

Concurrent Session 11: Trace Elements I

Zinc homeostasis – insights from inherited disorders of zinc metabolism

ML Ackland, AA Michalczyk

Deakin University, Centre for Cellular and Molecular Biology, Deakin University VIC 3125

Background – Zinc is an essential trace element required for growth and development. Nutritional zinc deficiency causes dermatitis, diarrhoea, reduced wound healing, neurological disturbances and increased susceptibility to infections. Zinc deficiency rates within the top 20 selected leading risk factors in relation to global deaths (1), however the extent of zinc deficiency is difficult to determine as there is no reliable indicator of body zinc status. Genetic factors can cause zinc deficiency and individuals with inherited disorders of zinc metabolism show similar features to nutritional deficiency. The genetic disorders provide an opportunity to understand the underlying pathology of zinc deficiency. A severe form of zinc deficiency is seen in some premature breast-fed babies, caused by reduced levels of zinc in maternal milk (2). We hypothesised firstly that cellular zinc transporters may be present in the mammary gland to mediate secretion of zinc into milk and secondly, that defects in one of these zinc transporters may underlie the condition leading to the production of zinc-deficient milk.

Approach – We analysed human breast tissue for the presence of the SLC30 family of zinc transporters that are predicted to cellular zinc efflux. We found that 5 members of the SLC30 family of zinc transporters were expressed in the breast. The multiplicity of zinc transporters in the lactating breast was surprising and may be consistent with the requirement for processing of zinc for different cellular functions including secretion. We then investigated three families where the lactating mothers produced milk with reduced zinc levels (25% of age-matched controls). Breast-fed infants on these mothers who produced zinc-deficient milk developed infected dermatitis, sparse hair, weakness and failure to thrive (3). Analysis of cells from mothers producing zinc-deficient milk showed reduced expression of two genes, SLC30A5 and SLC30A6.

Conclusion – The human breast expresses 5 zinc transporters belonging to the SLC 30 family. Two of these have altered patterns of expression in cells from women with inherited disorders of zinc secretion into milk. We postulate that the tissue-specific expression of different types of zinc transporters may account for the variability in zinc levels seen between different organs and tissues. Understanding the function of individual zinc transporters will facilitate the development of indicators for zinc status. Due to the multiplicity of cellular zinc transporters, genetic factors may interact with dietary factors to influence the susceptibility or predisposition individuals to zinc deficiency.

References

1. WHO World Health Report 2002
2. Michalczyk AA, Varigos G, Catto Smith T, Blomeley, R, Ackland ML 2003 *Human Genetics* 113: 202-210.
3. Agnes Michalczyk, George Varigos, Lance Smith and M Leigh Ackland. 2004 *Biotechniques* 37(2):262-4, 266-269.