



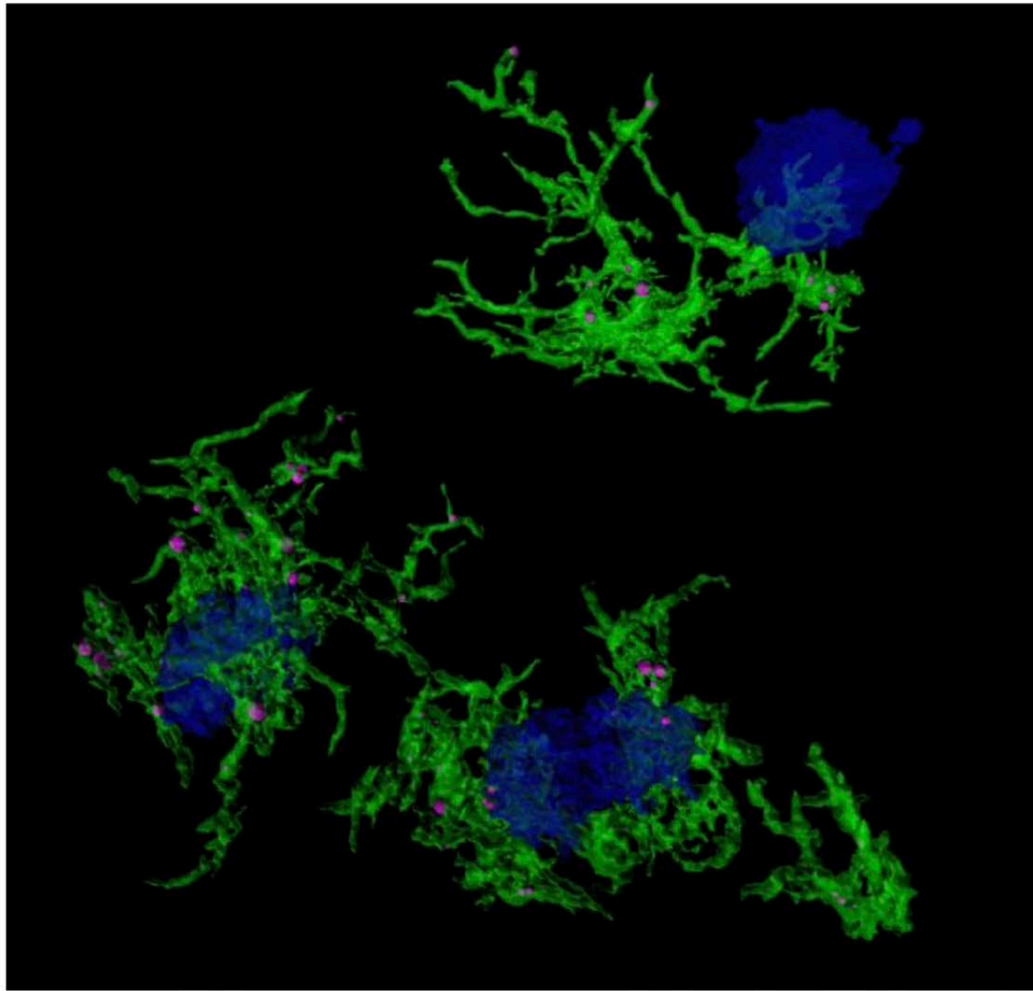
Development of ^{18}F -OP-801: a novel hydroxyl dendrimer PET tracer for imaging maladaptive inflammation in the whole body and brain

Mackenzie Carlson

James Lab | Stanford University

Departments of Bioengineering, Radiology, Neurology and Neurological Sciences

Immune Dysfunction in Neurological Diseases



Confocal microscopic image of microglia (green) engulfing amyloid plaques (blue).
CREDIT: Duke-NUS Medical School

- Innate immune dysfunction plays a critical role in many neurological diseases.
- Gold standard PET target for neuroinflammation (TSPO) lacks specificity.
- There is a huge unmet need to visualize and quantify innate immune activation *in vivo*.

What is [¹⁸F]OP-801?

- This is **PAMAM hydroxyl dendrimer** targeting activated microglia and macrophages (>95%)
- Tested in over 30 animal models

