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First proof in patients of an improved 'magic bullet' for cancer detection and radio-therapy

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Oncologists have long sought a powerful "magic bullet" that can find tumors wherever they hide in the body so that they can be imaged and then destroyed. Until recently scientists accepted the notion that such an agent, an agonist, needed to enter and accumulate in the cancerous cells to act. An international research team has now shown in cancer patients that an investigational agent that sticks onto the surface of tumor cells without triggering internalization, an antagonist, may be safer and even more effective than agonists.

One of the Salk Institute's leading researchers, Dr. Jean Rivier, professor in The Clayton Foundation Laboratories for Peptide Biology and holder of the Frederik Paulsen Chair in Neurosciences and his Swiss collaborator, Dr. Jean Claude Reubi, University of Berne and Adjunct Professor at Salk, co-authored a pilot study, published in the September issue of the Journal of Nuclear Medicine, of five patients and demonstrated that their "antagonist", 111In-DOTA-BASS, outperformed the "agonist" agent, OctreoScan, that is widely used in the clinic to image neuroendocrine tumors bearing somatostatin receptors.

"This is the first proof of principle in humans that labeled peptide antagonists can effectively image tumors. Additional research suggests that we could one day use a different radioactive metal to effectively kill the tumors," said Dr. Rivier.

Dr. Reubi, a molecular pathologist, and Dr. Rivier, a chemist, collaborated in the design and selection of natIn-DOTA-BASS for

human testing, and Dr. Helmut R. Maecke, a radio chemist, loaded DOTA-BASS with its radioactive marker and tested the compound before use in human. Afterward, the "first in man" study with the radioactive loaded DOTA-BASS was performed at the University Hospital in Freiburgby Drs. Damian Wild, Melpomeni Fani, Martin Behe, Ingo Brink, Helmut R. Maecke, and Wolfgang A. Weber.

The genesis of this study goes back to 1973, when a team of Salk researchers, which included Drs. Brazeau, Vale, Burgus, Rivier, and Roger Guillemin, a 1977 Nobel laureate, isolated and characterized somatostatin, a peptide produced by neuroendocrine glands. The scientists found that the normal function of somatostatin is to block the release of growth hormone throughout the body, which includes inhibiting the release of thyroid-stimulating hormone (TSH) from the thyroid.

Drs. Rivier, Reubi and their colleagues from Germany showed that 111In-DOTA-BASS bound to a greater number of somatostatin receptors on cancer cells than the agonist OctreoScan, and that it did accumulate in normal tissue (liver and kidney) to a lesser extent.

The prototype antagonist therapy has been revamped, and the version studied in the Journal of Nuclear Medicine publication, 111In-DOTA-BASS, detected 25 of 28 metastatic neuroendocrine tumors in the patients, whereas OctreoScan detected only 17.

In-DOTA-BASS has been licensed to a pharmaceutical company for clinical trial development, according to Rivier, who adds that other researchers are exploring an antagonist approach for other G-protein coupled receptors that are abundantly expressed on cancer cells.

Provided by Salk Institute