

Genomic approach to PET imaging of prostate cancer: from mouse to man.

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The need is compelling for early and accurate diagnosis of prostate cancer (PC), non-invasively. The goal is to PET image PC using ⁶⁴Cu-TP3805, specific for VPAC1 receptors, expressed in high density on PC cells, but not on normal cells.

⁶⁴Cu-TP3805 has (i) high affinity for VPAC1 (Kd = 3.1x10⁻⁹M), (ii) excellent stability in-vivo, and (iii) ability to image spontaneously grown PC in transgenic (TRAMP) mice that mimic pathophysiology of human PC.

Patients (n=25) scheduled for radical prostatectomy, who signed consent form, were PET imaged preoperatively. The images were compared to pathologic analysis of whole mount, excised prostate. Deparaffinized whole mount pathology slides (n=68) from 6 VPAC1 PET imaged patients, 3 benign prostatic hyperplasia (BPH) patients (n=9), one malignant lymph node (LN, n=3), and one benign LN (n=3) were incubated with Cu-64-TP3805, washed, and subjected to digital autoradiography (DAR). Slides were then H&E stained, read microscopically and marked as PC, benign, cyst, or prostatic intraepithelial neoplasia (PIN), and compared with DAR images.

DAR identified 105/107 (98%) histologically known PC foci, 9 previously unknown PC foci, 18 high grade prostatic intraepithelial neoplasia (HIGPIN), 2/2 ejaculatory duct, and 5/5 urethra verumontanum, but missed 2/107 (1.8%) PC foci due to artifact. DAR was positive for positive LN and negative for benign LN, for three BPH patients, and for 5/5 cysts.

Detection of HIGPIN was consistent with early expression of VPAC1. With excellent PPV (98%) and NPV(100%), Cu-64-TP3805 is worthy of imaging PC.

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