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Researchers help in search for new ways to image, therapeutically target melanoma

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Because the incidence of malignant melanoma is rising faster than any other cancer in the U.S., researchers at Moffitt Cancer Center in Tampa, Fla., and colleagues at Tampa-based Intezyne Technologies, Inc., Western Carolina University and the University of Arizona are working overtime to develop new technologies to aid in both malignant melanoma diagnosis and therapy. A tool of great promise comes from the world of nanomedicine – where tiny drug delivery systems are measured in the billionths of meters and are being designed to deliver targeted therapies.

Which therapies are appropriate to be loaded into nano-sized vehicles to attach to the right receptors for targeting purposes is an issue.

"Melanoma progression is associated with altered expression of cell surface proteins, including adhesion proteins and receptors," said study co-author David L. Morse, Ph.D., whose work at Moffitt includes experimental therapeutics and diagnostic imaging. "Eighty percent of malignant melanomas express high levels of the MC1R receptor, one of a family of five receptors."

Their study, published in a recent issue of the *Journal of Medicinal Chemistry*, tested the family of receptors, including MC1R, to find out which receptors would respond best when the right ligand was loaded into a nano-sized spherical delivery device resembling a Koosh Ball called a "micelle."

According to study co-author Robert J. Gillies, Ph.D., director of

Molecular and Functional Imaging and vice chair of Radiology Research at Moffitt, MC1R has been in the past investigated as a target for selective imaging and for potential therapeutic agents and is known to play a role in skin pigmentation and hair color. The search for the right "ligand" (a substance that forms a complex with a biomolecule) for use in targeting the right receptor, is ongoing.

"The development of ligands that can be attached to micelles and/or nanoparticles to target cancer cells relative to healthy organs is a subject of great research and great potential," said Gilles.

However, failures in this effort can emerge when attachments lose affinity, when poor stability results in collapse before the nano-sized vehicle gets to the vicinity of the tumor, or when the nanoparticle size is too big to escape the body's vascular system. Each issue needs to be addressed, said Gillies.

In this study, Gilles and Morse and colleagues tested one ligand that was found to have "high affinity and selectivity" for MC1R. That ligand was subsequently modified for attachment to a polymer micelle. Noting the three hurdles to be overcome – ligand affinity, nanoparticle stability and right nanoparticle size – the authors concluded that their chosen ligand "remained selective after attachment" and that the increased binding affinity of the ligand to MC1R demonstrated the stability of the system.

"We are also confident that our micelles are of sufficient size to escape the vasculature, and studies in mice are underway to evaluate the selectivity and stability of this targeted micelle system," concluded Morse.

The Moffitt researchers and their colleagues also feel that this development is a step in the right direction toward more effective imaging of malignant melanoma as well as the development of better

targeted therapies for individualized treatment of the disease using nano-sized drug delivery systems.

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