Séminaire

Département des sciences de l'imagerie médicale et des radiations

In Vitro Evaluation of a 64Cu-Labeled PSMA-Terpyridine Conjugate for Prostate Cancer

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Prostate cancer (PCa), particularly in its metastatic form, remains difficult to manage due to limited diagnostic and therapeutic options. We previously developed 64Cu-NOTA-terpyridine (64Cu-NOTA-TP), a radiotheranostic with selective cytotoxicity toward cancer cells. To improve efficacy and tumor specificity, we synthesized a new conjugate by coupling a prostate-specific membrane antigen (PSMA) ligand to the terpyridine core, generating 64Cu-NOTA-TP-PSMA. The compound was produced in 30–40% yield and radiolabeled with 64Cu in >99% efficiency. In PSMA-positive LNCaP cells, it demonstrated strong PSMA binding (IC_{50} ≈ 41 nM), higher uptake (66%) and internalization (45%) at 24 h than either 64Cu-NOTA-TP (40%; 36%) or 64Cu-NOTA-PSMA (23%; 16%), with improved retention (52% vs. ~39% for controls), while HEK-293 showed minimal accumulation. Subcellular studies revealed markedly greater nuclear localization (7%) compared with <1% for monomers. Cytotoxicity assays confirmed potent selectivity in LNCaP (IC_{50} = 10–24 nM over 24–72 h) compared to reduced activity for 64Cu-NOTA-TP (27–53 nM) and 64Cu-NOTA-PSMA (93–145 nM), and little effect in HEK-293 (IC_{50} >250 nM). Non-radioactive [NatCu]Cu-NOTA-TP-PSMA and cisplatin were inactive (>16,000 and >22,000 nM). These findings highlight 64Cu-NOTA-TP-PSMA as a promising radiotheranostic candidate with enhanced uptake, retention, nuclear localization, and cytotoxic selectivity for PCa, warranting further in vivo evaluation.