Newborn screening for severe combined immunodeficiency: experiences and pitfalls

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DNA-based newborn screening for severe combined immunodeficiency (SCID) started in August 2019. Based on a novel method for fast and cost efficient nucleic acid extraction, 407,000 newborns were screened for SCID until January 2022. Nine newborns were found and confirmed with T cell deficiency (T lymphocytopenia). T-cell excision circles (TREC) were assessed for SCID screening and an exon 7 deletion in the survival of motor neuron 1 (SMN1) gene for spinal muscular atrophy (SMA) screening in a multiplexed real-time PCR. Primers and probe for the detection of a mutation in the ß globin gene indicative of sickle cell disease were added to the assay in October 2021.

Out of these three parameters, the TREC assay exhibited the most problems regarding interpretation.

Factors influencing the TREC copy numbers from sample processing before nucleic acid extraction to the PCR assay per se will be shown. Pitfalls in the interpretation of low TREC copies, e.g. from preterm newborns and possible false negative results due to contaminations will be discussed.