Abstract Title: Effect of genotype on treatment of newborn with metabolic disorders

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Abstract: A newborn can present with any organ involvement and an acute metabolic crisis such as hyperammonemia or seizures needing immediate management, or with a more chronic clinical picture such as cholestatic liver disease. Metabolic disorders can be challenging to diagnose and early detection of treatable metabolic conditions is important for initiation of therapy to improve outcomes. Whole exome sequencing (WES) or whole genome sequencing (WGS) has emerged as a powerful tool for identifying genetic disease in critically ill neonates admitted to the neonatal intensive care unit (NICU). Rapid whole genome sequencing (rWGS) of critically ill neonates in intensive care units with suspected genetic diseases has been associated with increased rate of diagnosis (rWGS diagnosed 43% versus 10% by microarray ± gene panels, $p = 0.02$) and a net reduction in cost of care post testing. The interpretation of results can benefit from parental testing. Knowing the specific genetic mutations causing the metabolic disorder is crucial for developing targeted treatments such as enzyme replacement therapy, drugs or dietary modifications. Genotype information can provide insights into the severity of the metabolic disorder and the potential long-term complications.

Several large-scale studies have been conducted of rapid diagnostic whole genome sequencing of sick newborns and several national programs exist of rapid trio genome sequencing in NICUs in countries such as Israel, and Japan. Advances in genetic research and personalized medicine continue to enhance our ability to provide targeted interventions for complex conditions and plan for appropriate long-term management strategies.

I will review the literature and also share the diagnostic efficacy and clinical utility of results of rapid WGS testing from a cohort of patients from one NICU in California, USA

Area of expertise: Translational genetics, metabolic, lysosomal, natural history, undiagnosed genetic diseases