Streszczenie w j. angielskim

"Molecular analyses of oncogenic differentiation using proteogenomic data sets obtained from 12 tumor types"

Over the past decade there has been growing evidence indicating that progression and therapeutic resistance in cancer have been strongly associated with the acquisition of a stemness phenotype by cancer cells. Although the oncology field continues to evolve, there is still an urgent need to discover new biomarkers and drug targets for personalized anti-cancer therapy. Previous studies linking genomics with the molecular mechanisms of cancer development point to a knowledge gap that still exists. To overcome the existing limitations, this study links cancer stemness concept with proteomics that adds a new layer of molecular insight into mechanisms driving cancer progression. In this study, a new protein expression-based stemness index (PROTsi) was applied to assess the degree of oncogenic dedifferentiation that is associated with tumor histopathology features and clinical outcome in tumor samples. The data for analyzed tumor samples were collected for the Clinical Proteomic Tumor Analysis Consortium (CPTAC) from twelve types of primary tumors: breast cancer, clear cell renal cell carcinoma, endometrial cancer, glioblastoma multiforme, pediatric brain tumors, head and neck cancer, lung adenocarcinoma, lung squamous cell carcinoma, pancreatic ductal carcinoma, colrectal cancer, ovarian cancer, early-onset gastric carcinoma. Integration of the stemness index computed using proteomic data with gene expression, DNA methylation, microRNA, copy number alteration and protein post-translational modification identified coherent proteogenomic stemness association and indicated that proteins play a role of active nodes of signaling pathways and transcriptional networks that drive aggressiveness of the primary tumors that cause cancer progression and resistance to existing therapies. The correlation between the stemness index and protein expression led to the identification of potential drug targets for anti-cancer therapy both tumor-specific and shared among different tumor types. Moreover, the identified stemness-associated proteins carry a predictive value of clinical outcome across analyzed tumor types. Eventually, a set of stemness-associated protein targets were validated by immunohistochemistry in independent samples to confirm the association with patients' clinical outcome. The validation carried out for clear cell renal cell carcinoma and head and neck squamous cell carcinoma samples indicated that PROTsi is an effective tool for predictive protein target selection that is an essential step to tailor the anti-cancer therapy and for clinical development of effective cures for cancer patients.