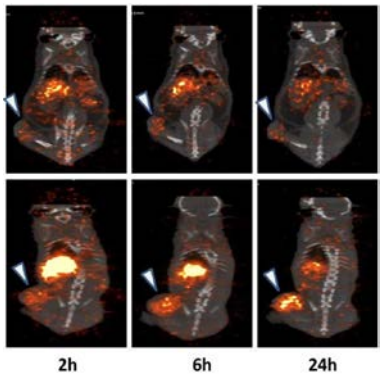
HOUSTON METHODIST INVENTION:

Multivalent ligands targeting VEGFR



Invention

The invention consists of novel compounds for angiogenesis-targeted therapy and imaging particularly for diseases such as cancer where increased angiogenesis is deleterious. The compounds target the VEGF receptor (VEGFR) with 100-fold improvement in binding affinity, higher specificity and tumor cell uptake and improved blood clearance. The compounds can be used to improve the targeting of imaging agents and therapeutic agents to tumor cells.

Background

Angiogenesis is a critical component for growth and metastatic spread of tumors and one of the most important regulators of angiogenesis is VEGFR. Binding of VEGF to VEGFR induces endothelial cell proliferation, promotes cell migration, inhibits apoptosis and is associated with advanced tumor growth and induction of tumor angiogenesis. Numerous drugs are in development to target the VEGF signaling pathway with a wide variability in the patient response to treatment being observed in clinical trials. Imaging agents that can determine VEGFR expression levels and identify patients that are most likely to respond to these anti-angiogenic drugs would be extremely useful. The imaging agents developed to date have had limited success due to slow clearance from blood, high uptake in non-targeted tissues such as kidney, and poor extravasations and diffusion into the extracellular space resulting in high background. There is a need for better imaging agents targeted to the VEGFR and the targeting agents may also improve the delivery of therapeutic agents to tumors.

Advantages

- The multivalent ligands are more potent binding agents for the VEGFR and increase tumor cell uptake of the imaging agents or therapeutics attached to them.
- The multivalent ligands are small molecules and so have faster, more specific binding to tumor cells than traditional large antibody constructs.
- The multivalent ligands are cleared from the blood pool faster than antibodies and are more stable so there is less non-specific background and better imaging.
- The multivalent small molecule ligands are easier to radiolabel and purify than larger antibody–based imaging agents.

For more information, contact the Office of Technology Transfer by e-mail at OTT@HoustonMethodist.org.

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