G6PD, EXON 12 IS AN EXONIC SPLICING SILENCER CONTAINING/SUBSTITUTED DEFINE CODON REGIONS INVOLVED IN THE G6PD MRNA[i]

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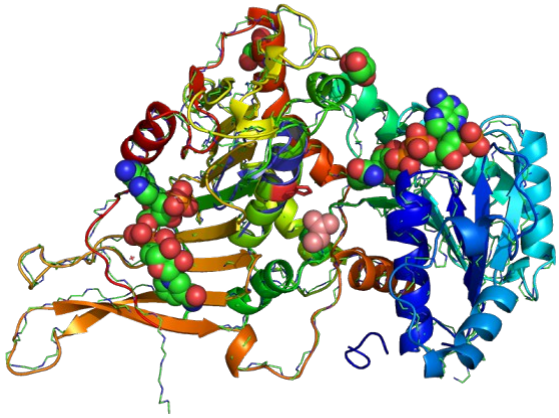
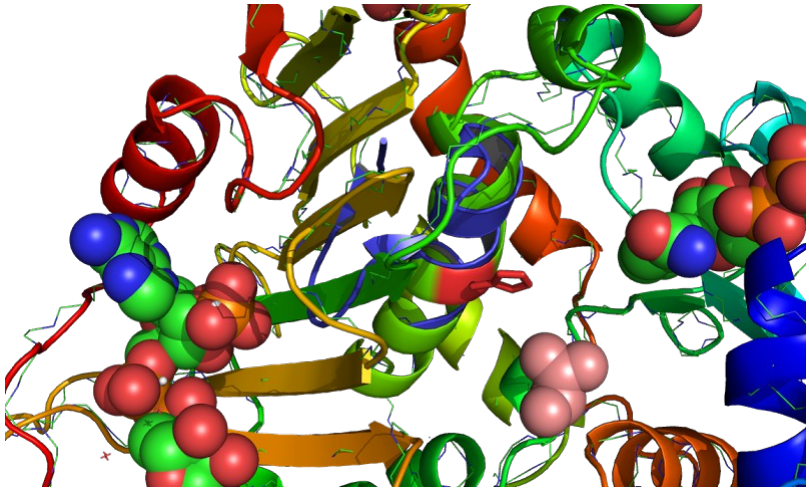
G6PD (EC 1.1.1.49) glucose-6-phosphate dehydrogenase [§§; †, ‡], situated at Xq28 locus-coding region is the rate-limiting enzyme, of the (PPP) pentose phosphate pathway. G6PD deficiency and its X-linked gene mutations exons 2-13 (160 different mutations) are the most common inborn error of metabolism, in human red blood cell (RBC) enzymopathy, among humans. G6PD is divided into 12 segments and involves an exonic splicing enhancer (ESE) in exon 12 with 13exons and an intron present 5' UTR, proximal to the 5' bkp-breakpoint region. Intron comparisons from the second to the thirteenth exons of G6PD gene, 3′ UTR towards the 3' end of the gene to exon 1 located in 5' UTR G6PD is a region of deleted alleles (ASO-PCR) or G-6-PD the many population genetics variants/wild-type (160 different mutations and 300 G6PD variants) assuming that, at exon2 (2,3-BPG* levels) are hypothesized that G6PD partly 'overlaps' the IKBKG gene confined to the blood. The subunit (G6PD), consists of the biochemical-characteristics of 531 amino acids. This enzyme is the only process in mature red cells for NADPH-generation it involves oxidation of glucose as a » hexose « (OBJ xenobiotic compounds) pathway ('naturally found in D-* and the unusual L- Monosaccharide forms or between 2,3-BPG*) pentose and hexose phosphates, an alternative to glycolysis, converts glucose in which ATP is produced' from the conversion of glucose-6-phosphate into ribulose 5-phosphate in liver cytosol in which a residue in the dimer interface (@ 37° C) structural G6PD is a NADP+ dependent. At the tetramer interface an Apoenzyme (PDB:2BH9), that stimulates G6PD to produce (reversible enzyme transketolase (TK) presence is necessary) more NADPH. Hemolytic crises or dysregulated NADPH oxidase located in the 3' dependent 5' UTR G6PD in humans determines the response, in which G6PD deficiency is prevalent with development of chronic hemolytic «« anemia (CNSHA-HNSHA) associated with food-induced or a exogenous-agent and drug-induced º" ª hemolytic crises which led to the discovery of G6PD deficiency. Sulfatase (STS, EC 3.1.6.2) catalyzes Phenyl-Piracetam OBJ it also stacks well and involves the phosphoinositide 3-kinase (PI 3-kinase) pathway in the employed doses in related induction of certain enzyme (Glucose 6PD) synthesizing activities (glycolysis) five metabolite levels of insulin signal transduction. These include, Sulforaphane OBJ or broccoli-sprout extracts increased cell-lysate NAD(P)H:quinone oxidoreductase (NQO1) phase II activities (Tanshinone IIA⊕), administered to cells and in human supplementation studies, were found to be in balance with green tea extract (GTE), (EGCG) epigallocatechin-3-gallate OBJ to generate detoxifying reactions to hepatotoxicity (can be prevented by amalika, Emblica officinalis OBJ which supports the chemopreventive action of the silymarin extract Silibinin OBJ, of the milk thistle) preventing nitric oxide-mediated lipid peroxidation (LPO) and antioxidant defense system (GSH) glutathione (GSH-Px and GR) depletion, via an antioxidant response element (ARE OBJ⊕) mechanism-based inhibitor, element (NRF2) regulates (ARE)-regulated genes. A lack of NQO1 protein predisposes cells to benzene toxicity and to various forms of leukemias and toward therapeutic modulation (Acetylcysteine OBJ and acetaminophen) of pulmonary oxygen toxicity. G6PD-deficient variants is the result of various enzymopathies (but not GPI-chronic hemolysis), that glucuronidated-bilirubin values (UGT1A1 genotype) tended to parallel, (CNSHA) hyperbilirubinemia with hemolytic anemias, single amino acid substitutions resulting in 'mutation of variants'. Or to inherited³ and acquired physiologic changes in red cell enzyme G6PD deficiency leading to favism (an A- variant reaches the polymorphism level the commonest a Mediterranean form, other alleles A, A+, the primordial human type B cell and normal B+ and a rare B- phenotype are neutral. Malaria-infected human red cells possess at least two pathways (in a dimer -- tetramer equilibrium) where carbonic anhydrase (CA) isoenzymes (allozymes are variants often neutral) the native structure may serve different roles [malaria resistance] in the G6PD-deficient erythrocyte) and transmitted biochemical poly(A) characteristics (58 different -missense-mutations account for 97, poly(A) -substitutions-towards mutation of variants) divided into 5 classes of

