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IODINE 123 LABELLED STEROIDS FOR NEGATIVE CONTROL OF STEROID RECEPTORS CONTAINING TUMORS.

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In the process of their decay, some radioisotopes release cascades of low Energy Auger electrons possessing a subcellular range of action (a few nm.). If the decay occurs in the vicinity of the DNA it will induce double strands breaks and less than 100 disintegrations are enough to kill a cell. On the contrary if it occurs at the cell surface or within the cytoplasm, it has a negligeable effect on the cell survival. One way to bring these radioisotopes near the DNA is to attach them to steroids with high affinity for the nuclear associated steroid receptor. We have synthesized an estrogen derivative with very high affinity for the estrogen receptor (ER), the Z isomer of the 11ß-chloromethyl-17α-iodovinyl-estradiol (11ßCMIVE). It was labelled with Iodine 123, an Auger electron emitting radionuclide of short half-life (13.21 h). This agent demonstrates a very selective biodistribution in ER. containing tissues. In vitro cytotoxicity was assessed using a modified MTT assay and a clonogenic assay on human cancer cells and normal bone marrow cells. In vivo experiments were performed on nude mice bearing human tumors. A very selective tumor growth inhibition was obtained both in vitro and in vivo. These results indicate that the hormone superfamily of receptors could be suitable targets for radiotherapy of receptors containing tumors.