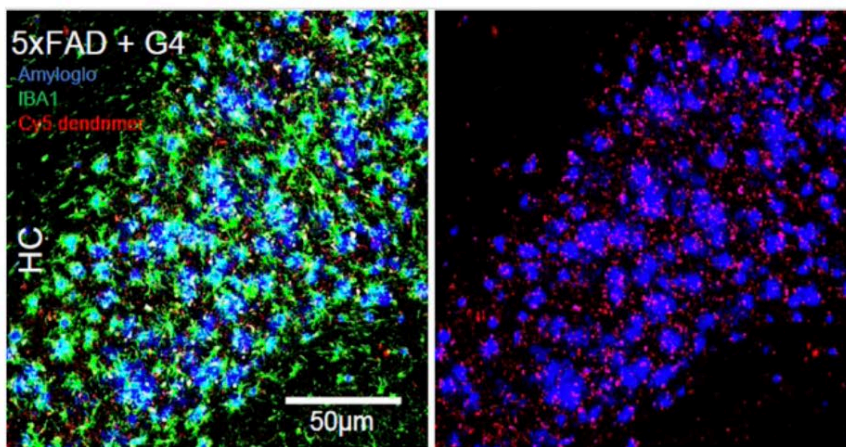
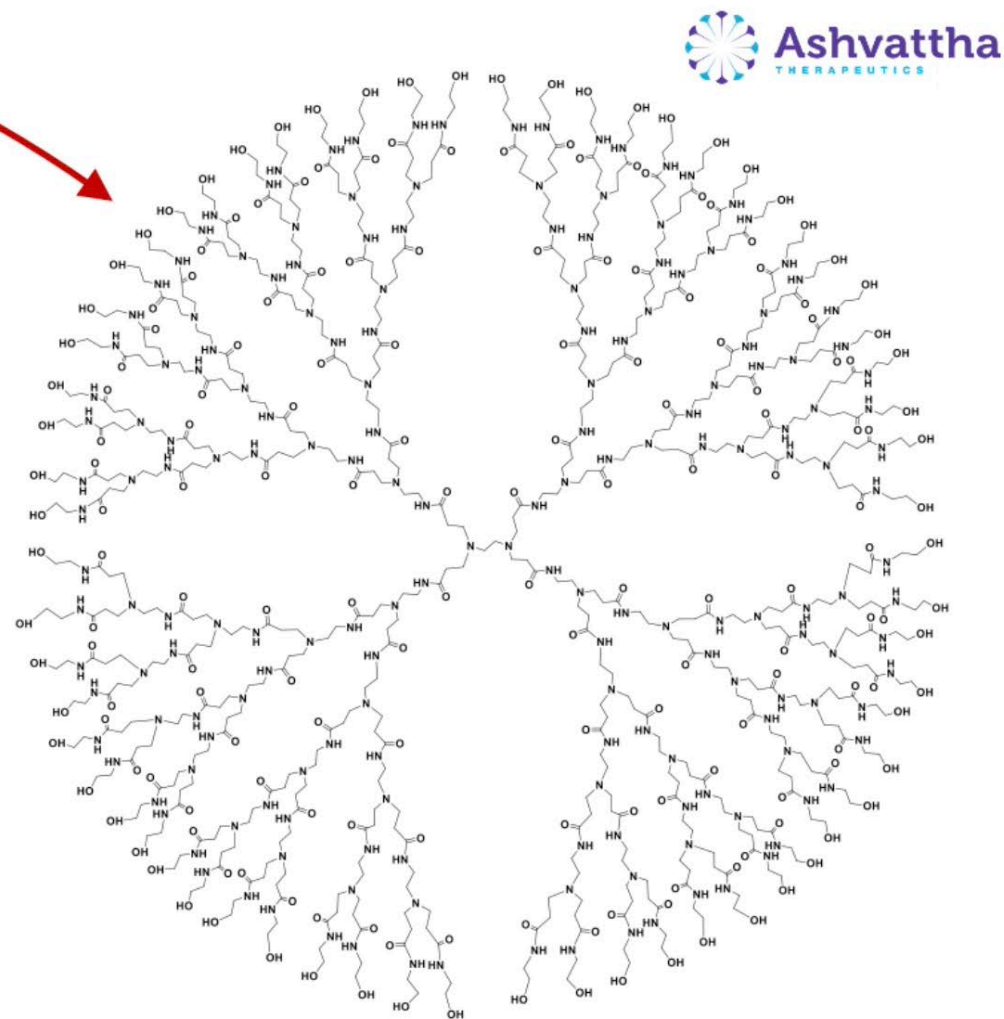


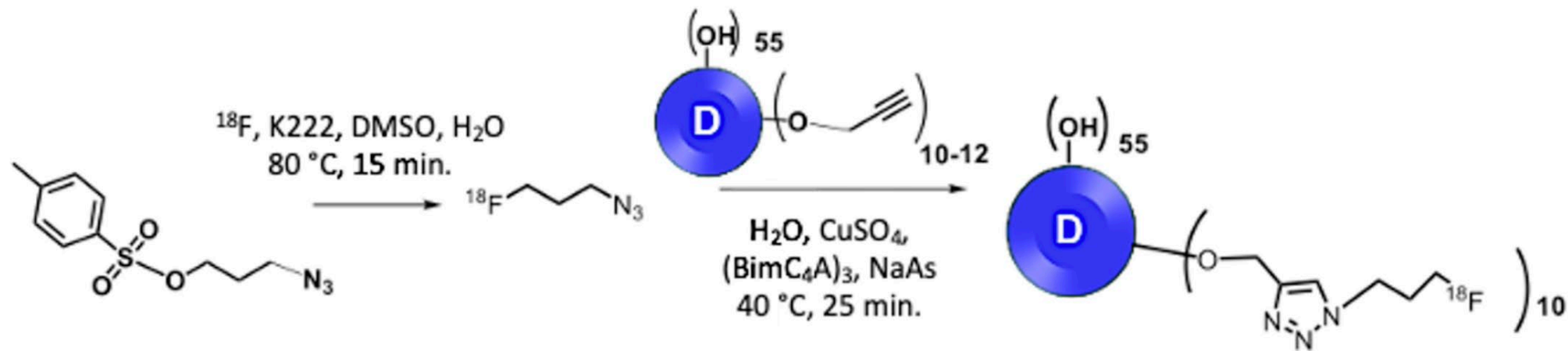
Image courtesy of Ashvattha Therapeutics, Henningfield 2020.

