High proportion of transient neonatal zinc deficiency (TNZD) causing alleles in the general population

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Abstract

Loss of function (LoF) mutations in the zinc transporter SLC30A2/ZnT2 result in impaired zinc secretion into breast milk consequently causing transient neonatal zinc deficiency (TNZD) in exclusively breastfed infants. However, the frequency of TNZD causing alleles in the general population is yet unknown. Herein we investigated 115 missense SLC30A2/ZnT2 mutations from the ExAC database, equally distributed in the entire coding region, harbored in 668 alleles in 60,706 healthy individuals of diverse ethnicity. To estimate the frequency of LoF SLC30A2/ZnT2 mutations in the general population, we used bioinformatics tools to predict the potential impact of these mutations on ZnT2 functionality, and corroborated these predictions by a zinc transport assay in human MCF-7 cells. We found 14 missense mutations that were markedly deleterious to zinc transport. Together with 2 conspicuous LoF mutations in the ExAC database, 26 SLC30A2/ZnT2 alleles harbored deleterious mutations, suggesting that at least 1 in 2,334 newborn infants is at risk to develop TNZD. This high frequency of TNZD mutations combined with the World Health Organization-promoted increase in the rate of exclusive breastfeeding, highlights the importance of genetic screening for inactivating SLC30A2/ZnT2 mutations in the general population for diagnosis and prevention of TNZD.