energy metabolism {chart} enzymes. Where GSH represents red cell enzymes involved in glycolysis, enolase (ENO), phosphoglycerate kinase (PGK), phosphofructokinase (PFK [OBJ] that phosphorylates fructose 6-phosphate (PHI)), hexokinase (HK), aldolase (ALD), and pyruvate kinase (PK)) activity. From class 1--chronic variants with administration of 8-azaguanine to class IV--increased enzyme activity. NADP-linked enzymes, malic enzyme (ME, EC 1.1.1.40) malic dehydrogenase (MDH) that catalyzes (NAD-ME) by the chemical reaction to NADP-ME and ATP:citrate lyase (ACL) and (IDH)-isocitrate dehydrogenase (NADP-ICD) channeled NADPH into the fatty acid biosynthesis influences carbohydrate metabolism and partly account for stimulated nucleotide synthesis. Poly(A) RNA by carnitine- palmitoyl (CPT) and acyl (ACO) mRNA, or HMG-CoA oxidase donating activities in inhibition of meiotic maturation, acetyl-CoA carboxylase (ACC) was also measured in the forming DNA adducts. The metabolism of xylitol remains intact to complete the NADPH cycle. The G6PD gene is X-linked, G6PD synthesis leading to G6PD deficiencies which occurs in the oocyte where X-inactivation (Xq13-XIST; 314670) large deletions or a loss-of-function mutation does not occur or might be lethal, had affected the red cell and white cell series differently, in the mouse presumably the polymorphisms of hemoglobin are on the X chromosome in man, according to hybrid cell studies of a number of domesticated species.

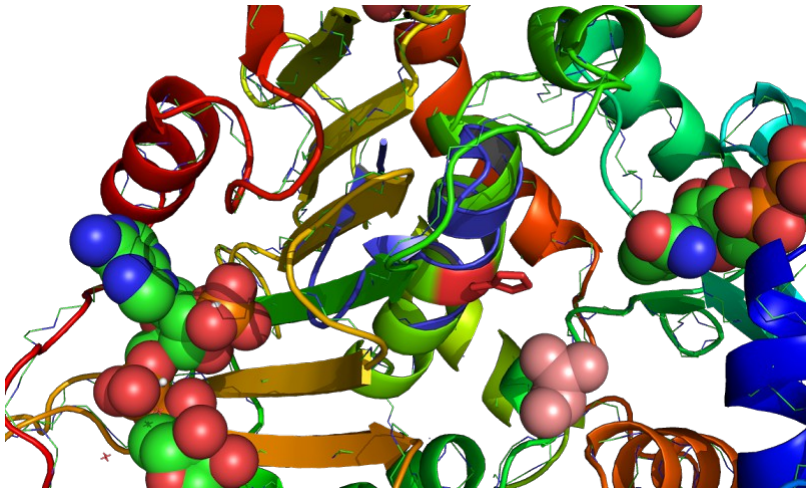
Exon 12 is an exonic splicing silencer containing other-(exons II, III-IV, V, VI-VII, VIII, IX, X, and XI-XIII)-spliced exons regions and an exonic splicing enhancer (ESE) in exon 12. Using the G6PD model, Exon 12, may define *12 base pairs*, or two DNA base substitutions in the deamano-NADP (EC 1.1.1.49) utilization.