- Mechanism of uptake: fluid-phase endocytosis
- 5.5 hr biologic half-life, 15 kDa molecular weight



[¹⁸F]OP-801 Radiosynthesis

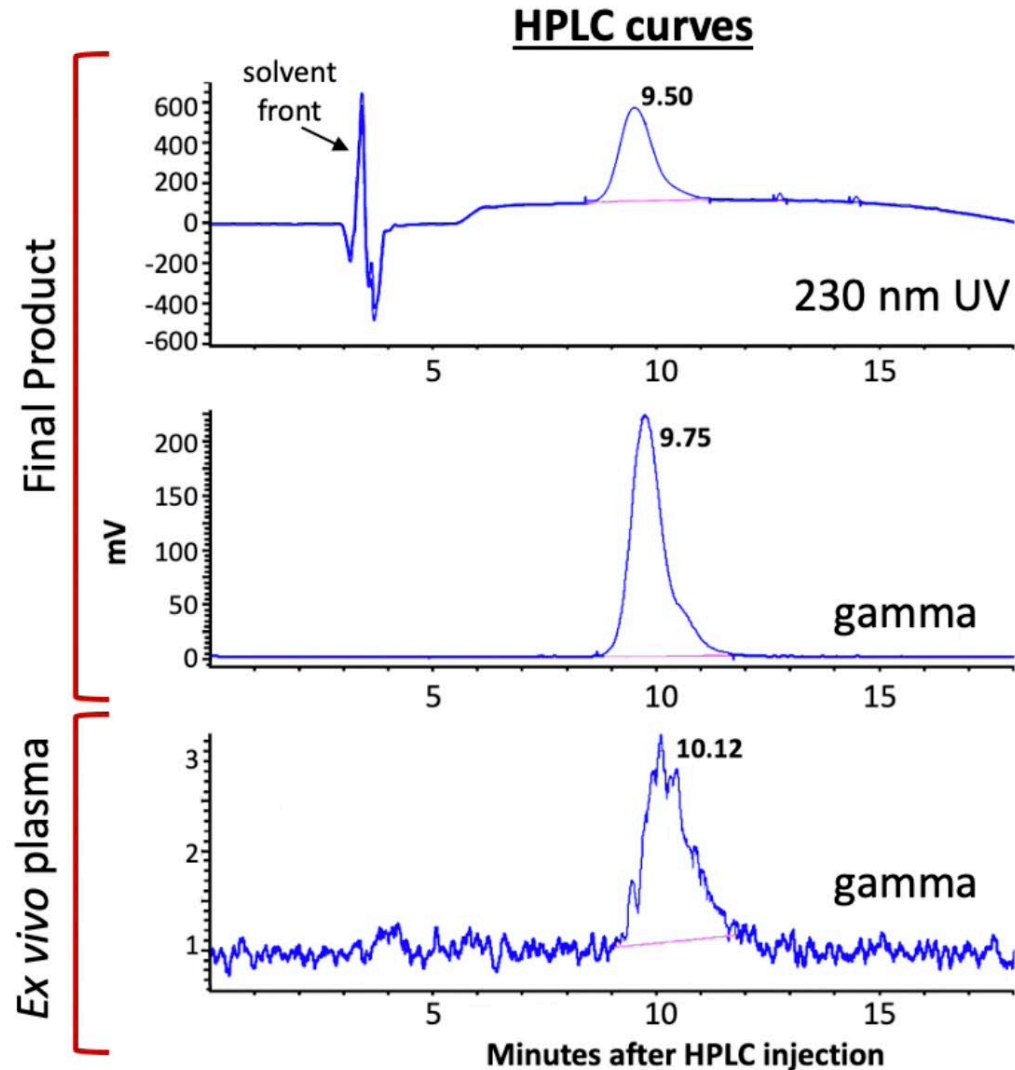
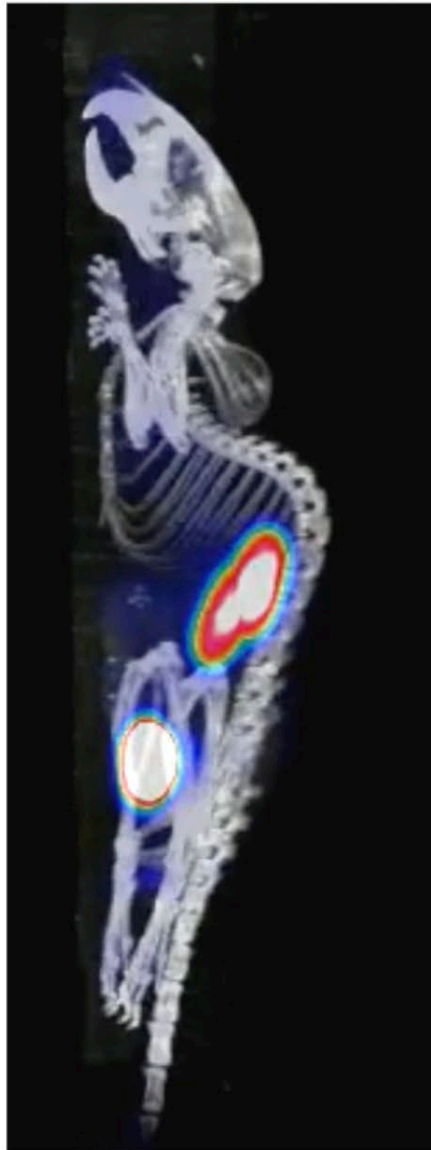
2-step azide fluorination and copper-catalyzed click reaction



