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Abstracts

GENOMICS

GENO-01. MOLECULAR INTERROGATION OF GLIOBLASTOMA MULTIFORME TUMORS IDENTIFIES A COMPLEX NETWORK OF CELL SIGNALLING PATHWAYS WITH POSSIBLE THERAPEUTIC IMPLICATIONS

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The precise molecular mechanism behind Glioblastoma Grade IV with extremely poor treatment outcome for patients with even intensive therapy regimen is yet to be completely understood. GBMs represent approximately 17% of all primary brain tumours diagnosed worldwide, and 60-75% of astrocytomas, increasing in frequency with age (WHO and IARC, 2008). Recent research has revealed four distinct subtypes based on multiple genetic alterations which have prognostic and therapeutic implications. Present study was performed to characterize global genomic analysis from ten GBM patients to study the molecular mechanisms and pathways associated with tumorigenesis and to understand the cause of therapy failure. Here we show that molecular interrogation clearly identifies GBM subtypes which seem to have distinct prognostic outcomes. Importantly, pathways known to play a role in the cancer stem cell (CSC) proliferation were found to be activated in several tumor specimens. Significantly, CSCs have been implicated in tumor maintenance and relapse after surgical resection. Most current anti-cancer drugs, small molecule inhibitors and monoclonal antibodies are designed to target rapidly proliferating cells which represent committed cancer cells but not CSCs and hence may partly explain cause of therapy failure. Further, multiple pathway activation in the GBM population calls for immediate attention to consider development of combination regimens / new target based drug development in GBMs. This could be an alternative to the template regimen which has now resulted in plateaued overall survival. We also observed a possible abetment by the metabolic engine in tumor progression and would need more study to consider its importance in GBM grading. Study further supports the urgent need for identifying global molecular signatures in GBM patients to align treatment for better outcomes and improved overall survivals.