

Measuring oncogene signaling in prostate cancer with transferrin-based PET

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Background: Non-invasive tools that measure the activity of central oncogenes could be broadly useful for cancer detection and management. We have shown that radiolabeled transferrin molecules can be used to measure mTORC1 and MYC signaling in prostate cancer models, because the transferrin receptor is a MYC target gene. The purpose of this study was to complete the preclinical assessment of ⁸⁹Zr-transferrin, as well as demonstrate that clinical disease harbors avidity for transferrin using ⁶⁸Ga-citrate.

Methods: Human prostate cancer cell lines have been manipulated pharmacologically and genetically to alter mTORC1 and/or MYC signaling, and radiolabeled transferrin has been used to study the impact of aberrant oncogene signaling on transferrin biology. A first in man study with ⁶⁸Ga-transferrin PET was also performed at UCSF using a GE SIGNA PET/MR. A dose escalation study was performed in eight patients with castration resistant prostate cancer to identify the optimal signal to noise ratio.

Results: Activation of mTORC1 or MYC resulted in higher transferrin receptor expression and higher transferrin uptake into cells, as expected. Pharmacological inhibition of either oncogene suppressed transferrin uptake in vitro and in vivo. ⁶⁸Ga-transferrin PET/MR resolved ~75% of lesions that were detectable by CT or bone scan. Approximately 4 mCi and >3.5 hours post injection was required to visualize tumor lesions.

Conclusions: These experiments establish that like MYC, mTOR activity can be quantified in prostate cancer models with ⁸⁹Zr-transferrin. Moreover, our first in human study with ⁶⁸Ga-transferrin shows that human disease is generally avid for the radiotracer, but the uptake is variable among lesions, consistent with a molecularly diverse disease.

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