50. THE ROLE OF TYROSINE-PROTEIN KINASE RECEPTORS IN TRIGGERING DIFFERENT TYPES OF CANCER

Author: Ceban Tatiana

Scientific adviser: Eugeniu Simionică, Doctor of biology, Department of Biochemistry and Clinical Biochemistry, *Nicolae Testemitanu* State University of Medicine and Pharmacy of the Republic of Moldova.

Introduction. Tyrosine-protein kinase receptors (RTK) are proteins on the surface of the cell membrane that are encoded by a large group of genes in the eukaryotes body. RTK plays an important role in controlling the most fundamental cellular processes, such as cell cycle, metabolism and survival, migration, proliferation, and cell differentiation. Mutations in RTK and the aberrant activation of intracellular signalling pathways caused by them, lead to the onset of various types of cancer.

Aim of study. Synthesis of current studies aimed at identifying the role of tyrosine-protein kinase receptors and the causes that lead to the onset of different types of cancer, as well as potential targeted therapy.

Methods and materials. The bibliographic study was realised on the basis of scientific articles published in the period 2018-2021 in the databases PubMed, NCBI, and BioMed Central using key phrases "Tyrosine-kinase receptors", "RTK in oncogenesis", "targeted therapy on RTK".

Results. Tyrosine-protein kinase receptors include 58 different types that are classified into 20 families according to their structure and ligand. In human cancers, there are 4 mechanisms that lead to the constitutive activation of RTK: genomic amplification, gain-of-function mutations, chromosomal rearrangements, and autocrine activation. Genomic amplification has been identified in a variety of cancers: EGFR in glioblastoma, esophageal, lung, thyroid cancer; HER2 / ErbB2 in breast cancer, bladder cancer; MET in gastric and lung cancer. Activation by gain-of-function mutations can occur in extracellular, transmembrane, and juxtamembrane domains of RTK. FGFR3 extracellular domain point mutations have been reported in cervical carcinomas. Transmembrane HER2 mutations have been identified in non-small cell lung cancer. The KIT V560G and PDGFRA V561D mutations in the juxtamembrane domain are found in gastrointestinal stromal tumours. Chromosomal rearrangements occur in patients with chronic myeloid leukemia-fusion of the gene encoding tyrosine kinase ABL1 on chromosome 9 with the BCR gene on chromosome 22 (BCR-ABL). Autocrine activation of various RTKs has been well characterised in various cancers, including TGFα-EGFR. Over the years, numerous studies have been performed on targeted therapy. Thus, there are currently 61 RTK inhibitors approved by the Food and Drug Administration starting from July 22, 2020.

Conclusion. Malignant tumours have always been a serious problem for human life. Thus, RTK studies are an important perspective on oncology and subsequently the development of targeted therapies.