

CELL DEATH, SENCESCENCE AND SURVIVAL

VÍCTOR YUSTE MATEOS

PROFILE

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RESEARCH

RESEARCH INTERESTS/STRATEGIC OBJECTIVES/MAIN RESEARCH LINES

Apoptosis is a complex but highly defined cellular program of cell demolition. Deregulation of apoptosis conducts to a number of serious diseases, including cancer. Biochemical events lead to characteristic cell changes and death. Activation of cysteine proteases called caspases plays a major role in the execution of apoptosis. These proteases selectively cleave vital cellular substrates, which results in the two hallmarks of apoptosis: nuclear chromatin condensation and internucleosomal DNA fragmentation. These hallmarks are achieved by a specifically activated DNase termed DFF40 or CAD (death fragmentation factor 40 or caspase-activated DNase). We are interested in the molecular mechanisms involved in the regulation of this endonuclease and the consequences for a cellular population derived from an abnormal or defective activation of DFF40/CAD.

The most aggressive manifestation of gliomas is the glioblastoma multiforme (GBM), characterized by diffuse invasion, angiogenesis and extensive necrosis. Due to their robust apoptosis resistance, the clinical progression is dramatically rapid and patients are committed to death often within 12-24 months after diagnosis despite aggressive surgery, radio- and chemotherapy. These are an example in which the actual combinatorial therapies are inefficient.

LAB FEATURED PUBLICATIONS

Sánchez-Osuna M, Martínez-Escardó L, Granados-Colomina C, Martínez-Soler F, Pascual-Guiral S, Iglesias-Guimarais V, Velasco R, Plans G, Vidal N, Tortosa A, Barcia C, Bruna J, Yuste VJ. An intrinsic DFF40/CAD endonuclease deficiency impairs oligonucleosomal DNA hydrolysis during caspase-dependent cell death: a common trait in human glioblastoma cells. *Neuro Oncol.* 2016 Jul;18(7):950-61. doi: 10.1093/neuonc/nov315. Epub 2016 Jan 10. PMID: 26755073; PMCID: PMC4896542.

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Sánchez-Osuna M, García-Belinchón M, Iglesias-Guimarais V, Gil-Guiñón E, Casanelles E, Yuste VJ. Caspase-activated DNase is necessary and sufficient for oligonucleosomal DNA breakdown, but not for chromatin disassembly during caspase-dependent apoptosis of LN-18 glioblastoma cells. J Biol Chem. 2014 Jul 4;289(27):18752-69. doi: 10.1074/jbc.M114.550020. Epub 2014 May 17. PMID: 24838313; PMCID: PMC4081919.

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Gozzelino R, Sole C, Llecha N, Segura MF, Moubarak RS, Iglesias-Guimarais V, Perez-Garcia MJ, Reix S, Zhang J, Badiola N, Sanchis D, Rodriguez-Alvarez J, Trullas R, Yuste VJ, Comella JX. BCL-XL regulates TNF-alpha-mediated cell death independently of NF-κB, FLIP and IAPs. Cell Res. 2008 Oct;18(10):1020-36. doi: 10.1038/cr.2008.76. PMID: 18591962.