Oxidative stress occurs early in Down syndrome pregnancy: A redox proteomics analysis of amniotic fluid.


Department of Biochemical Sciences, "Sapienza" University of Rome, Rome, Italy.

Abstract

Purpose: The present study aims to evaluate a set of oxidative stress biomarkers in the amniotic fluid (AF) of women carrying Down syndrome (DS) fetuses that could prove in vivo the early occurrence of oxidative damage in DS. Experimental design: To assess the extent of protein oxidation in DS AF, we measured protein carbonylation and protein-bound HNE by slot-blot analysis, total and oxidized GSH levels by enzymatic assay and heat shock proteins (HSPs) thioredoxin (Trx) induction by Western blot. Further, by a redox proteomics approach specific targets of protein carbonylation were identified. Results: We found increased levels of oxidative stress, as indexed by increased protein oxidation, lipid peroxidation, reduction of GSH and Trx levels and induction of the HSP response. By a redox proteomics approach, we identified selective proteins which showed increased oxidation in DS fetuses compared with healthy controls. The identified proteins are involved in iron homeostasis (ceruloplasmin and transferin), lipid metabolism (zinc-α2-glycoprotein, retinol-binding protein 4 and apolipoprotein A1) and inflammation (complement C9, α-1B-glycoprotein, collagen α-1V chain) with critical relevance in the clinical outcome of DS. Conclusions and clinical relevance: Our results indicate that oxidative damage is an early event in the DS pathogenesis and might contribute to the development of deleterious DS phenotypes, including abnormal development and AD-like neuropathology.

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