ANTI-CD138 ANTIBODY NANOPLATFORM AS NEW ACTIVE DRUG DELIVERY SYSTEM FOR MULTIPLE MYELOMA (MM)

Tangredi C.*[1,2], Busato D.[1], Macor P.[2], Cavalli R.[3], Dal Bo M.[1], Toffoli G.[1]
[1]Experimental and Clinical Pharmacology Unit, National Cancer Institute (CRO), IRCCS, 33081Aviano (PN), Italy, carmela.tangredi@cro.it; [2]Department of Life Science, University of Trieste, Piazzale Europa 1, 34127 Trieste (TS), Italy, carmela.tangredi@phd.units.it; [3]Department of drug science e technology, University of Torino, 10125 Torino (TO), Italy

Background: Multiple myeloma (MM) is the second most common hematologic malignancy causing more than 10000 annual deaths. Treatment of MM usually involves high-dose chemotherapy, often with potent side-effects that limit dosing. Syndecan-1 (SDC-1 or CD138) may be a useful immunotherapeutic target because it is highly expressed on the surface of MM cells, whereas it is not expressed or only expressed at low levels in healthy B cells.

Methods: A mouse monoclonal antibody of the IgG class directed against an epitope of CD138 was obtained from previously harvested hybridoma cells and purified by high affinity chromatography (HPLC). The antibody ability to target CD138 antigen on the MM cell line RPMI 8226, was tested by flow cytometry and immunofluorescence analysis. A cytotoxic assay was performed with three different drugs: Lenalidomide, Doxorubicin and Monomethyl-Auristatin E (MMAE), and cell death was assessed by Cell Titer and Ann-V/7-AAD assays. The synthesis, loading and conjugation of Chitosan Nanobubbles (CNs) was performed in collaboration with University of Torino and characterized by dynamic side scattering (DLS).

Results: Immunofluorescence analysis showed the CD138 presence on the RPMI cell membrane, while flow cytometric analysis revealed a specific fluorescence signal for CD138 with 98% of positive cells, compared to CD138 negative cells. Moreover, an antibody competition assay shows that our antibody recognizes a different epitope than commercial antibodies. Of the three drugs, doxorubicin and MMAE strongly induced cell death with apoptosis mechanisms (Doxo: 70% late apoptosis at 1μM; MMAE: 70% early apoptosis at 1nM) compared to lenalidomide (20% cell death at 1μM). Doxorubicin was loaded into CNs then functionalized with our antibody. The synthesized CNs showed an average diameter of 360nm and a positive charge.

Future target: the cytotoxic activity of CNs will be tested in vitro and then the localization, toxicity and killing ability evaluated in-vivo.