Gene Section
Review

PRXL2C (Peroxiredoxin like 2C)

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Abstract

Review on PRXL2C, with data on DNA, on the protein encoded, and where the gene is implicated.

Keywords

PRXL2C; oxidation; reduction; Mutation; Overexpression; Cancer; Gastric cancer; Attention-deficit/hyperactivity disorder

Identity

Other names: C9orf21, AAED1

HGNC (Hugo): AAED1

Location: 9q22.33

DNA/RNA

Description

Six exons, four splice forms, one of which codes for a protein:

Transcription

Coding transcript: 2863bp

Protein

Description

A selenoprotein is a protein containing selenocysteines (Sec), with an atom of selenium SHE taking the place of the sulfur SH of the cysteine. Decoding of UGA into a selenocysteine (Sec) is alternative to the stop signal in the canonical genetic code.

The human selenoproteins (SelU family) are composed of three Cys-containing members, one of which being PRXL2C (Ensembl ENSG00000158122) (Castellano et al., 2004). PRXL2C amino acids 68-71 are: CYIC, a CXXC motif. According to InterPro http://www.ebi.ac.uk/interpro/protein/Q7RTV5, PRXL2C signature matches with thioredoxin-like superfamily in amino acids 35-135 (or 21-90) (with a thioredoxin CXXC motif at aa 68-71 (CYIC); the two cysteines can forms a disulfide bond), and also matches with peroxiredoxin-like 2A/B/C in aa 86-196 (or 40-150). Peroxiredoxins and thioredoxins are involved in oxidation-reduction process (antioxidants). Peroxiredoxins form a family of thiol oxidoreductases and play a role in peroxides detoxification (see Figure2). A peroxidatic cysteine reduces the peroxide to water. Thioredoxin system reduce peroxiredoxins restoring to them their catalytically active form (West et al., 2018).

Expression

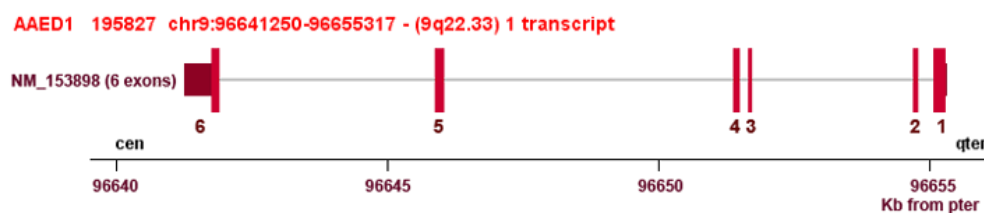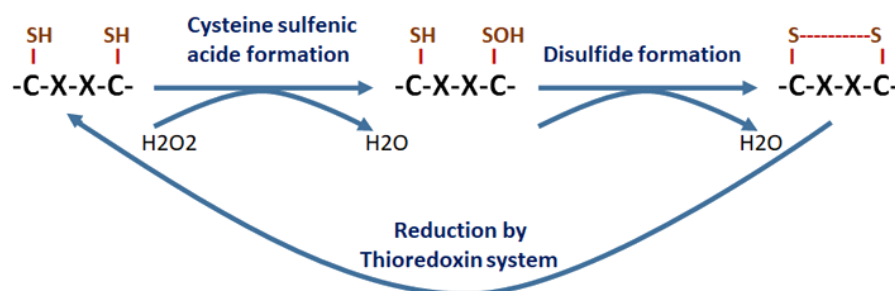PRXL2C is widely expressed (The Human Protein Atlas).

Figure 1 PRXL2C gene

Figure 2 Peroxides detoxification by Peroxiredoxins motifs -C-X-X-C-

Function

Aaed1 was found to be one of the few primitive endoderm transition markers in preimplantation mouse embryos (Gerovska and Arauzo-Bravo, 2016).

Mutations

Somatic

According to Cosmic
Glioma astrocytoma grade IV amino acid (aa) mutation: p.V91A from CDS mutation c.272T>C
Papillary thyroid carcinomas aa mutation p.I81S (c.242T>G)
Thyroid carcinomas NOS aa mutations: p.V95L (c.283G>T); p.G183V (c.548G>T)
Lung small cell carcinoma aa mutation: p.E136K (c.406G>A) (Rudin et al. 2012)
Lung adenocarcinoma aa mutations: p.H145N (c.433C>A) (Imielinski et al. 2012); p.S152L (c.455C>T)
Skin melanoma aa mutations: p.M131I (c.393G>A); p.S148L (c.443C>T); p.W159* (c.476G>A)
Colon adenocarcinoma aa mutations: p.E76D (c.228G>T); p.L110Q (c.329T>A) (Giannakis et al. 2016); p.S143I (c.428G>T) (Giannakis et al. 2016); p.Q208H (c.624G>T) (Wood et al. 2007); p.P221H (c.662C>A)
Duodenum adenoma aa mutations: p.K201N (c.603A>C) (Yachida et al. 2016); p.T218A (c.652A>G) (Yachida et al. 2016)
Prostate adenocarcinoma aa mutation: p.H214R (c.641A>G)

Implicated in

Gastric cancer

(AhpC/TSA antioxidant enzyme domain containing 1), which is upregulated in gastric cancer cells. Silencing of PRXL2C inhibited cancer cell proliferation in vitro in gastric cancer cell lines. Possibly though MAPK signaling, PRXL2C upregulates HIF1A (hypoxia inducible factor 1 subunit alpha), a transcriptional activator of many genes, including glycolytic enzymes and glucose transporters in aerobic glycolysis (Zhang et al., 2018).

Renal cancer

PRXL2C High expression is related with an unfavourable prognosis according to the Human Protein Atlas https://www.proteinatlas.org/ENSG00000158122-AAED1/pathology

Attention-deficit/hyperactivity disorder (ADHD)

A rare variant of PRXL2C (rs151326868) amino acid p.H200D (c.598C>G) was found to segregate with ADHD in one of the families with an apparent dominant inheritance that was studied (Corominas et al., 2018).
PRXL2C binds PICK1 (Protein Kinase C-Alpha-Binding Protein) and PICK1 binds SLC6A3 (solute carrier family 6 member 3, also known as DAT, the dopamine transporter 1), regulating SLC6A3 trafficking in presynaptic sites of dopaminergic neurons, and DRD3 (dopamine D3 receptor 3). PICK1 also has a role in glutamate receptor regulation (Corominas et al., 2018).

Disease
ADHD is characterized by of lack of attention, impulsivity, hyperactivity and distractibility.
It is a highly heritable (80%-90%) childhood behavioral disorder with a prevalence estimated at 5-7% in children, male predominance, and half of them have persisting symptoms in adulthood.
In addition to genetic factors, environmental factors (adverse circumstances in maternal or children life) have been implicated in the etiology of ADHD.

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