Istituto di Biomedicina e Immunologia Molecolare "Alberto Monroy" - CNR

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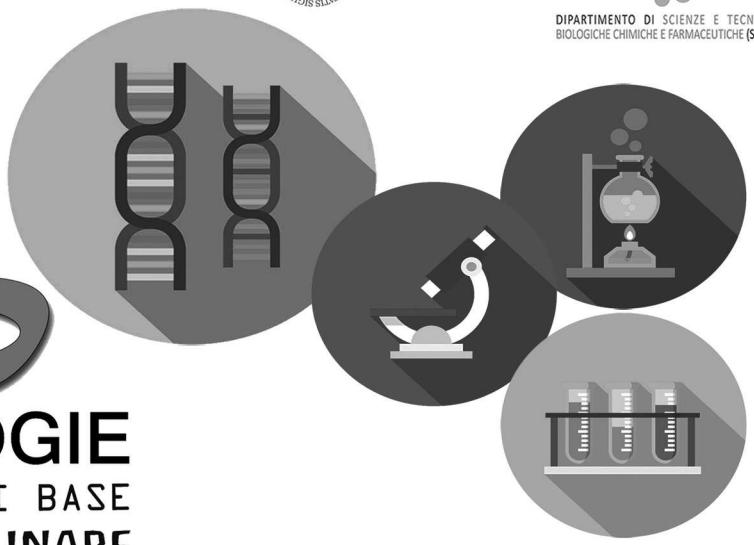

Bio TECNOLOGIE

RICERCA DI BASE
INTERDISCIPLINARE
TRASLAZIONALE
IN AMBITO BIOMEDICO

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

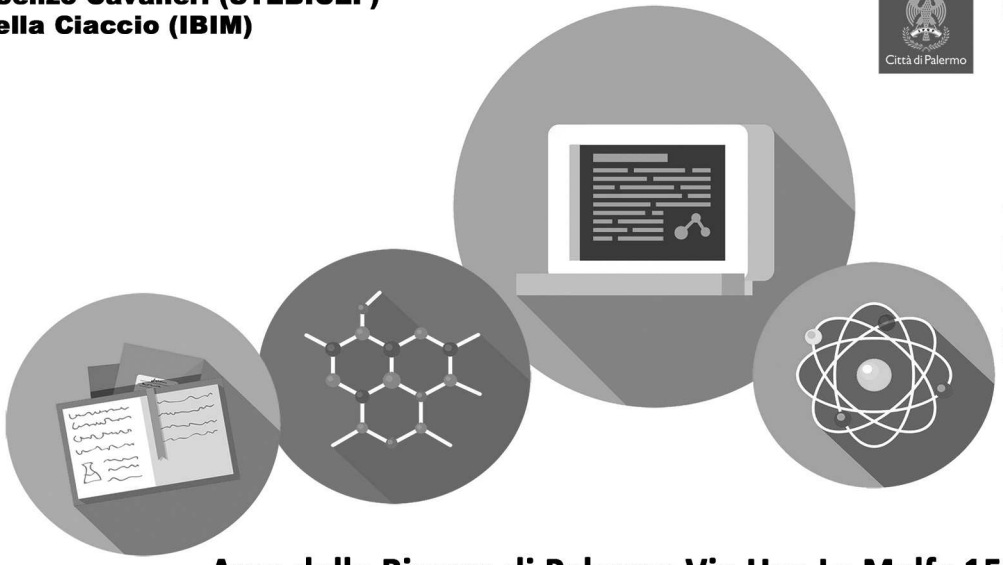
LIBRO degli ABSTRACT

5° Meeting

Comitato Scientifico
Marta Di Carlo (IBIM)
Vincenzo Cavalieri (STEBICEF)
Mirella Ciaccio (IBIM)

Città di Palermo

PALERMO
2018
CAPITALE ITALIANA DELLA CULTURA



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Area della Ricerca di Palermo Via Ugo La Malfa 153

PALERMO 5-6 LUGLIO 2018

A-1210477 sensitizes TRAIL-induced apoptosis in MDA-MB-231 Triple Negative Breast Cancer cells

