Basic Research

Doi: 10.4274/jus.galenos.2019.06.21

Re: Molecular Landmarks of Tumor Hypoxia Across Cancer Types

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Nat Genet. 2019 Feb;51(2):308-318. doi: 10.1038/s41588-018-0318-2. Epub 2019 Jan 14.

EDITORIAL COMMENT

Tumor microenvironment plays an important role in tumor initiation and progression. Sub-regions of hypoxia arising due to a decreased oxygen supply associated with irregular tumor vasculature as well as increased oxygen demand associated with changes in tumor metabolism may vary in size and extent. Tumor adaptation to this imbalance is associated with poor clinical prognosis. Hypoxia strongly affects apoptosis and DNA repair systems and thus leads to increased mutagenesis and genomic instability. In this research, the authors reported associations with hypoxia at the genomic, transcriptomic levels with a focus on localized prostate cancer, for which whole-genome-sequencing data linked to direct intratumoral oxygen measurements were available. They confirmed that abundance of miR-133a-3p and several tumor suppressor proteins was strongly associated with hypoxia and, higher hypoxia scores were significantly associated with more advanced tumor extent (T category). Additionally, the total amount of somatic single nucleotide variants was elevated in tumor hypoxia. Tumors with mitochondrial genome mutations also had elevated hypoxia. Phosphatase and tensin homolog (PTEN) loss may occur in hypoxic tumors and this is associated with elevated genomic instability and aggressive disease. According to the research, one of the strongest gene-hypoxia associations was allelic loss of the tumor-suppressor gene PTEN. Their data showed that hypoxic prostate tumors were associated with dysregulated PTEN, which is strongly correlated with decreased TERT expression and shortening of telomeres. These data show that the tumor microenvironment and hypoxia can play a role in tumor evolution and progression and may affect response to therapy.

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