University of Cyprus
Department of Biological Sciences

Postgraduate Seminars

Seminar Series 2018-2019

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"The cellular response to hypoxia in health and disease: metabolic role, regulation and targeting of HIF-1"

Friday, 12 October 2018, at 13:30
Building CTF 02, Room 014, Panepistimioupoli Campus

This seminar is open to the public

Hypoxia (oxygen deficiency) characterizes physiological development and activities as well as many pathological conditions. Adaptation of cells to hypoxia is mainly mediated by the hypoxia-inducible transcription factors HIF, which are, therefore, valid therapeutic targets in cancer and other diseases. HIF-1, specifically, is responsible for the activation of genes that support reprogramming of cellular metabolism and inhibit apoptosis under hypoxia. The inducible subunit HIF-1α is regulated predominantly at post-translational level. Proline hydroxylation triggers degradation of HIF-1α under normal oxygenation conditions while inhibition of hydroxylation represents the main activation mechanism of HIF-1 upon hypoxia. An important role is also played by phosphorylation, which can act either positively or negatively. Our studies have led to the identification of kinases that target HIF-1α and determination of the corresponding modification sites. Phosphorylation of HIF-1α by CK1δ inhibits its heterodimerization with HIF-1β (ARNT) and impairs formation of HIF-1 and activation of its gene targets implicated in triglyceride accumulation, a process that is necessary for cellular proliferation under hypoxic conditions. Modification of HIF-1α by ERK controls its intracellular trafficking between nucleus and cytoplasm and determines the balance between its genomic activity, mediated through binding to chromatin proteins, and its non-genomic function that involves interaction with mortalin and other anti-apoptotic proteins of the outer mitochondrial membrane. Cell-penetrating HIF-1α-derived peptides that inhibit its phosphorylation also inhibit proliferation and migration of cancer cells and trigger their apoptotic death only under hypoxic conditions, confirming the importance of ERK-dependent regulation and opening prospects for the development of specific HIF-1 inhibitors with anti-cancer activity.