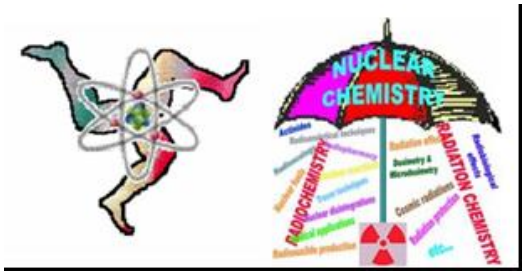

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99mTc(N)-DBODC(5) from cardiology to oncology: preliminary in vitro study

Thursday, 22 September 2011 17:05 (15 minutes)

99mTc(N)-DBODC(5) is a lipophilic cationic mixed-compound currently under clinical investigation as potential myocardial imaging agent. The findings that this complex accumulates in mitochondrial structures through a mechanism mediated by the negative mitochondrial membrane potential, and that the rapid efflux of 99mTc(N)-DBODC(5) from non-target tissues seems correlated to the Pgp/MDR-Pgp transport function opens the possibility to extend the clinical applications of this class of complexes to tumor imaging and non invasive multidrug resistance studies.
Standing on this ground, the kinetic of uptake at 4 and 37 ℃ of 99mTc(N)-DBODC(5) was evaluated in vitro in suitable human cancer cell lines, and in the corresponding sub-lines, before and after MDR-modulator treatment, using 99mTc-Sestamibi as reference.
Results from this study clearly indicated that: ì) the uptake of both 99mTc(N)-DBODC(5) and 99mTc-Sestamibi was correlated to metabolic activity of the cells. In fact, low temperature inhibited the cellular uptake of both 99mTc-tracers indicating that there was no binding to the cell membranes or to the hydrophobic regions of the cell membrane protein. ìì) The cellular accumulation is correlated to the level of Pgp/MRP expression, in fact an enhancement of uptake in resistant cells was observed after treatment with a MDR inhibitor/modulator, indicating the selective blockade of Pgp/MPR prevents efflux of the tracers.
This study give a preliminary indication on the applicability of 99mTc(N)-DBODC(5) to tumour imaging and to the detection of MDR-mediate drug resistance in human cancer.

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