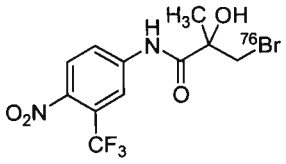
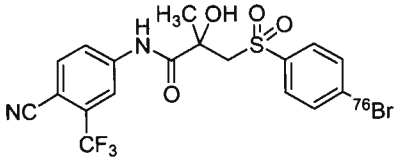
Imaging Prostate Cancer: Synthesis and In Vivo Testing of Androgen Radiopharmaceuticals

Ephraim Parent and John A. Katzenellenbogen

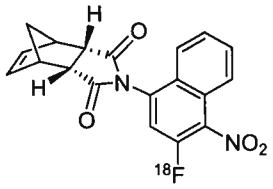
Prostate cancer is the most frequently diagnosed cancer and the second leading cause of cancer death in American men. The role of androgens in prostate tumor growth has been well established and androgen receptors (AR) are over-expressed in most primary and metastatic prostate cancers. AR radiopharmaceutical ligands capable of external diagnostic imaging of tumor sites using positron emission tomography (PET) have been developed. To date however, these studies have principally focused on using fluorinated steroid ligands with no published studies utilizing non steroidal anti-androgens as the core diagnostic agent. We have prepared several clinically relevant ^{76}Br- and ^{18}F-labeled non-steroidal androgen antagonists and studied their respective tissue distribution in androgen-depleted rats.



[^{76}Br] 3-Bromo-hydroxyflutamide

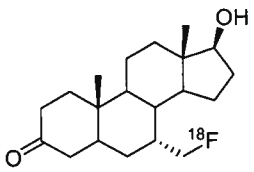


[^{76}Br] Bromobicalutamide

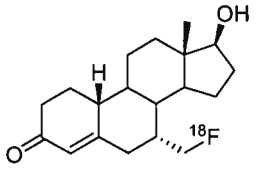


[^{18}F] 3-Fluoro-BMS 22

In addition to our non-steroidal work, we have designed and synthesized some high affinity steroidal compounds to probe the mechanism of androgen delivery to the cellular AR transcription mechanism. Sex hormone binding globulin (SHBG) binds testosterone, the principal circulating androgen, in high affinity and is believed to be directly involved in delivery of the hormone to cytoplasmic AR. Other high-affinity AR compounds, such as nor-testosterone, do not bind SHBG and their potential as imaging agents is not clear. We have prepared two classes of high affinity AR, ^{18}F-labeled steroidal compounds, one of which binds to SHBG and studied their tissue distribution in androgen-depleted rats.



[^{18}F] 7α-Fluoromethyl-dihydrotestosterone



[^{18}F] 7α-Fluoromethyl-nortestosterone