Mutations in PI3K-AKT-mTOR signaling pathway result in developmental mosaic disorders

Mutation in *PIK3CA*, one of the genes involved in the PI3K-AKT-mTOR pathway, is associated with developmental mosaic disorders which are now collectively termed as PIK3CA-Related Overgrowth Spectrum (PROS). PROS can be further divided into two subgroups based on the affected body systems, which are body asymmetrical overgrowth and central nervous system (CNS) overgrowth respectively. Body asymmetrical overgrowth includes diseases such as CLOVES Syndrome, Klippel-Trenaunay Syndrome, Cystic Hygroma and Fibroadipose Hyperplasia. More than 90% of these patients have somatic mutations in one of the 4 mutation hotspots in *PIK3CA*. CNS overgrowth includes diseases such as Megalencephaly-Polymicrogyria-Polydactyly-Hydrocephalus Syndrome (MPPH) and Megalencephaly-Capillary Malformation Syndromes (MCAP). Nowadays, it is known that germline/somatic mutations in other genes in the PI3K-AKT-mTOR signaling pathway can also result in to CNS overgrowth. Patients who have CNS overgrowth have megalencephaly and at the same time developmental delay and/or autistic spectrum disorder. In this lecture, I will present the clinical spectrum of this group of developmental mosaic disorders, and discuss the challenges for genetic diagnosis.

Acknowledge:
This work was supported by SK Yee Medical Research Fund and Society for Relief of Disabled Children.