Nencki Institute of Experimental Biology

New Measures of Cancer Stemness and its Impact on Cancer Progression - publication in Cell Journal Co-Authored By Prof. Bożena Kamińska from Nencki Institute

2018-04-12

Professor Bożena Kamińska, head of the Laboratory of Molecular Neurobiology, is a co-author of a paper entitled: "Machine Learning Identifies Stemness Features Associated with Oncogenic Dedifferentiation", published in Cell Journal.

Tumors are traditionally evaluated and classified according to their histopathological features. The microscopic manifestation of a tumor reflects the sum of its underlying genomic alterations, however, morphologically, similar tumors can have distinct genomes, and give different outcomes and responses to therapy. The Cancer Genome Atlas (TCGA), was a big international effort to understand the molecular underpinnings of cancer, and introduce molecular classifications. TCGA projects identified previously unrecognized molecular subgroups, and have provided the knowledge to more accurately classify cancers. The resulting resources are extensive, containing almost 12,000 samples of 33 tumor types, and allows to inquire about novel molecular mechanisms characterizing cancer, its heterogeneity, and interactions with microenvironment.

Cancer formation involves the accumulation of genetic alterations in undifferentiated cells, or the loss of a differentiated phenotype and acquisition of progenitor and stem-cell-like features. While cancer stem cells have been discovered in many cancer types, their origin, identity and specific markers have been debated. The team of international researchers (including prof. Bozena Kaminska from the Nencki Institute, Warsaw) led by Prof. Maciej Wiznerowicz sought to find universal characteristics of cancer stemness, along with its associations with patient's survival and host immune responses. In the Cell paper (5th April, 2018, https://doi.org/10.1016/j.cell.2018.03.034) the team demonstrated, that analyzing molecular markers of normal pluripotent cells led to differentiate, molecular indices of "stemness" could be computed and applied to TCGA data to assess the degree of dedifferentiation in 33 types of cancer. Using machine-learning algorithms trained on transcriptomic and epigenetic features, the researchers were able to identify previously undiscovered biological mechanisms associated with the oncogenic dedifferentiation. Analyses of the tumor microenvironment revealed unanticipated links between cancer stemness and tumor immune

evasion mechanisms influencing infiltration and functions of immune cells. The dedifferentiated oncogenic phenotype was most prominent in metastatic tumors. Using molecular correlates of stemness and underlying signaling pathways, the researchers identified novel targets and postulated therapies targeting cancer stemness.