arbors. Through the use of specific inhibitors targeting each of the known physiological pathways of choline, synthesis of phosphatidylcholine from choline was found to be the most important pathway in bringing about the changes seen in choline-supplemented *MECP2*-knockdown neurons. Rescue of the morphological defects could lead to enhanced neurotransmission, as suggested by an observed trend of increased expression of selected synaptic proteins in choline-supplemented cells and differences in dendritic spine density and shape between wild type and *MECP2*-knockout mice, with choline or vehicle supplementation. In addition, choline supplementation to cultured hippocampal neurons restored mini excitatory postsynaptic current frequencies in *MECP2*-knockdown cells to control levels, while the amplitude was unchanged. Choline treatment to *MECP2*-knockout mice also rescued deficits in motor coordination, anxiety-like behavior and social interaction. Taken together, these data reveal a role of choline in modulating neuronal plasticity, possibly leading to behavioral changes and hence, a potential for using choline to treat RTT.3

Biography

Eyleen Goh is a Senior Research Scientist at the National Neuroscience Institute and an Assistant Professor with the Duke-NUS Medical School in Singapore.

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