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Small Molecule PET Radiotracer for Imaging TREM1-Positive Myeloid Cells

Stanford researchers have developed the first small molecule PET radiotracer targeting triggering receptor expressed on myeloid cells-1 (TREM1), a cell surface receptor selectively upregulated on pro-inflammatory myeloid cells. The agent is designed to cross the blood-brain barrier, enabling non-invasive imaging of maladaptive innate immune activation in the central nervous system as well as throughout the body.

PET imaging of innate immune activation currently relies largely on translocator protein 18 kDa (TSPO), which is expressed across endothelial cells, astrocytes, and tumor cells in addition to myeloid cells, and therefore cannot resolve immune cell phenotype or function. TREM1 is a far more selective marker of toxic innate immune responses, but the tracers explored for this target to date have been antibody-based, with limited brain penetrance and high cost of goods. Starting from a small molecule TREM1 antagonist with physicochemical properties predictive of good CNS exposure, the Stanford team designed and synthesized a novel labeling precursor and established a carbon-11 radiolabeling route that delivers the tracer in high radiochemical purity. Preclinical work has demonstrated TREM1-dependent binding in cell-based assays and rapid brain uptake followed by washout in healthy mice, supporting further evaluation in disease models of neuroinflammation.

Stage of Development
Research - in vitro

Applications

- Imaging innate immune activation in neuroinflammatory and neurodegenerative disease (e.g., multiple sclerosis, Alzheimer's disease, Parkinson's disease)
- Pharmacodynamic and patient-selection biomarker for clinical trials of immunomodulatory therapeutics
- Disease staging and treatment monitoring in inflammation-driven conditions
- Whole-body assessment of myeloid cell involvement in oncology and systemic inflammatory disease
- Preclinical research tool for tracking myeloid cell responses in vivo

Advantages

- Myeloid cell specificity beyond what TSPO-based imaging can provide
- Blood-brain barrier penetrant, unlike existing antibody-based TREM1 tracers
- Small molecule format with lower cost of goods and a more commercially viable path than antibody tracers
- Compatible with standard cyclotron and clinical PET infrastructure
- First reported small molecule tracer for this target

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