Metric	Quantity	Unit
Radiochemical Yield	>4.7±2.66%	Decay corrected
Radiochemical Purity	>95%	
Molar Activity	>50	mCi/mg
Mass injected per mouse	~5	ng
Time from EOB	2	hours

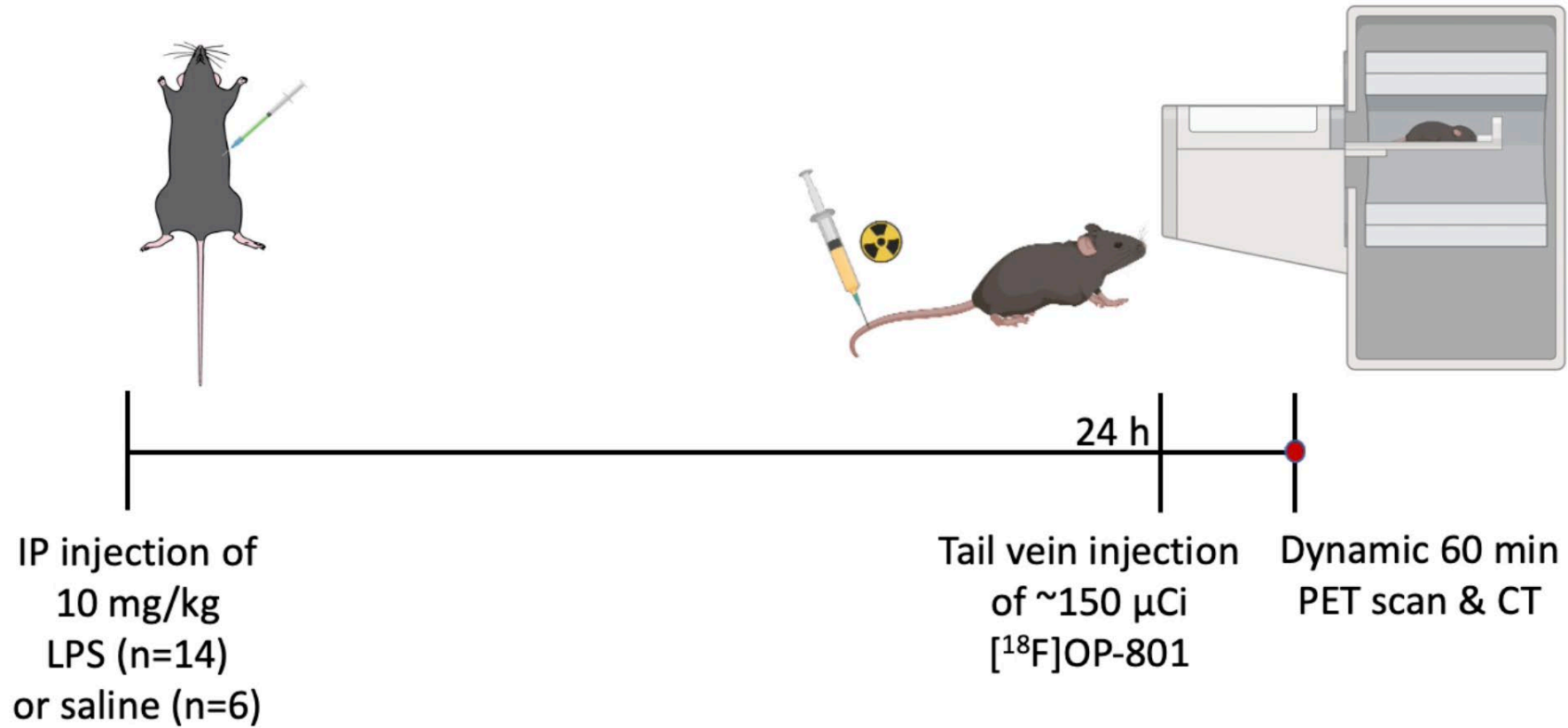
Assessing [^{18}F]OP-801 in Healthy Mice

