Epigenetics

Epigenetics is the study of heritable changes in gene function that do not involve changes in the DNA sequence.

The Greek prefix epi- (ἐπι- “over, outside of, around”) in epigenetics implies features that are “on top of” or “in addition to” the traditional genetic basis for inheritance.

Epigenetics often refers to changes in a chromosome that affect gene activity and expression, but can also be used to describe any heritable phenotypic change that does not derive from a modification of the genome, such as prions. Such effects on cellular and physiological phenotypic traits may result from external or environmental factors, or be part of normal developmental program. The standard definition of epigenetics requires these alterations to be heritable, either in the progeny of cells or of organisms.

Incremental hypoxia inside the growing tumor mass drives epigenetic drug resistance by activating non-genetic repair of anti-apoptotic DNA, which could be impaired by drug treatment. Hence, rescuing inter-tumor hypoxia by oxygen-generating microparticles may promote susceptibility to anti-tumor drugs. Moreover, a tumor-on-a-chip model a enables user-specified alternation of clinic-derived samples. This study utilized patient-derived glioblastoma tissue to generate cell spheroids with size variations in a 3D microchannel network chip (Glioblastoma chip). As the spheroid size increased, epigenetic drug resistance was promoted with inward hypoxia severance, as supported by the spheroid size-proportional expression of hypoxia-inducible factor-1a in the chip. Loading anti-hypoxia microparticles onto the spheroid surface significantly reduced drug resistance by silencing the expression of critical epigenetic factor, resulting in significantly decreased cell invasiveness. The results were confirmed in vitro using cell line and patient samples in the chip as well as chip implantation into a hypoxic hindlimb ischemia model in mice, which is an unprecedented approach in the field [1].

In each glioblastoma Glioblastoma, hundreds of genes are subject to DNA hypermethylation at their CpG island promoters. A subset of Glioblastomas is also characterized by locus-specific and genome-wide decrease in DNA methylation, or DNA hypomethylation. Other epigenetic alterations, such as changes in the position of histone variants and changes in histone modifications are also likely important in the molecular pathology of Glioblastoma, but somewhat surprisingly there are very limited data about these in Glioblastoma. Alterations in histone modifications are especially important to understand, given that histone deacetylases are targets for drugs that are in clinical trial for Glioblastomas. The technological wave of next-generation sequencing will accelerate Glioblastoma epigenome profiling, allowing the direct integration of DNA methylation, histone modification and gene expression profiles. Ultimately, genomic and epigenomic data should provide new predictive markers of response and lead to more effective therapies for Glioblastoma [2]

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Nagarajan RP, Costello JF. Epigenetic mechanisms in glioblastoma multiforme. Semin Cancer Biol. 2009 Jun;19(3):188-97. doi: 10.1016/j.semcancer.2009.02.005. Epub 2009 Feb 20. Review. PubMed PMID: 19429483.