Effect of Folate on Endoplasmic Reticulum Stress Caused by Hypoxia

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Introduction: Endoplasmic reticulum (ER) stress is involved in the pathogenesis of congenital cardiac defects, intrauterine growth restriction, craniofacial anomalies, and many common diseases. The purpose of this study was to test if folic acid (FA) can mitigate ER stress or improve recovery of cells from ER stress.

Methods: Human dental pulp stem cells (HDPSC, Celprogen) were cultured in the presence or absence of folate (Molecular Products). Alpha MEM cultivation medium was supplemented with 10% human serum, L-glutamine, and penicillin/streptomycin mixture. Folic acid concentrations were 0.002 µg/ml, 0.2 µg/ml, 2 µg/ml, and 20 µg/ml. Cells were grown in triplicates in atmospheric oxygen and in 0.5% oxygen (Biopherix chamber) with adequate controls.

Results: HDPSC were cultivated in 0.5% oxygen for 1, 2, 4, and 6 hours. An optimal timing was determined. HDPSC were cultivated in different concentrations of FA in atmospheric oxygen for 3 days. Compared to controls, no difference in cell counts was observed. HDPSC were subsequently exposed to 0.5% oxygen for two hours in different concentrations of folic acid. A significant decrease in the number of dead cells was found when HDPSC were maintained in a medium containing 2 µg/ml or 20 µg/ml of folic acid.

Conclusions: FA maintained the viability of approximately half of HDPSC in 0.5% oxygen for two hours. This study will enable us to better understand the underlying molecular mechanisms and processes attenuating ER stress.