12
% ID/g
0



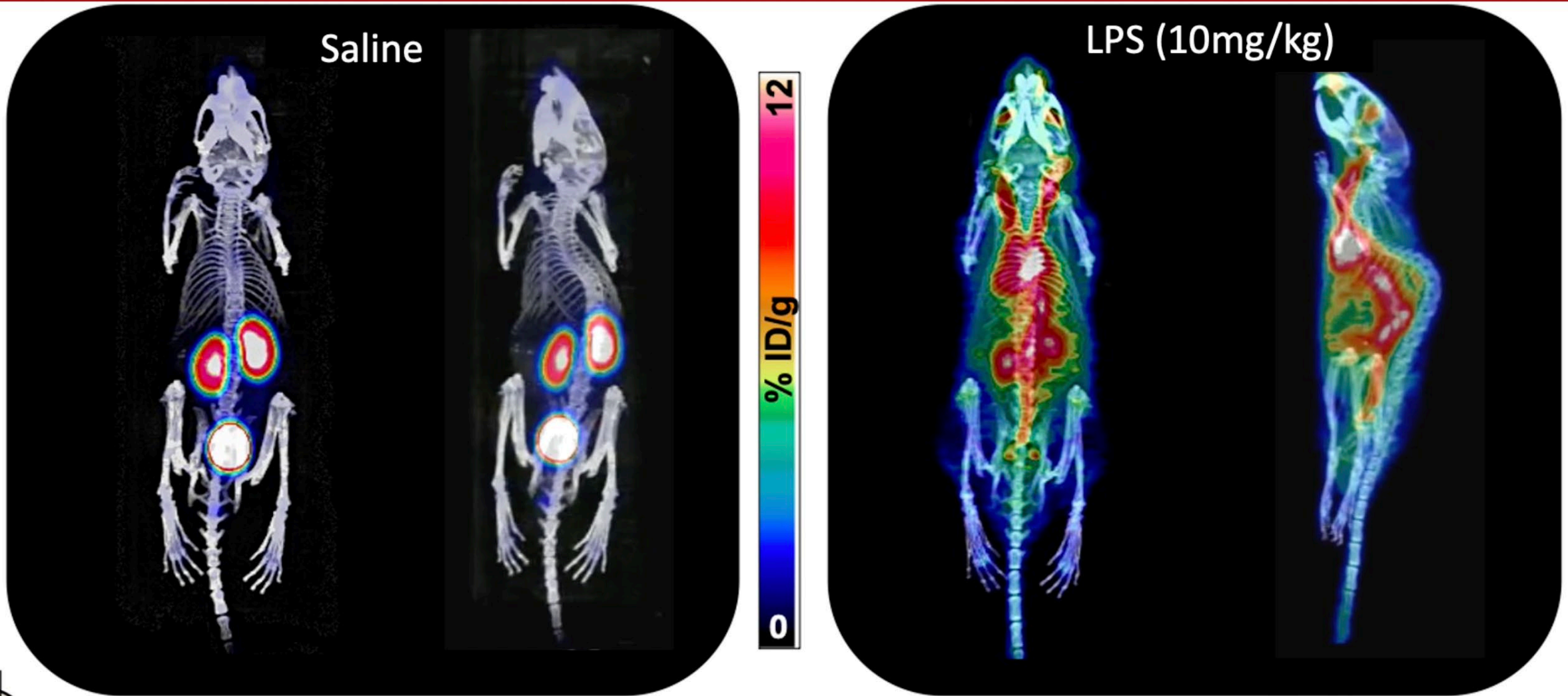
Plasma collected 150 minutes post-injection in n=4 female mice.
97±3% intact

Study Design: Assessing OP-801 in a model of sepsis



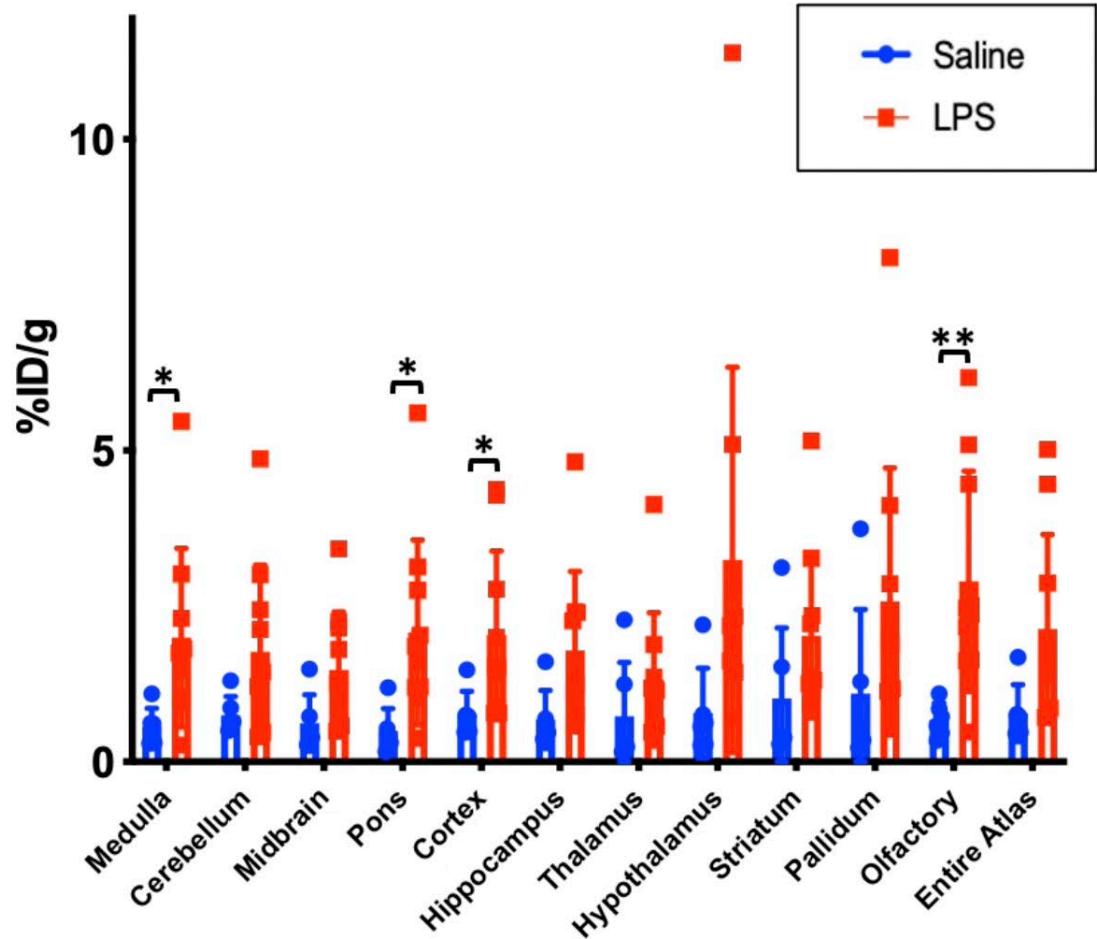
Well characterized model of systemic and neuroinflammation.

