

MAGNESIUM DEFICIENCY ACCELERATES CELLULAR SENESCENCE IN HUMAN FIBROBLASTS

David W. Killilea (P) and Bruce N. Ames

Children's Hospital Oakland Research Institute, Oakland, California, USA and University of California, Berkeley, California, USA

Magnesium deficiency is surprisingly common. In the United States, 70% of the population has an average magnesium intake below the national recommended daily allowance (RDA), while 20% has an average magnesium intake that is even below half the RDA. Long-term magnesium deficiency is associated with cardiovascular disease, hypertension, and diabetes, though the molecular mechanisms are not understood. Altered cellular function likely has an etiological role, but few studies have investigated long-term magnesium deficiency in isolated cells. Therefore, primary human fibroblasts were cultured under magnesium deficient conditions throughout their entire lifespan. Magnesium deficiency decreased replicative capacity and increased biomarkers of cellular senescence in these cultures in a time and dose-dependent manner. The changes did not appear to be related to increased cell death. Further investigation of these cells revealed evidence of altered sensitivity to oxidative stress and changes in mitochondrial physiology. When studied in human fibroblasts that had been SV40-transformed, the pro-senescence effects of magnesium deficiency were not observed. Thus, magnesium deficiency alters cellular and mitochondrial function and accelerates the senescent phenotype in normal human fibroblasts. It is possible that these changes induced by long-term magnesium deficiency may promote or exacerbate age-related disease.