Multi-Disciplinary Validation of CNS and Cancer Biomarkers and Imaging Probes

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Highlight A: Cancer Imaging Tracer Development:

Cancer cells consume a large amount of oxygen to produce energy to maintain their proliferative status and require a constant supply of new DNA. Nuclear bases made in cancer cells for DNA replication are under oxidative stress and are damaged much more frequently than in normal cells. Dysfunctional redox regulation and increased reactive oxygen species (ROS) in cancer cells cause oxidative damage either directly or indirectly to DNA. Upregulation of MTH1, an oxidized purine nucleoside triphosphatase that specifically hydrolyzes oxidized purine nucleoside triphosphates, occurs in various cancers to repair oxidized DNA and suppress the accumulation of oxidatively damaged nucleic acids. ROS causes cellular dysfunctions such as cell death and mutagenesis by exerting oxidative damage to lipids, proteins, and nucleic acids in living cells. Oxidative damage to nucleic acids can potentially alter nuclear and mitochondrial DNA. *In vivo* measures of these processes could provide a critical metric of disease progression and a target for drug engagement. MTH1 has been reported to be a crucial enzyme in cancer proliferation and resistance to cancer therapy.

The first part of the talk will highlight the development and validation of MTH1 radiotracers for imaging oxidative DNA stress in cancer.

Highlight 2: PET Radiotracers for Imaging Parkinson Disease

Parkinson Disease (PD), the second most common neurodegenerative disease, relentlessly and progressively causes substantial disability. Pathologically, abnormal α-synuclein deposition occurs in cytoplasmic inclusions (Lewy bodies) in residual neurons in regions such as substantia nigra pars compacta (SNpc) and in dystrophic neuronal processes in striatal or cortical regions (Lewy neurites). Development and validation of biomarkers that distinguish damage in striatal terminal fields from that in nigra cell bodies/dendrites are critical to target and test disease-modifying therapies.

The second part of the talk focuses on validating pre- and postsynaptic dopaminergic neuroimaging biomarkers for nigrostriatal neuron alterations involved in PD, using the functional imaging tools: in vivo PET and in vitro quantitative autoradiography.

Biography

Jinbin Xu, Ph.D., Associate Professor of Radiology at Washington University School of Medicine, is extensively experienced in the biomedical imaging sciences, focusing on the development and characterization of probes/therapeutics for receptor- and enzyme-based central nervous system (CNS) and oncology imaging/therapy using in vivo Positron Emission Tomography (PET) and in vitro quantitative autoradiography. Dr. Xu developed a novel autoradiography procedure for measuring dopamine D2 and D3 receptor density ratios. He also played a crucial role in validating the sigma-2 receptor as an imaging biomarker for cell proliferation and developing sigma-2 receptor antagonists against Aβ oligomer toxicity in human neurons as therapeutic agents in Alzheimer disease. Dr. Xu is leading a diverse team and conducting innovative pre-clinical research via modern technologies such as quantitative imaging, biochemistry, genetics, radiomics, and proteomics.