Static 50-60 min summed whole-body PET/CT images

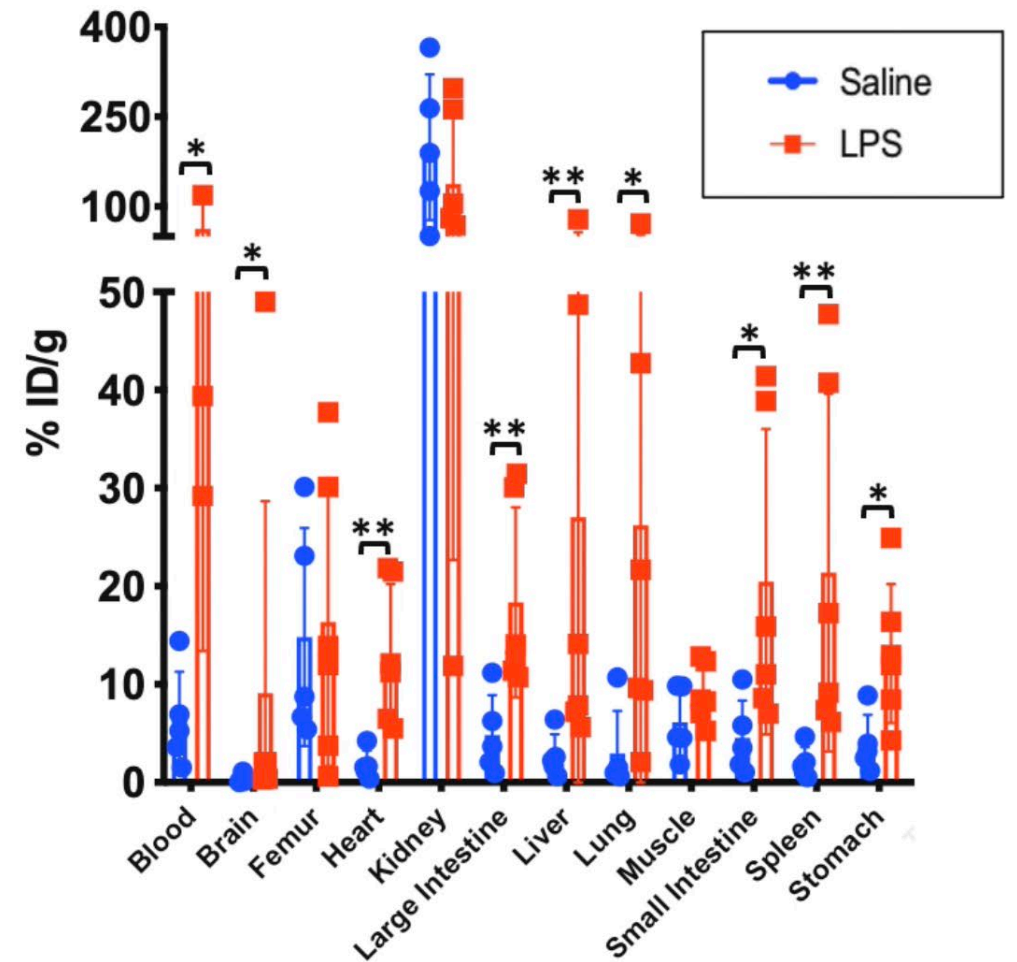


In vivo PET and Ex vivo biodistribution

PET Quantitation



Ex vivo biodistribution



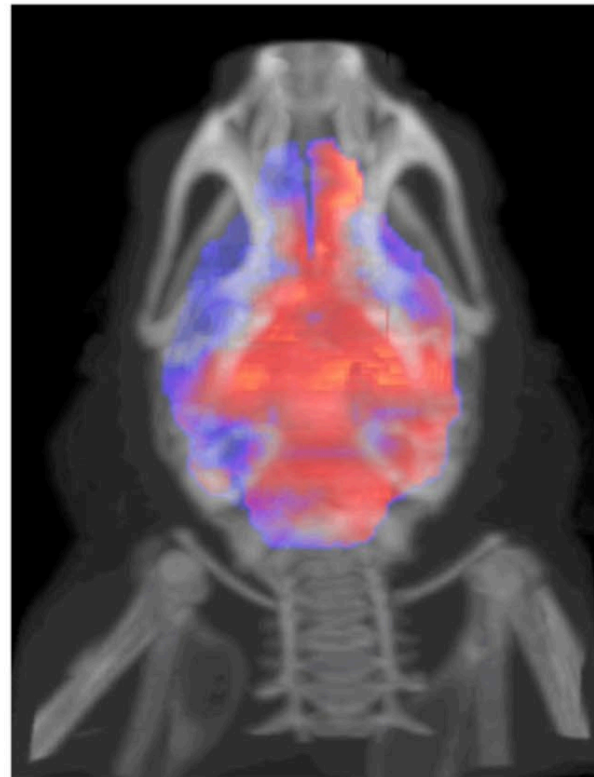
* P<0.05 ** P<0.01

