MOLECULAR-GENETIC BASIS OF DOWN SYNDROME

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Motivation and Aim: Down syndrome is very hard hereditary disease that leads to intellectual disabilities and developmental delays that vary by individual. Physical features of this disease include short, stocky build, slightly bent 5th finger, small nose, mouth and ears, almond-shaped eyes with skin fold covering inner corner (epicanthus), white spots on colored part of eyes and flat, round face. There are 200 thousands – 250 thousands births of children with Down syndrome every year around the World which is approximately 1 in 700 of newborns worldwide, this number varies by different regions and countries. The average lifespan of people suffering from Down syndrome is significantly increased in last decades and now it is 50-60 years.

Materials and methods: literature review and theoretical analysis of scientific articles from the Pubmed database (https://pubmed.ncbi.nlm.nih.gov/), World Health Organization (https://www.who.int/home) and books by topic for the last 10 years.

Results: we have found that the most common cause of Down syndrome is the presence of extra copy of chromosome 21, which is the trisomy 21 (aneuploidy): 95% of cases. The second cause is Robertsonian translocation: 3-4% of cases. In this case a part of chromosome 21 breaks off and attaches to another chromosome (usually chromosome 14). The third type of the syndrome is mosaic genotype: 1-2% of cases.

Some cells have the extra copy of the chromosome 21 while other cells do not have, varying severity of symptoms. Down syndrome is not typically inherited. It results from a random violation of chromosome segregation during meiosis (gamete formation, the egg or sperm cells). However, the risk of having a child with Down syndrome increases with maternal age. The total diagnosis of this disease includes prenatal diagnosis, molecular-biological techniques and post-natal diagnosis. Prenatal diagnosis is provided by classical ultrasound detection of physical markers and maternal serum screening that measures levels of specific hormones and proteins. Molecular-biological techniques include non-invasive prenatal testing (NIPT) that analyzes fetal DNA in maternal blood, chorionic villus sampling (CVS) that analyzes placental tissue, and amniocentesis that analyzes amniotic fluid for chromosomal abnormalities. Postnatal diagnosis includes karyotyping which confirms the presence of extra copy of chromosome 21 and fluorescence *in situ* hybridization (FISH) that detects specific chromosomal abnormalities. Medical and therapeutic interventions

for treatment and managing symptoms include monitoring and treatment of heart defects, addressing digestive issues and feeding difficulties, addressing hearing loss and vision problems. Rehabilitation strategies for the syndrome include early intervention, special education and social integration.

Conclusion: gene therapy for Down syndrome is still in its early stages, but holds promising potential for future treatments. Researchers are exploring strategies to modify the expression of genes related to Down syndrome, aiming to improve cognitive function and reduce health risks. Research is ongoing to target specific genes on chromosome 21 (*DSCR1, DYRK1A*) to mitigate cognitive deficits. CRISPR-Cas9 and other gene-editing tools are being explored but are not yet clinically available.

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