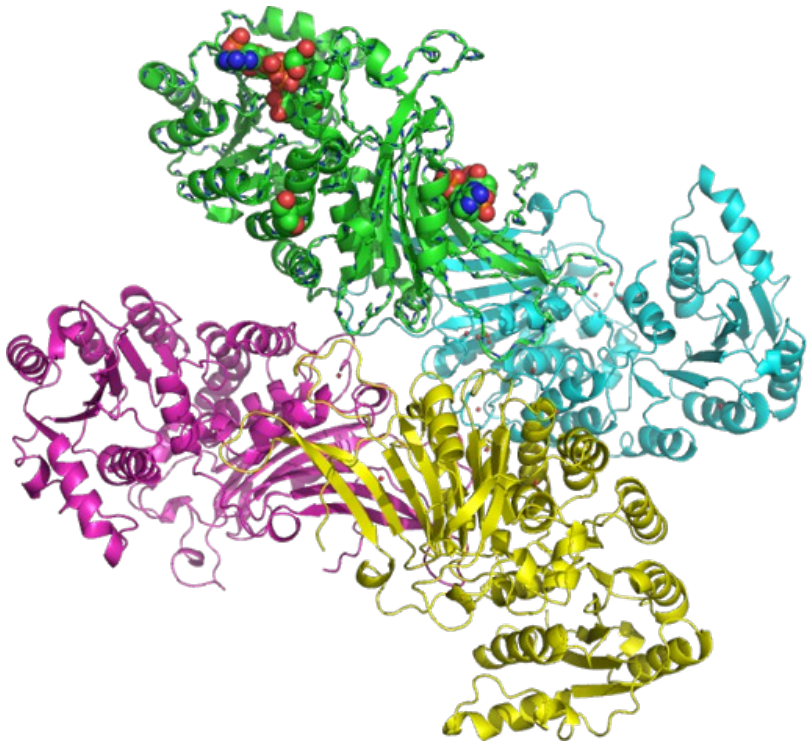
A regulatory element within exon 12 controls splicing efficiency and the rate of intron removal. The UGT1A1 gene and the exon 12 of G6PD gene and the polymorphisms of UGT1A1 two DNA base substitutions C1 and C2 for example Gly71Arg from Arg to His are the mutational activities (dimer **pink** PDB: rasmol_php SNP: L235F, Figs. 1-2 and 3) of serine-arginine-rich (SR), proteins located in exon 12 of the G6PD gene.



The most common mutations are: 1376 G-->T substitution abnormality (C1) and 1388 G-->A (G6PD Kaiping) abnormality (C2) is A-->G in exon2, both in exon 12 binding to the C-rich motifs (ESE) blocked binding of the serine-arginine-rich splicing factor 3 (SRSF3) but not SRSF4, PDB-2I2Y.



Where G6PD partly 'overlaps' the IKBKG gene PDB: 2JVX-**blue**-cartoon located in the ribbon with the ESE-**red**-exon (XII) 12. The G6PD gene is 18 kb long divided into 12 segments ranging in size from *12 base pairs* to 236 bp and interacts with elements in the beta-globin HBB common polymorphism site C1311T/IVS-II promoter are more common forms of the protein hemoglobin in the beta-globin HBB derived from the 3'-end of intron 7 is one of the 2 types of subunits in human red cell (RBC) G6PD. An ratio between heterozygote and hemizygote in males and between hetero and homozygote in females of cellular components evident from the state of G6PD activity modified by the rate of (GdX PMID: 8786131, PDB:2BH9 a deletion variant of G6PD PMID-17637841) intron removal , shows that an intron present on the 5' UTR (located on Fig. A, the end of **blue** cartoon situated near the broken **blue** strand) of G6PD the first intron of the G6PD genome isozymes can be observed, 'GdA and GdB'[3] can be bound by NADP by a direct source of ROS effects of high glucose, inhibition of PKA decreased ROS can use a direct repeat-3 (DR3) vitamin D response element liganded vitamin D receptor.



i Szeszel-Fedorowicz, Wioletta, Indrani Talukdar, Brian N Griffith, Callee M Walsh, and Lisa M Salati. “An Exonic Splicing Silencer Is Involved in the Regulated Splicing of Glucose 6-Phosphate Dehydrogenase mRNA.” *The Journal of Biological Chemistry* 281, no. 45 (November 10, 2006): 34146–34158. doi:10.1074/jbc.M603825200.