Brain uptake in representative mice

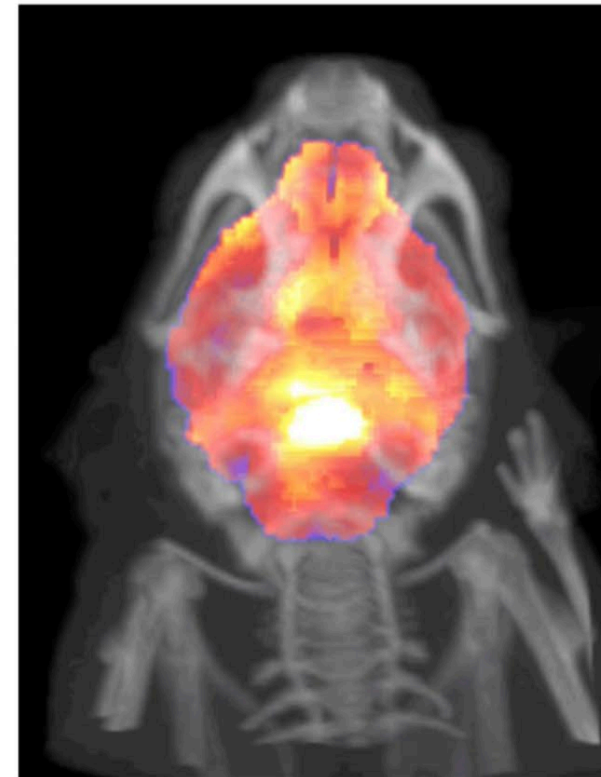
Saline Control



Moderate LPS



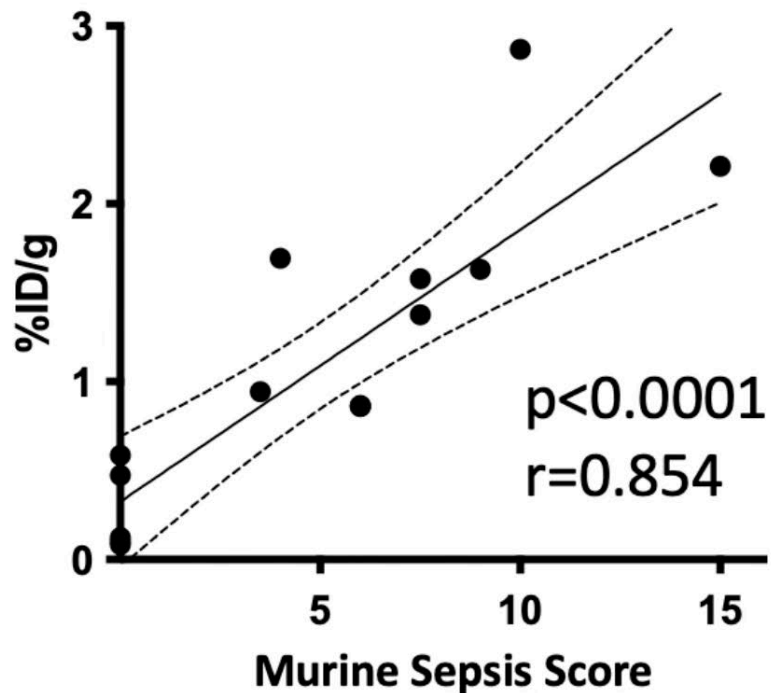
Severe LPS



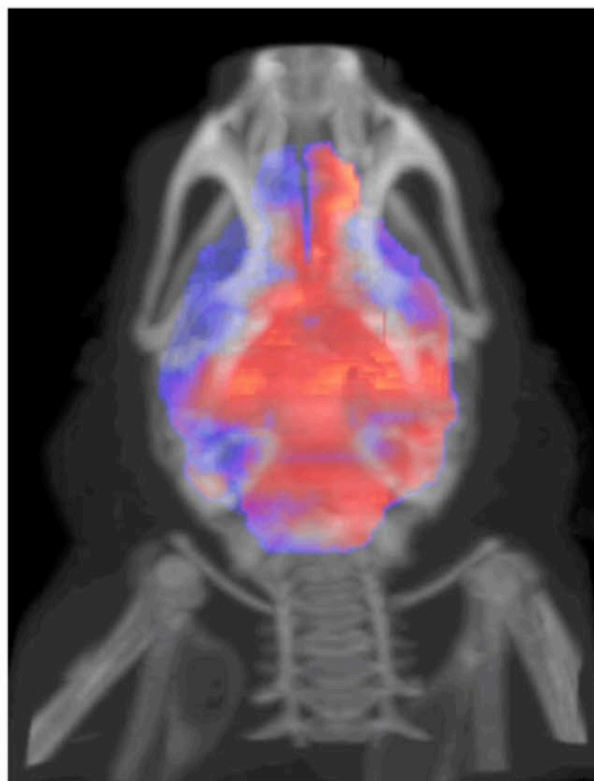
Brain uptake in representative mice

Whole brain uptake

(n=15)

