Children's National Health System

Research at a Glance

Clinicopathology of DIPG and its redefined genomic and epigenomic landscape

Gene (alteration)	Protein	Biological consequences
H3F3A (mutations)	H3.3	Up to 70 percent of DIPGs; associated with poor survival
HIST1H3B and *HIST1H3C* (mutations)	H3.1	18 percent of patients; majority are WHO III–IV astrocytomas; K27M are concurrent with ACVR1, PPM1D mutations, downregulation of PAX3, and ALT phenotype
ACVR1 (mutations)	ACVR1	21 percent to 32 percent of patients; concurrent with H3.1 mutations
TP53 (mutations)	P53	40 percent to 77 percent of patients; concurrent with H3F3A-ATRX-DAXX mutations
ATRX (mutations)	ATRX	9 percent to 31 percent of patients; concurrent with ALT phenotype
NF1 (mutations)	NF1	Loss of function mutations in 4 percent of patients; mutations in PI3KMAPK pathway occur in 46 percent of patients
PPM1D (mutations)	PPM1D	Concurrent with H3.3 K27M mutation; mutually exclusive with P53 mutations
PIK3CA (mutations)	PIK3CA	First mutated oncogene reported in 15 percent of patients; mutually exclusive with PDGFRA amplifications and PTEN deletions
EGFR (mutations)	EGFRvIII	Presence of EGFR variant III leads to unregulated growth, survival, and invasion
TERT (promoter mutations)	TERT	Mutually exclusive with ATRX mutations and ALT phenotype
NTRK (gene fusions)	NTRK	NTRK-activating fusions are associated with RTK-RAS-PI3K signaling
PAX3 (up-regulation)	PAX3	Concurrent with H3.3 K27M, alterations in TP53 and PDGFR-a, and amplification of cell cycle regulatory genes
IL13RA2 (up-regulation)	IL-13Ra2	Binds IL-13 and inhibits STAT6 via the JAK/STAT pathway
PARP1 (up-regulation)	PARP-1	Signals DNA damage repair proteins; overexpression leads to temozolomide and radiation resistance
MYCN (up-regulation)	N-Myc	Activation is higher in H3.3 compared with H3.1 mutants; corresponds to hypermethylated genomes
PTEN (deletions)	PTEN	Loss of function activates AKT, leading to resistance to radiation therapy and chemotherapy
PDGFRA (amplification)	PDGFR-*α*	13 to 36 percent of patients; majority are WHO II–IV astrocytomas
EGFR (amplification)	EGFR	Restricted to high-grade BSG; overexpression correlated with increasing WHO grade
*CCND*1,2,3 and *CDK*4,6 (amplification)	CCND1,2,3 and CDK4,6	Amplification of these cell cycle regulatory genes leads to uncontrolled Rb phosphorylation
MET (amplification)	c-Met	Associated with RTK-RAS-PI3K signaling

Source: *"Clinicopathology of Diffuse Intrinsic Pontine Glioma and Its Redefined Genomic and Epigenomic Landscape." E. Panditharatna, K. Yaeger, L.B. Kilburn, R.J. Packer, and J. Nazarian. Published by Cancer Genetics on May 1, 2015.*