Gene expression disorders / Questions and case reports

Questions

1. **Translation of 2200 bp mRNA results in a product the size of:**
   - A – 1100 bp
   - B - 494 amino acid residues
   - C – 196 kDa
   - D - 985 amino acid residues
2. **Tissue-specific mRNA editing is provided mainly by:**
   - A - mitochondrial specific tRNAs
   - B - eRNA
   - C - gRNA
   - D - ribosomal RNA (rRNA)
3. **A frameshift mutation does not usually lead to this change:**
   - A - New cap creation or the placement of the cap in a new place
   - B - Elongated protein
   - C - Altered biological half-life of the protein
   - D - New stop codon creation
4. **Which answer is incorrect? Nuclear gene expression is regulated:**
   - A - By transcription factors
   - B - In the promoter region
   - C - Using nuclear receptors
   - D - Via negative feedback according to the amount of mRNA in mitochondria

Aswers

Question 1.

- A - Wrong. During translation, a polypeptide is formed.
- **B - Correct. One amino acid is encoded by a triplet. Part of the mRNA consists of regions that are not subject to translation (5´UTR is 100 bp on average, while the 3´UTR is 600 bp on average).**
- C - Wrong. One amino acid contributes to approximately 100 Da. Carbohydrates, for example, are unlikely to account for 75% molecular weight.
- D - Wrong. The maximum number of amino acids in a polypeptide is theoretically 2200/3 = 733.

Question 2.

- A - Wrong. Mitochondrial tRNAs have no effect on editing.
- B - Wrong. There are no eRNAs.
- **C - Correct. Specific gRNAs are involved in editing by recognition and anchoring polyU sequences.**
- D - Wrong. Ribosomal RNAs have a different function in proteosynthesis.

Question 3.

- **A - Correct. The shift of the reading frame occurs behind the signal site for the cap, usually in the first exon.**
- B - Wrong.
- C - Wrong.
- D - Wrong.

Question 4.

- A - Wrong. Transcription factors are commonly involved in the regulation of gene expression.
- B - Wrong. This region is typical for the regulation of gene expression.
- C - Wrong. Gene expression is sometimes regulated, for example, by nuclear hormone receptors.
- **D - Right. The amount of mitochondrial mRNA has no effect on the regulation of nuclear gene expression.**

Case reports

Newborn with focal seizures

The patient, 4 days old, was left in the neonatal unit for focal seizures. Biochemical examination was repeatedly normal. Epileptic activity was detected by EEG. The pediatric neurologist evaluated the finding as benign focal neonatal epilepsy. Extensive family history has shown a frequent occurrence of epilepsy in the family. The patient was diagnosed with a 283insGT mutation in KCNQ2.

Questions:

1. What biochemical tests have been performed?
2. What is the biochemical basis of hereditary epilepsy?
3. What does 283insGT stand for and what does such a mutation lead to?

Answers

1. S-Ca, S-K, S-Na, β-glucose, S-Mg, β-lactate, S-bilirubin, blood gases, blood pH, urine for ketone bodies.
2. “Depolarization war" between potassium and sodium channels, caused for example by mutations in genes for the alpha subunit of potassium channels, e.g., KCNQ2 (20q13.3), KCNQ1, KCNQ3, HERG (Ikr), KCNA1.
3. Insertion of two nucleotide pairs into triplet (codon) 283, which results in a frameshift mutation (generation of a polypeptide with a meaningless amino acid sequence from the mutation site onwards and formation of an early or late stop codon).

Patient with hypertension and the metabolic disorder

The patient, 4 years old, was admitted to the pediatric ward because he lost consciousness. The examination revealed hypotension, S-K level of 2.6 mmol/L, 7.8 pH, and HCO3 level of 52 mmol/L. The Nordin index was 1.4. The P124L mutation in CLC-Kb was detected.

Questions:

1. What disease could it be? And what would be the laboratory findings necessary to confirm the diagnosis?
2. What is the Nordin Index?
3. What is the cause of this syndrome?
4. What is CLC-Kb and what does the abbreviation P124L mean?

