Reactive Oxygen Species (ROS)-related gene expression

Reactive Oxygen Species (ROS)-related gene expression in glioma

Reactive Oxygen Species (ROS)-related gene expression encompasses the transcriptional regulation of genes involved in the production, detoxification, and response to ROS, as well as the cellular signaling pathways they influence. ROS are key molecules in various physiological processes, such as cell signaling, immune response, and apoptosis. Dysregulation of ROS levels can lead to oxidative stress, contributing to diseases like cancer, neurodegeneration, and cardiovascular disorders.

Genes Associated with ROS Production

Mitochondrial ROS Production:

MT-ND1, MT-ND2: Encode components of Complex I in the electron transport chain, where superoxide is generated.

CYCS (Cytochrome C): Links the mitochondrial electron transport chain to ROS-induced apoptosis.

NADPH Oxidase Complex (NOX Family):

NOX1, NOX2, NOX4, NOX5: Catalyze the production of superoxide from oxygen using NADPH.

DUOX1, DUOX2: Generate hydrogen peroxide and play roles in thyroid function and epithelial defense.

Xanthine Oxidase (XDH):

Converts hypoxanthine to xanthine, producing superoxide as a byproduct.

Cytochrome P450 Enzymes (CYPs):

Byproducts of these monooxygenases include ROS, particularly in drug metabolism.

Genes Associated with ROS Detoxification

Superoxide Dismutases (SODs):

SOD1 (cytosolic): Converts superoxide to hydrogen peroxide in the cytoplasm.

SOD2 (mitochondrial): Protects mitochondria from oxidative damage.

SOD3 (extracellular): Detoxifies superoxide in extracellular spaces.

Catalase (CAT):

Breaks down hydrogen peroxide into water and oxygen, preventing oxidative stress.

Glutathione Peroxidases (GPXs):

GPX1, GPX4: Reduce hydrogen peroxide and lipid peroxides using glutathione.

Peroxiredoxins (PRDXs):

PRDX1-6: Detoxify peroxides and contribute to cellular redox signaling.

Thioredoxin (TXN) System:

TXN1, TXN2: Reduce oxidized proteins and ROS through electron donation.

Genes Regulating Cellular Responses to ROS

NRF2 Pathway (NFE2L2):

Activates a broad antioxidant response, inducing genes like:

HMOX1 (heme oxygenase 1): Antioxidant and anti-inflammatory effects.

NQO1 (NAD(P)H quinone oxidoreductase 1): Detoxifies quinones and reduces ROS.

GCLC, GCLM: Catalyze glutathione biosynthesis.

Hypoxia-Inducible Factor (HIF-1α):

Regulates genes involved in the adaptation to oxidative stress under low oxygen conditions.

AP-1 (FOS, JUN):

Transcription factor complex that modulates gene expression in response to oxidative stress.

p53 (TP53):

Activates genes involved in DNA repair, cell cycle arrest, and apoptosis in response to ROS-induced damage.

FOXO Family (FOXO1, FOXO3):

Induce antioxidant genes like CAT, SOD2, and others to mitigate ROS damage.

ATF4 (Activating Transcription Factor 4):

Regulates genes in response to oxidative and endoplasmic reticulum stress.

Disease Implications of ROS-Related Gene Dysregulation

Cancer:

Overexpression of NOX4 promotes tumor growth by increasing ROS.

Downregulation of NRF2 or overactivation may lead to oxidative damage or chemoresistance.

Neurodegenerative Diseases:

SOD1 mutations are linked to amyotrophic lateral sclerosis (ALS).

Increased ROS contributes to mitochondrial dysfunction in Alzheimer's and Parkinson's disease.

Cardiovascular Diseases:

Overactive NOX2 and reduced SOD2 exacerbate oxidative damage in ischemia-reperfusion injury.

Diabetes:

Increased ROS in mitochondria and reduced detoxification by CAT and GPX1 lead to endothelial dysfunction.

Experimental Tools for ROS-Related Gene Expression

RT-qPCR: To quantify expression of ROS-related genes.

RNA-Seq: For a comprehensive analysis of gene expression changes in response to ROS.

ChIP-Seq: To study transcription factor binding (e.g., NRF2, p53) on ROS-related genes.

Western Blot: To measure protein levels of ROS detoxifying enzymes (e.g., SOD, catalase).

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