Epigenetic reprogramming

Epigenetic reprogramming is the process by which an organism's genotype interacts with the environment to produce its phenotype and provides a framework for explaining individual variations and the uniqueness of cells, tissues, or organs despite identical genetic information.

Epigenetic reprogramming drives tumorigenesis in pediatric Diffuse midline glioma H3 K27-altered by altering the canonical functions of chromatin remodeling complexes. These studies (i) identified BRG1 (encoded by SMARCA4), the catalytic subunit of the mammalian SWI/SNF (BAF) chromatin remodeling complex, as a novel dependency in pediatric H3K27M glioma; (ii) investigated the molecular mechanisms underlying the maintenance of the progenitor state; and (iii) demonstrated efficacy for BRG1 inhibitors. The authors identified the BRG1 ATPase as a dependency in pediatric H3K27M-mutant DMG. SOX10 recruits BRG1 to regulatory elements to drive progression. Pharmacologically targeting BRG1 reduced tumor volume and improved survival in vivo. Inhibiting BRG1 ATPase represents a potential therapeutic strategy for pediatric H3K27M DMG [1)]

DNA Methylation patterns are largely erased and then re-established between generations in mammals. Almost all of the methylations from the parents are erased, first during gametogenesis, and again in early embryogenesis, with demethylation and remethylation occurring each time. Demethylation of early embryogenesis occurs in the preimplantation period in two stages – initially in the zygote, then the first few embryonic replication cycles of morula and blastula. A wave of methylation then takes place during the implantation stage of the embryo, with CpG islands protected from methylation. This results in global repression and allows housekeeping genes to be expressed in all cells. In the post-implantation stage, methylation patterns are stage- and tissue-specific with changes that would define each individual cell type lasting stably over a long time.

1)
Beytagh MC, Weiss WA. Epigenetic Rewiring Underlies SMARCA4-Dependent Maintenance of Progenitor State in Pediatric H3K27M Diffuse Midline Glioma. Cancer Discov. 2022 Dec 2;12(12):2730-2732. doi: 10.1158/2159-8290.CD-22-1030. PMID: 36458436.