Answers

1. Bartter's syndrome. Recurrent hypokalaemic alkalosis, increased urinary salt loss, hyperreninemia and hyperaldosteronism, hypercalciuria, hyperprostaglandinuria, normomagnesemia.
2. U-calcium/U-creatinine ratio (mmol/mmol).
3. Mutations in chloride or potassium transport protein genes in the outer or inner membrane of renal duct cells (e.g., in the thick part of the ascending arm of the Henle's loop): CLC-Kb, ROMK (ATP sensitive inwardly rectifying K + channel), NKCC2 (bumetanide-sensitive Na- K-2Cl cotransporter).
4. The CLC-Kb chloride channel belongs to the family of about 10 voltage-gated chloride channels (CLC). Another type of chloride channel includes ELG (extracellular ligand-gated) and CFTR. P124L stands for proline to leucine substitution at the position 124 of the polypeptide chain.

A patient with colorectal cancer

A patient, 52 years old, was examined on an outpatient basis for fatigue, subfebrile illness, gastrointestinal problems, and recurrence of fresh blood and sometimes mucus in the stool. A biopsy was performed from a suspected tumor site during rectoscopy. The biopsy sample was examined histologically (adenocarcinoma) and molecular genetically for the presence of mutations in the K-ras gene (substitution at position 2 of codon 12, GGT → GCT).

Questions:

1. What other laboratory tests would be appropriate to monitor the patient?
2. What is the K-ras gene and what is its significance?
3. What is the consequence of this point mutation?

Answers

1. E.g., CEA, FW (erythrocyte sedimentation), acute phase proteins.
2. Point mutations in the K-ras gene are associated with a multi-stage process of colorectal cancer development. K-ras gene expression leads to the synthesis of the p21ras protein, which is an essential component of cellular signaling cascades. Functionally related to cytoplasmic receptors. Point mutations in exon 1 (codons 12 and 13) and exon 2 (codon 61) of the K-ras gene inhibit the GTPase activity of the p21ras protein and thus contribute to the uncontrolled proliferation and malignant transformation of intestinal cells.
3. This is a point substitution that results in the exchange of one amino acid for another, in this case Gly12Ala. This amino acid substitution leads to a reduction in the GTPase activity of the RAS protein (resulting in a slow inactivation of the GTP-RAS signal, which leads to an excessive cellular response to the receptor signal).

A patient with liver cirrhosis

A patient, 55 years old, visited her family doctor for persistent weakness, lethargy, loss of libido, and joint pain. She was diagnosed with diabetes mellitus six months ago. Hepatomegaly and hyperpigmentation of the skin were found on physical examination. There were signs of cardiomyopathy on the ECG. Biochemical examinations and liver biopsies were performed. DNA was isolated from peripheral leukocytes and examined for the presence of the C282Y mutation in the HLA-H (HFE) gene.

Questions:

1. What biochemical tests should be performed? What histological examination was performed on the biopsy specimen?
2. What disease is it and how is it treated?
3. What is the cause of this disease?
4. What does C282Y stand for?

Answers

1. Serum: AST 1.1 ukat/L, ALT 0.9 ukat/L, Fe 60 umol/L, ferritin 630 ug/L, transferrin 2.57 g/L. Staining of the preparation for the presence of iron.
2. Hereditary hemochromatosis. He is treated with controlled venipuncture and Desferal.
3. Excessive deposition of Fe ions in tissues. This is caused by mutations in the HFE gene, formerly known as HLA-H. The protein product of this gene shows homology to HLA class I proteins, including binding to β2-microglobulin. Under physiological conditions, the HFE protein occupies transferrin receptors on the cell surface, thereby regulating the transition of the iron-transferrin ion complex into the cell. Mutation of the HFE gene C282Y in a homozygous arrangement was found in 85% of cases of hereditary hemochromatosis. The second protein, whose erroneous overproduction is probably associated with hemochromatosis, is a product of the SFT (stimulator of Fe transport) gene.
4. Substitution of cysteine with tyrosine at codon site 282 of the polypeptide.

References

Related articles

- Gene expression
- Control of gene expression and proteosynthesis in eukaryotes
- Transcription
- Translation

Other chapters from the book MASOPUST, J., PRŮŠA, R .: Pathobiochemistry of metabolic pathways

Source

- MASOPUST, Jaroslav and Richard PRŮŠA. *Pathobiochemistry of metabolic pathways.* 1st edition. Prague: Charles University, 1999. 182 pp. 214–218. ISBN 80-238-4589-6 .

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