Why 21? The significance of selenoproteins for human health revealed by inborn errors of metabolism.

Schweizer U¹, Fradejas-Villar N².

Author information

Abstract
Selenocysteine is the 21st proteinogenic amino acid in mammals. The human genome contains 25 genes encoding selenoproteins, and their significance for human health is increasingly recognized through the identification of patients with inborn errors in selenoprotein biosynthetic factors or in individual selenoproteins. Mutations in selenoprotein N (SEPN1) lead to a spectrum of disorders collectively called SEPN1-related myopathy, and mutations in glutathione peroxidase 4 (GPX4) cause respiratory failure and bone defects, and mutations in thioredoxin reductase 2 (TXNRD2) are associated with familial glucocorticoid deficiency. Pathogenic mutations in selenocysteine synthase (SEPSECS) cause neurodevelopmental disorders, but also other factors epistatic to selenoprotein biosynthesis, such as SECIS-binding protein 2 (SECISBP2) and tRNA^[Ser]^[Sec], are known to cause complex disorders. Mutations in the latter 2 genes involve impaired metabolism and action of thyroid hormones, which lead to delayed bone growth and maturation. Mutations in SECISBP2 sometimes affect nervous system development, muscle, inner ear, skin, and immune system function, underlining the significance of selenoproteins for the organism. Mouse models helped to delineate the functions of selenoproteins and explain pathomechanisms. For brevity, this review is focused on human genetic disorders associated with selenoprotein deficiency and only briefly touches on health effects of nutritional selenium deficiency.-Schweizer, U., Fradejas-Villar, N. Why 21? The significance of selenoproteins for human health revealed by inborn errors of metabolism.

KEYWORDS: Sedaghatian; brain development; deiodinase; epilepsy; interneuron

PMID: 27473727 DOI: 10.1096/fj.201600424

[Indexed for MEDLINE]