Abstract 32. Jahrestagung der Deutschen Gesellschaft für Neugeborenenscreening

Titel : Erfahrungen aus aktuellen Pilotprojekten

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Einleitung und Ziel:
Newborn screening reliably identifies several rare diseases (RD) in Germany, allowing affected children to receive early treatment. But multiple other RD's lack methods for early identification, despite new treatment options, leading to a long diagnostic journey and significant delays in treatment initiation.
Since approx. 80% of all rare diseases are genetically determined, integration of Next Generation Sequencing (NGS) into newborn screening appears to be a promising approach to bridge the gap between expanding therapeutic options and current lack of biomarkers for early detection.

Methoden:
ENTIRE, a prospective pilot study, will enroll 1000-3000 newborns born in Berlin/Dresden, performing NGS from dried blood spot cards. Written consent must be obtained beforehand. Exclusion criteria are defined as missing written consent and age > 28 days.
Analysis will be restricted to predefined target genes. ACMG 4/5 variants in disease-causing constellations will be flagged and curated by a multidisciplinary Task Force. If the variant is reported, the family will be invited for confirmatory testing. If a disease is confirmed, treatment will be initiated in a timely manner. Statistical analysis will mostly be descriptive.

Resultate:
We have created workflows for patient recruitment, sample collection and confirmatory analysis and integrated these workflows into clinical routine at the sides involved. Furthermore, we have defined core criteria for target diseases and selected diseases based on these criteria. For validation of core genes we programmed a large language model that gathers comprehensive information from open source data. Moreover, we are currently assembling a Scientific Task Force with specialists from each addressed field, human geneticists and screening facilities alongside with patient organizations. Our workflows have been tested by temporarily recruiting for Screen4Care, a European multicentric research project on genetic newborn screening. Recruitment for ENTIRE is planned to start in Q4/26.

Schlussfolgerung:

Genomic screening measures might be an important opportunity to presymptomatically detect numerous inborn diseases in small children and thereby improve pediatric care. But, feasibility and utility in regional settings still need to be determined. Moreover, a close collaboration of newborn screening facilities, pediatric subspecialies and human geneticists is required. As a pilot study ENTIRE aims at providing a scaffold for integration of NGS methods into newbornscreening.

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