Looking for hypoxia fingerprint in malignant tumors

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Hypoxia, a decreased availability of oxygen, is a feature of most tumors, which increases patients treatment resistance and favors tumor progression. Although several pathways have been identified to regulate hypoxic adaptation of cells, the primary mediators of this response are HIF-1 (hypoxia inducible factor 1) transcription factors. The aim of our research was to identify the hypoxia signature in malignant tumors. For our research we have chosen two types of tumors. Malignant melanoma, developing in constantly hypoxic environment, and multiple myeloma, which develops in an environment where only hypoxic niches occurs. In the first step, cancer cell lines were cultured under normoxic (21%O_2) and hypoxic (1%O_2) conditions for 16h. The presence of hypoxia was confirmed by the stabilization of HIF-1α subunit and detection of protein-pimonidazole adducts. Next, the panel of HIF-1 target genes, selected based on the literature, was examined using RT-PCR. All the studied genes were confirmed as HIF-1 targets and contained hypoxia response elements (HRE) in their promoters. Next, we determined molecular hypoxia signature using the genes with low basal expression and significant induction in hypoxia. Subsequently, using binominal Bernouli distribution, the molecular signature was verified on patients transcriptomic data to answer the question of whether a group of hypoxic patients is actually present in a given tumor. Our work has shown that hypoxia molecular signatures vary between different types of cancer, and that for each type of tumor the molecular signature must be determined individually. The approach we proposed may constitute an universal tool that will allow for searching for hypoxia fingerprint in transcriptomic data of cancer patients.