Title "Functionalized silica nanoparticles in the detection and treatment of Her2-positive breast cancer "

Rainone Paolo[1], Riva Benedetta[2], Belloli Sara[1], Sudati Francesco[3], Ripamonti Marilena[1], Prosperi Davide[2,] Gianolli Luigi[3], Maria Carla Gilardi[1] and Moresco Rosa Maria[4]
[1] *Institute of Molecular Bioimaging and Physiology (IBFM), CNR, Milan (Italy) ;*
[2]*Biotechnologies and Biosciences Department, University of Milan-Bicocca, Milan (Italy);*
[3]*Nuclear Medicine Department, San Raffaele Scientific Institute, Milan (Italy) ;*
[4]*Health Sciences Department, University of Milan-Bicocca, Monza (Italy).*

Introduction: Nanobiotechnology can provide the development of nanoparticles for diagnosis/treatment of human cancer. Aim of this work was to validate a silica nanoparticles (SNP)-based system functionalized with anti-Her2 antibody fragment and loaded with radioactive/fluorescent probes for detection of aggressive breast cancer.
Methods: SNPs carrying (ETZ-2) or not (ETZ-1, control) the Her2 antibody fragment were used in *in vitro* binding kinetic in Her2 positive (SKBR-3) and negative (MDA-MB-468) breast cancer cell lines. In parallel, the same SNPs were derivatized with nitril-triacetic acid and reacted with His-Tag, previously labelled with ^{99m}Tc-Tricarbonyl complex. Labelled SNPs were used for different experiments: *in vitro* uptake kinetic in SKBR-3 and MDA-MB-468 cells (20 min, 1 h, 4h and 24h); *ex vivo* distribution in tumour and peripheral organs in animals implanted with MDA-MB-468 or SKBR-3 cells, at 4h from ETZ-2 injection. SNPs binding in cells was expressed as percentage of the total radioactivity counted; uptake in tumours and tissues were calculated as percentage of injected dose per gram of tissue. Slices of tumour were also fixed with 4% PAF and observed by fluorescence. In parallel, additional animals bearing SKBR-3 or MDA-MB-468 lesions were treated with liposomal doxorubicin (3 mg/kg in 40µl) or vehicle, and tumour uptake of [^{18}F]FDG and [^{11}C]Choline was evaluated *ex vivo* with double autoradiography.
Results: ETZ-2 specifically binds SKBR-3 cells *in vitro*, reaching a maximum uptake ratio of 2,1 on MDA-MB-468 cells after 4h. The same result was confirmed in tumours, after the biodistribution study and observation in fluorescence. Standard treatment particularly affected SKBR-3 lesions growth, in which we observed a 12,4% decrease of [^{18}F]FDG and a 14.3% increase of [^{11}C]Choline uptake, compared to control. Comparison with NPSs filled with doxorubicin are in progress.
Conclusion: Labelled SNPs resulted a useful detection system for Her2 positive breast cancer and could be used for targeted therapy.