BIO TECNOLOGIE
RICERCA DI BASE
INTERDISCIPLINARE
TRASLAZIONALE
IN AMBITO BIOMEDICO

3°Meeting

IBIM-CNR

STEBICEF-UNIPA
UNIVERSITÀ DEGLI STUDI DI PALERMO

BIOINFORMATICA IMMUNOLOGIA
MALATTIE APPARATO RESPIRATORIO
MALATTIE METABOLICHE
MICROORGANISMI NELLE BIOTECNOLOGIE
NANOTECNOLOGIE NEUROSCIENZE
ONCOLOGIA SVILUPPO E DIFFERENZIAMENTO

LIBRO degli ABSTRACT

PALERMO 17-18 DICEMBRE 2015

Area della Ricerca di Palermo Via Ugo La Malfa 153

Progetto grafico:
Anna Bonomolo (IBIM-CNR)

predictive tests of tumor radiosensitivity and define therapeutic treatments targeted to individual tumor subtype.

Non-canonical roles of caspase-8 in MDA-MB-231 breast cancer cell line

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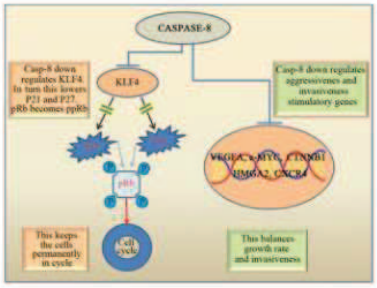
Caspase-8 (casp-8) is well known as an initiator caspase involved in cell death signalling, although its activity in many cancer cell types seems to work under non-apoptotic conditions. Moreover, in several types of cancer, casp-8 is only rarely mutated and often its expression is very elevated. Since cancer cell growth also depends on evasion of apoptosis, the upregulation of casp-8 in tumours may suggest one or more non-apoptotic roles (1). Here we report our recent studies carried out in MDA-MB-231 cells, derived from clinically aggressive forms of Triple-Negative Breast Cancer, where we have assessed the non-canonical roles of casp-8. Firstly, we evaluated casp-8 mRNA and protein levels in MDA-MB-231 cells, demonstrating that they were upregulated with respect to HMEC (normal Human Mammalian Epithelial Cells). Thereafter, to assess the role of casp-8, we silenced it by small interfering-RNA. Interestingly casp-8-knockdown, strongly decreased MDA-MB-231 cell growth by delaying G0/G1- to S-phase transition and increasing p21, p27 and hypophosphorylated/active form of pRb levels. No effects were evidenced on cell viability. To assess the metastatic capacity of MDA-MB-231 cells, the gene expression profiles of the relative markers after casp-8 knockdown were also measured. Surprisingly the expression of a number of genes and/or proteins such as VEGFA, C-MYC, CTNNB1, HMGA2, CXCR4, KLF4, VERSICAN V1 and MMP2 potently increased accompanied by migratory and metastatic capacities of cells, as shown by wound healing and matrigel assays. We suggest that among these genes, KLF4, a transcriptional factor with a dual role (activator and repressor), and responsible for p21 and p27 induction, could play critical roles (2). Casp-8 through KLF4 down-regulation, could manage the expression of critical proliferative and migratory/invasive genes. We suggest that these unusual roles played by casp-8 in MDA-MB-231 cells, should be better explored, in order to identify it as a molecular therapeutic target.



[1.] Stupack DG. Caspase-8 as a Therapeutic Target in Cancer. Cancer Lett 332:133–140, 2013.
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Ibuprofen containing mucus-penetrating nanoparticles as therapeutic tool for the treatment of inflammation in Cystic Fibrosis

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Conductance regulator protein (CFTR). The airways of CF patients are plugged with mucopurulent secretions containing abundant bacteria and neutrophils, and death results from progressive destruction of the lungs Cystic fibrosis (CF) is a lethal disease triggered by mutations in the gene encoding the CF transmembrane. Ibuprofen was found to significantly reduce this extreme inflammation, but despite the encouraging results obtained, in clinical the anti-inflammatory therapy is rarely practiced because of the poor penetration of drugs through mucus barrier. A novel approach could be allowed by designing particles with mucus-penetrating properties. Generally, particles with size lower than 500 nm and a neutral surface coated

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