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Role of hypoxia-inducible factor 1 (HIF1) in tumorigenesis

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Introduction

Cancer is one of the leading causes of morbidity and mortality worldwide. Proliferation, development and ***resistance of cancer cells*** are due to a specific microenvironment in which ***hypoxia*** is one of the key components.

Keywords

HIF1, tumorigenesis, hypoxia, cancer.

Purpose

Studying ***the role of HIF1 in tumorogenesis*** as well as the mechanisms by which it maintains the supervision of tumor cells to identify new strategies ***for diagnosis*** and targeted ***treatment of cancer***.

Material and methods

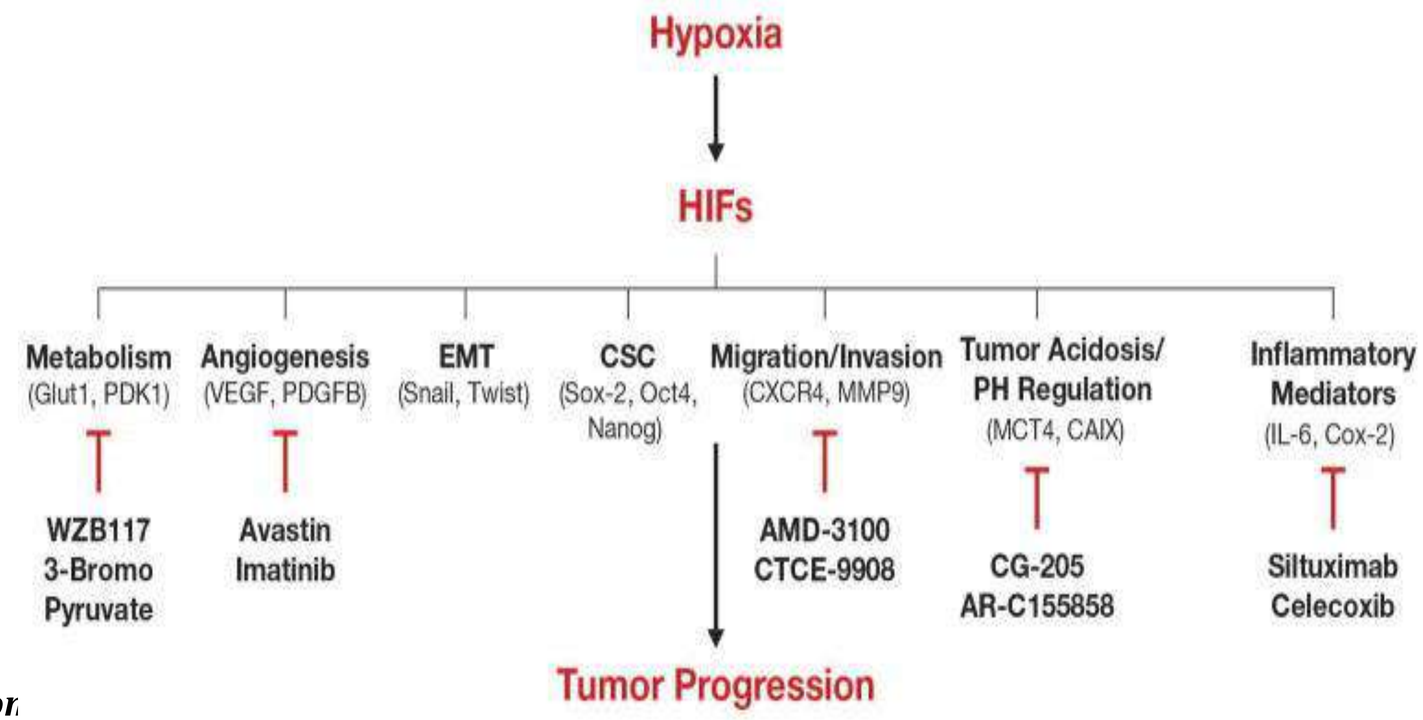
Literature analysis between 2015-2019 through the following search engines PubMed, BMC cancer, AACR publications, Google Scholar, using 12 bibliographic sources.

Results

- Rapid and uncontrolled proliferation of tumors limits the ***availability of O2*** and blood, triggering ***increased expressior*** and stabilization ***of HIF1α and HIF1β***, which in the nucleus ***induce*** the ***expression of glycolytic enzyme:*** (LDH-A) genes,VEGF gene, EPO, i-NOS and HO-1 genes, the inhibition of BAD and BID (proapoptotic) gene expression.
- LDH accumulation converts pyruvate to lactate by providing them with an energy substrate, VEGF induces angiogenesis, and EPO-erythropoiesis, inhibition of BAD and BID gives cells resistance to apoptosis. ***HIF-1 induces autophagy and inhibits mitochondrial biosynthesis to stop cell death*** by providing resistance.

Conclusions

High levels of HIF 1 in tumor cells can be used as a ***marker*** in the early detection ***of cancer***, and inhibition of the factor may stop the development of the tumor.



Scheme representing cellular functions regulated by HIF-1 and showing examples of direct target genes involved in various signaling pathways. Examples of existing inhibitors and/or FDA-approved drugs, which are specific to various HIF-1 regulated genes/pathways, are shown. CXCR4, Chemokine receptor 4; Nanog; Homeobox transcription factor; Oct-4, Octamer-binding transcription factor 4; Snail, Zinc finger transcriptional repressor; Sox-2, Sex determining region Y box-2; Twist, Basic helix-loop-helix transcription factor.