BIO TECNOLOGIE
RICERCA DI BASE
INTERDISCIPLINARE
TRASLAZIONALE
IN AMBITO BIOMEDICO

3°Meeting

IBIM-CNR

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MALATTIE APPARATO RESPIRATORIO
MALATTIE METABOLICHE
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LIBRO degli ABSTRACT

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vannamei (Liao et al., 2011) and in the Camponotus japonicus (Ishida et al., 2014). In this study, we report the identification of the first component of the ML superfamily in the invertebrate *Ciona intestinalis* by means of a subtractive hybridization strategy. Sequence homology and phylogenetic analysis showed that this protein forms a specific clade with vertebrate components of the Niemann-Pick type C2 protein and, for this reason, it has been named Ci-NPC2. The putative Ci-NPC2 is a 150 amino acids long protein with a short signal peptide, seven cysteine residues, three putative lipid binding site and a three-dimensional model showing a characteristic b-strand structure. Gene expression analysis demonstrated that the Ci-NPC2 protein is positively upregulated after LPS inoculum with a peak of expression 1 h after challenge. Finally, *in-situ* hybridization demonstrated that the Ci-NPC2 protein is preferentially expressed in hemocytes inside the vessel lumen.

Janus-Faced role of microRNA let-7d in osteosarcoma 3AB-OS cancer stem cells

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Osteosarcoma (OS) is the most common malignancy of bone in children and adolescents. It is a highly invasive and metastatic bone-malignancy because of which, despite therapeutic advances, 30%-50% of patients still die of pulmonary metastasis. As a consequence, there is an urgent need to identify new therapeutic strategies to improve the clinical outcome of the patients. Advances in OS treatment are inconceivable without better understanding of molecular mechanisms of osteosarcomagenesis and, especially, metastatic processes. Growing evidence suggests that cancer stem cells (CSCs), which have self-renewing and malignant potential, are at the root of tumor growth and relapse. Thus, a challenge for innovative therapy is their identification and eradication. Here, we have used the 3AB-OS CSCs, a cell line previously produced in our laboratory from the OS-MG63 cells, which was genetically, molecularly and functionally characterized. This study was focused on the role of let-7d miRNA –previously found by us to be downregulated in 3AB-OS-CSCs- in managing their stemness properties. We have found that let-7d-overexpression reduces cell proliferation by both decreasing CCND2 and E2F2 cell-cycle-activators and increasing p21 and p27 CDK-inhibitors. Let-7d also reduces sarcosphere- and colony-forming ability and the expression of Oct3/4, Sox2, Nanog, Lin28B and HMGA2, key regulators of cancer cell stemness. Moreover, let-7d induces mesenchymal-to-epithelium-transition, as shown by both N-Cadherin-E-cadherin-switch and vimentin decrease. Surprisingly, this switch was accompanied by enhanced migratory/invasive capacities and by increases in MMP9, CXCR4 and VersicanV1. Let-7d also reduced the resistance to serum starvation and chemotherapy. A decrease in caspase-3 with an increase in Bcl-2 was also observed. Overall, this study shows that let-7d -displaying both suppressor and oncogenic functions- behaves as a Janus-Faced miRNA. Thus, we suggest that, before prospecting new therapeutic strategies by let-7d modulation, it is urgent to better understand its functions.

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