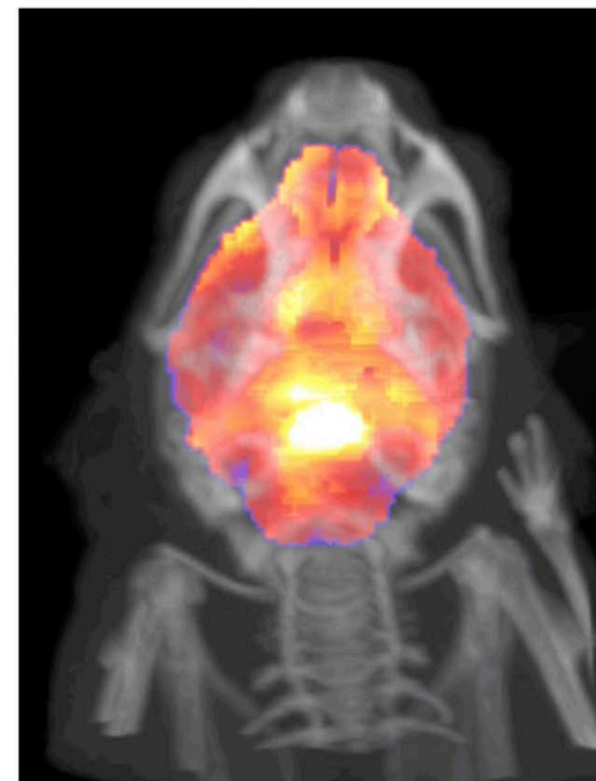


Moderate LPS



Invicro
A Konica Minolta Company

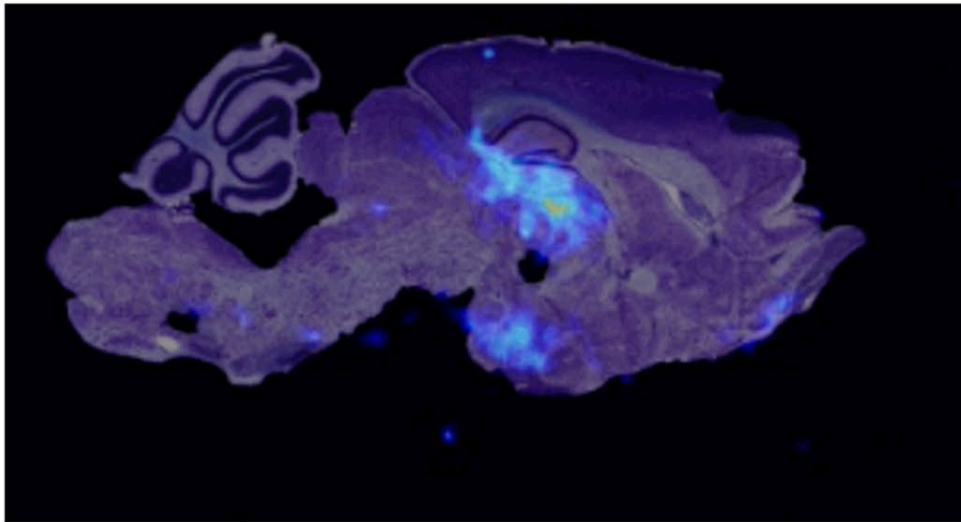
Severe LPS



Ex vivo mouse brain autoradiography

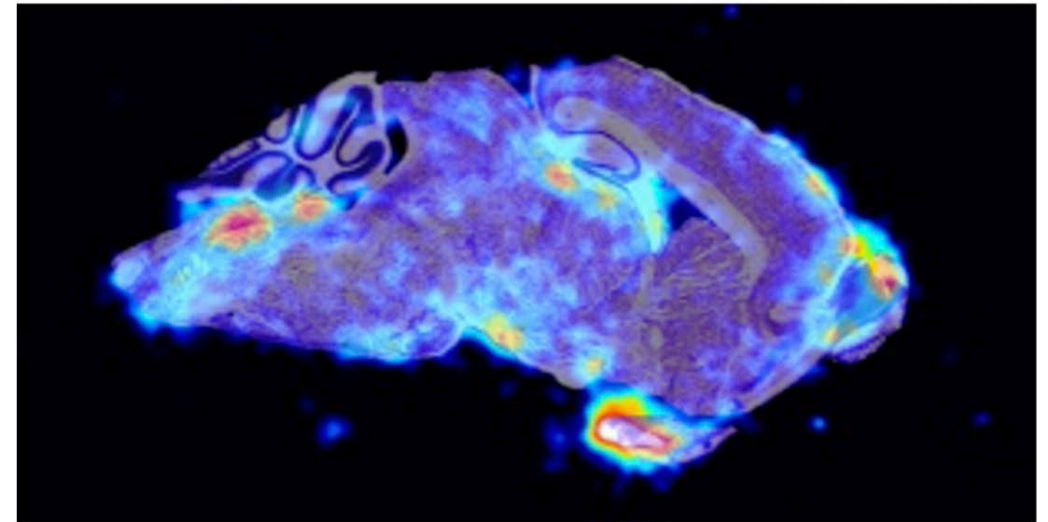
Overlaid on same 40 μ m section nissl stain.
Brain dissected 70min post-injection.
Autoradiography film developed for 19 hours.

Saline Control



low < radioactiv. > high

LPS



Conclusions and Next Steps

- [^{18}F]OP-801 enables sensitive and specific visualization of activated microglia and macrophages in the whole body and brain.
- We will use [^{18}F]OP-801 to evaluate response to anti-inflammatory dendrimer drugs in mouse models of Alzheimer's disease.
- Currently optimizing synthesis for routine clinical production.
- First clinical studies will be in ALS and AD patients, planned for 2022.

Acknowledgements

Dr. Michelle James Lab:

Carmen Azevedo
Samantha Reyes
Isaac Jackson
Dr. Israt Alam
Sydney Nagy
Dr. Mausam Kalita



Cyclotron and Radiochemistry Facility:

Dr. Bin Shen
Jessa Castillo
Rowaid Kellow



Ashvattha Therapeutics:

Jeffrey Cleland, CEO



Matthew Brewer, CBO

Dr. Rishi Sharma



Invicro:

Keryn Palmer

