Study points to personalized treatment opportunities for glioblastoma

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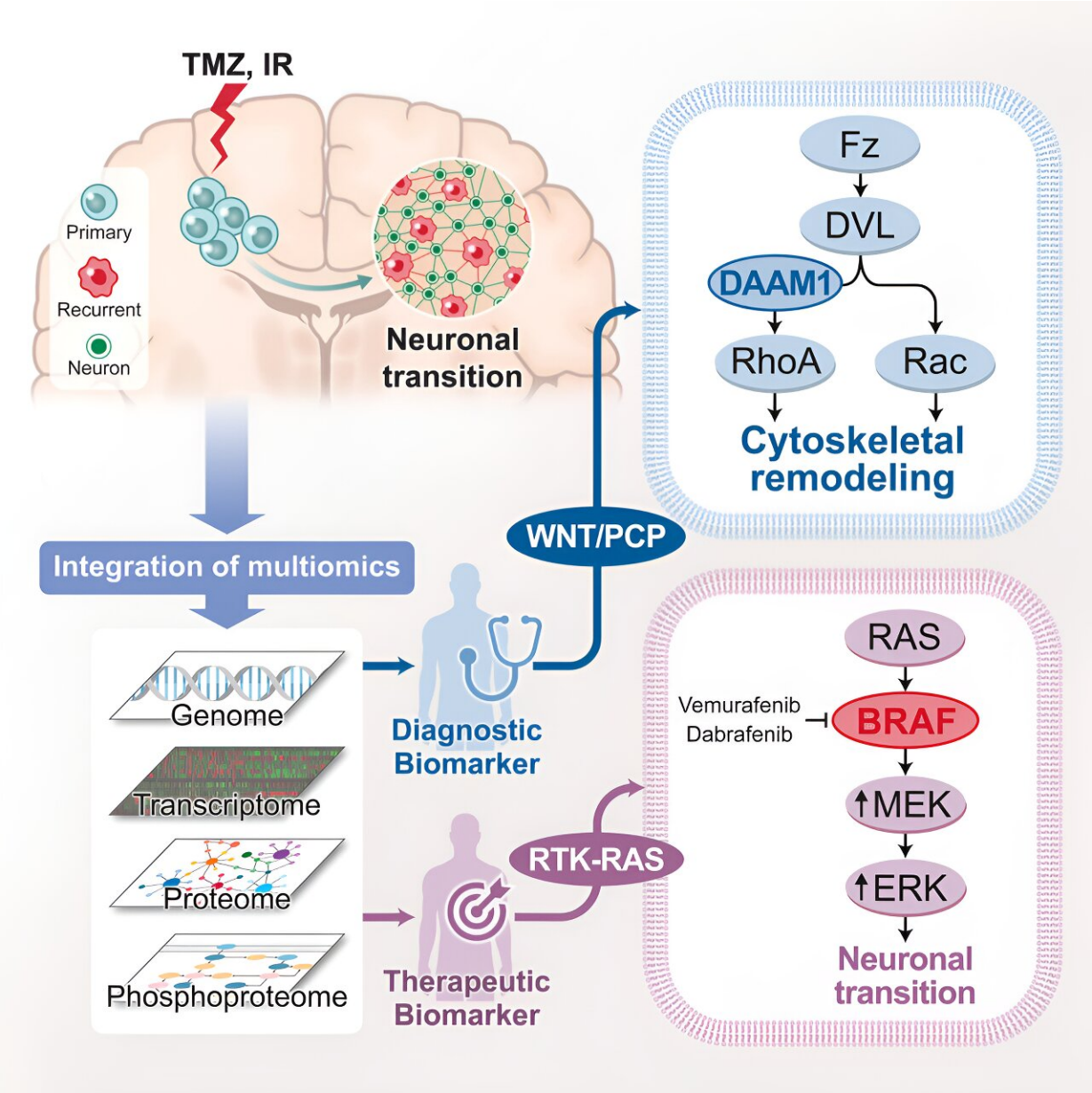

Credit: *Cancer Cell* (2024). DOI: 10.1016/j.ccell.2023.12.015

A study appearing in *Cancer Cell* uncovers the evolutionary dynamics of glioblastoma recurrence through proteogenomic analysis, offering potential therapeutic avenues.

The research team, led by Professor Jason K. Sa from Korea University College of Medicine's Department of Biomedical Informatics and Professor Jong Bae Park from the National Cancer Center, has elucidated the evolutionary process of glioblastoma recurrence through integrative proteogenomic analysis. They have provided new treatment opportunities based on their findings.

Glioblastoma is known for its complex genetic alterations and cellular capability to interact with surrounding neurons. It is particularly challenging due to its high recurrence rate and the prevalent resistance to standard treatments like chemotherapy and radiation therapy.

The research team meticulously analyzed the genomic, transcriptomic, and proteomic profiles of matched primary and recurrent glioblastoma from 123 patients. They discovered that the recurrent tumors have undergone neuronal transition (an interaction between cancer cells and nerve cells through neurotransmitters significantly affects the growth, progression, and metastasis of cancer) through activation of the WNT/PCP signaling pathway and the BRAF protein kinase.

The study also illustrated, through experimental validation with patient-derived cells and animal models, that the formation of synapses between normal neurons with tumor cells constituted a critical role in the recurrent tumor's resistance to standard therapy.

Moreover, the research highlighted that administering vemurafenib (a BRAF-inhibiting targeted drug) with temozolomide (a conventional chemotherapy drug) effectively impaired the neuronal transition and invasive capacity of the recurrent tumor cells, significantly prolonging survival in animal models. This outcome validates targeting the BRAF protein kinase as a novel strategy for combating recurrent glioblastoma, paving the way for innovative treatment opportunities.

Professor Sa stated, "The challenge with traditional genomic analysis was its inability to fully decipher the patterns of tumor evolution. This research, however, leverages a multidimensional data analysis approach, offering new therapeutic possibilities."

Professor Park explained, "This is the first time that we've been able to demonstrate, through the integration of genomic, proteomic, and clinical data, the role of neuron-brain tumor cell network formation in the recurrence of brain tumors."

More information: Kyung-Hee Kim et al, Integrated proteogenomic characterization of glioblastoma evolution, *Cancer Cell* (2024). DOI: 10.1016/j.ccell.2023.12.015

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