GeNeXpreSS

Molecular Diagnosis Aids in Specific Treatment of Rare Diseases

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Miransertib in Proteus syndrome (Keppler- Noreuil et al., 2019)

Proteus syndrome is an overgrowth disorder caused by somatic mosaicism of the variant c.49G>A (p.Glu17Lys) in *AKT1* gene. Miransertib, a small molecule that inhibits AKT1 has been tried in some cancers with the same variant in somatic cells. Noreuil et al. conducted a pharmacodynamic study of Miransertib in Proteus syndrome and concluded that a dose of 5mg/m^2/day resulted in a 50% reduction in phosphorylated AKT in tissues of five out of six individuals. The authors demonstrated that 5mg/m^2/day could be used as a starting dose of Miransertib for future drug efficacy trials in patients with Proteus syndrome.

CoQ_{10} treatment in nephrotic syndrome (Starr et al., 2018)

Majority of cases of monogenic forms of nephrotic syndrome are caused due to variations in *NPHS1*, *NPHS2* and *WT1* genes. Biallelic pathogenic variants in *COQ2*, resulting in CoQ_{10} deficiency have been reported in at least 20 patients with phenotypes ranging from isolated nephrotic syndrome to multisystem disease. Starr et al. described three children with nephrotic syndrome and biallelic variants in *COQ2*. Two of these three children responded well to CoQ_{10} supplementation at a dose of 30 to 50 mg/kg/day and had complete resolution of nephrotic syndrome. The authors concluded that early molecular diagnosis helped in initiating appropriate therapy.

Deep brain stimulation in patients with dystonia (Meyer et al., 2017)

Meyer et al. described 27 individuals with early onset progressive dystonia, specific findings on Magnetic Resonance Imaging (MRI) brain and heterozygous variants in *KMT2B* gene. None of the patients responded to common anti- dystonic agents like levodopa. Ten patients of this cohort responded well to bilateral globus pallidus interna deep brain stimulation (GPi-DBS). Patients had reduction in torticollis and improvement in gait and motor function. Patients who were wheel chair dependent became ambulant once DBS was inserted. The authors stressed the need for genetic evaluation of patients with early onset childhood dystonia and suggested that patients with heterozygous variants in *KMT2B* gene should be referred for deep brain stimulation.

References

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