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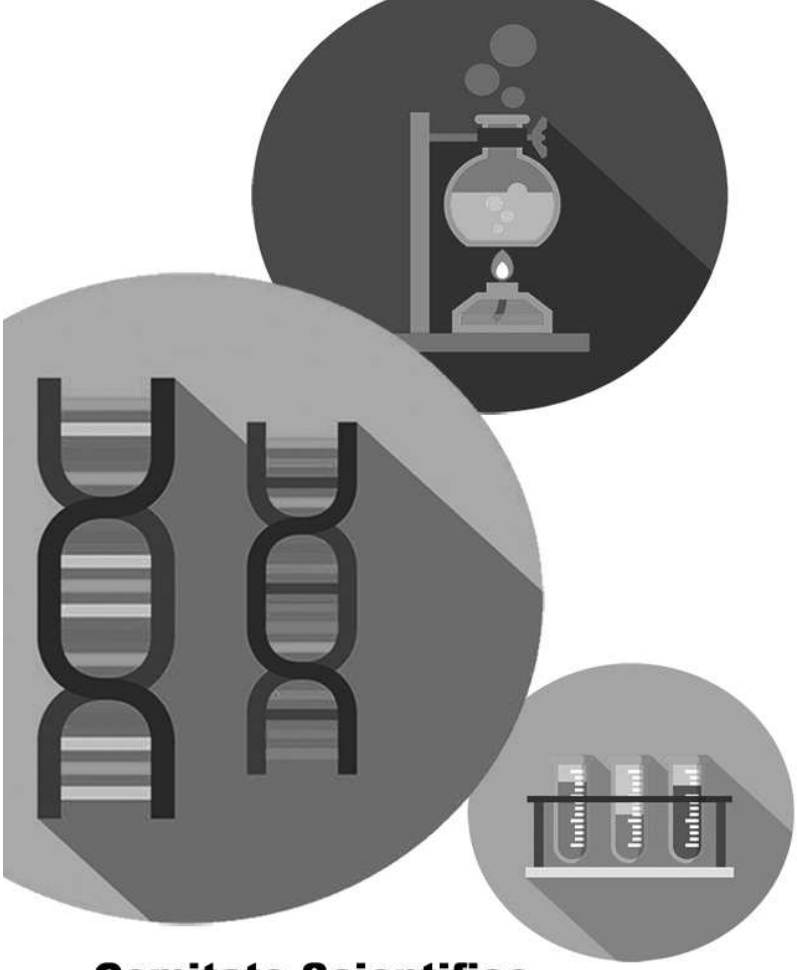
Triple negative breast cancer (TNBC) is a form of BC characterized by high aggressiveness, therapy resistance, short time to relapse, poor prognosis. The presence of Cancer Stem Cells (CSCs) could be responsible for TNBC resistance to therapy, recurrence and metastasis, and might explain the difficult of its eradication. Mcl-1 is one of the key regulators of CSCs self-renewal and its expression can limit the efficacy of antitumorigenic agents as TRAIL, a selective anticancer agent but with limited effects against some cancer cell lines. Here we investigated the expression profiles of Mcl-1 in TNBC tissue and cell lines. We also evaluated the effect of A-1210477, a selective Mcl-1 inhibitor, to enhance TRAIL-mediated apoptosis in MDA-MB-231 cells. We found Mcl-1 up-regulated in 43%, downregulated in 43% and no variations in 14% of analyzed TNBC tissues than normal ones. Moreover, analyzing TNBC cells in comparison to HMEC cells, we found that MDA-MB-231 cells show similar mRNA levels but higher Mcl-1 protein levels, whereas in MDA-MB-436 and BT-20 cells both mRNA and protein levels of Mcl-1 resulted downregulated. We also observed that, among the cell lines analyzed, MDA-MB-231 cells were the most resistant to rh-TRAIL. We showed that, in MDA-MB-231 cells, A-1210477 in combination with rh-TRAIL, drastically decreased cell viability, colony-forming ability and activated the apoptotic pathway. Finally, we found that the rh-TRAIL-A-1210477 combined treatment consistently reduced cell growth of 3D culture and tertiary spheres of MDA-MB-231 cells. Our findings suggest that rh-TRAIL-A-1210477 combined treatment could be particularly effective for overcome the rh-TRAIL-resistance.



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