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DEVELOPMENT AND AGING ARE OXYGEN-DEPENDENT AND ARE CORRELATED WITH HIF ALONG LIFE-SPAN

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Aging asa cumulative result of oxidative damage to cells which derives from aerobic metabolism and is influenced by environmental and genetic factors. Environmental factors include temperature, diet and oxygen availability. During development and aging vascular remodeling represent a critical adaptive response to tissue hypoxia. Hypoxic Inducible Factor (HIF) has a crucial role and is modulated by the oxygen levels with an age-dependent response in neonates, adult an aged people. HIF integrated the decrease in oxygen cellular levels with the gene expression. During hypoxia the degradation of HIF is reduced and HIF accumulates in the cells. ROS are generated under hypoxic conditions and the accumulation of free radicals during life reduces the ability of tissues to remove. We investigated through immunohistochemistry, the presence and location of HIF-1 and VEGF in human carotid bodies (CB) sampled at autopsy from three children (mean age +/- SD: 2 year +/- 66 days),four adult young subjects (mean age +/- SD: 44.3 +/- 3.4 years) andfour old subjects (mean age +/- SD: 67.3 +/- 3.4 years). Positive HIF immunoreaction was detected in the CB in the adult and aged subjects, respectively (1.7+/-03.4% versus 3.2+/-0.9%), whereas the children's CB tissues did not show a HIF-1 reaction. Positive VEGF immunoreactivity was significantly higher in the children's CB tissues (7.2+/-1.2%) and in the aged subjects (5.2.6+/-0.2%) than that in the adult (1.4+/-2.8%). The increase of HIF along the life axis suggests a possible involvement of HIF as an oxygen sensor in the aging process. Prevention of oxygen desaturation, reducing all causes of hypoxemia from neonatal life to aging would decrease the incidence of diseases in the elderly population with a lifespan extension.