

Supplemental Information: Monoamine oxidase binding would not be expected to significantly affect [¹⁸F]flortaucipir PET interpretation

Target Journal: European Journal of Nuclear Medicine and Molecular Imaging

Authors: Justin P. Wright¹, Jason R. Goodman¹, Yin-Guo Lin¹, Brian P. Lieberman¹, Jennifer Clemens¹, Luis F. Gomez¹, Qianwa Liang¹, Adam T. Hoye¹, Michael J. Pontecorvo¹, Kelly A. Conway^{1*}

*Corresponding author

Affiliations: ¹Avid Radiopharmaceuticals, a wholly owned subsidiary of Eli Lilly & Company, Philadelphia, PA, USA.

First author: Justin P Wright

Corresponding author: Kelly Conway

3711 Market Street

Seventh Fl Philadelphia, PA 19104, USA

conway@avidrp.com

Supplemental Methods

Quadrupole Time-of-Flight Mass Spectrometer (QTOF-MS)

Samples (15 μ L) were injected on a Waters Acquity UPLC system equipped with a Waters Acquity T3 HSS, 2.1 x 50mm, 1.8 μ m column at a mobile phase flow rate of 0.5 mL/min, and (MS) response was monitored with a Waters Xevo QTOF scanning 50-1200 Da. For each sample analysis, the column was equilibrated with 95:5 water with 0.1% formic acid (Mobile Phase A): acetonitrile with 0.1% formic acid (Mobile Phase B) for 0.25 minutes. Following injection, the gradient was changed to 70:30 Mobile Phase B: Mobile Phase A in a linear fashion over 1.75 minutes, and then to 100% Mobile Phase B over 0.2 minutes, held at 100% Mobile Phase B for 0.8 minutes, followed by 95:5 Mobile Phase A:Mobile Phase B over 0.1 minutes and held for 0.4 minutes. Masslynx QuanLynx™ software was used to analyze MS data. An internal standard was added to all samples to correct for instrument and sample processing variability.

Supplemental Results

[¹⁸F]Flortaucipir autoradiography in rat brain tissue using mild wash conditions

Experimental conditions as described in the Materials and Methods section of the manuscript “[¹⁸F]Flortaucipir Autoradiography: Comparison of Stringent and Mild Wash Conditions”. Under mild wash conditions, high background ARG signal is seen in rat brain tissue samples (male wild-type Sprague Dawley). The MAO-B inhibitor deprenyl (1 μ M) has no blocking effect on [¹⁸F]flortaucipir ARG signal. The MAO-A/B inhibitor pargyline (10 μ M), MAO-A inhibitor, clorgyline (1 μ M), and flortaucipir (1 μ M) partially block [¹⁸F]flortaucipir ARG signal.

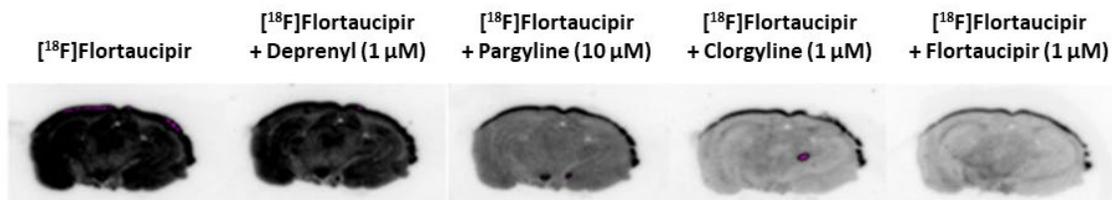
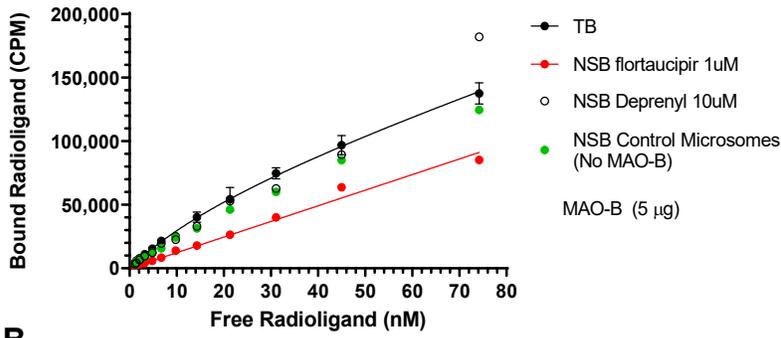


Figure S1. Autoradiography of [¹⁸F]flortaucipir in rat brain tissue with blocking by MAO-A/MAO-B inhibitors and flortaucipir.

Possible artifactual saturation binding curve

Saturation binding for [¹⁸F]flortaucipir against recombinant monoamine oxidase-B (MAO-B) when using 1 μM [¹⁸F]flortaucipir to define non-specific binding (A) generates an artifactual [¹⁸F]flortaucipir:MAO-B saturation binding curve with a K_d of 28 nM by artificially reducing the [¹⁸F]flortaucipir nonspecific binding below that of the control microsomes. A similar artifactual binding curve with a K_d of 16 nM is generated for [¹⁸F]flortaucipir curves run in binding buffer only, in which 10 μM flortaucipir is used to define NSB (B). This signal represents background binding of [¹⁸F]flortaucipir to the filter, which can be reduced by adding saturating amounts of non-radioactive flortaucipir.

A



B

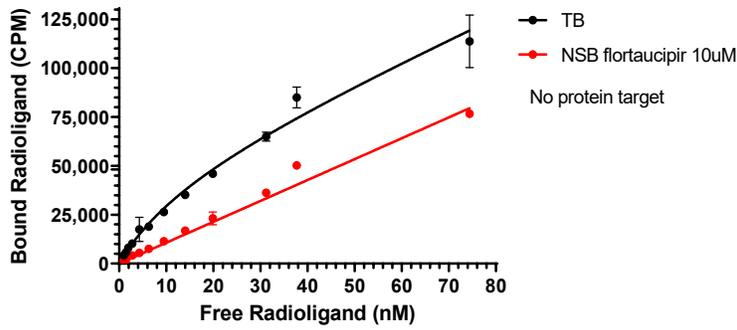


Figure S2. Artfactual [¹⁸F]flortaucipir binding curves generated by using high concentration of flortaucipir to define nonspecific binding.

Abbreviations: CPM, counts per minutes; MAO, monoamine oxidase; NSB, Non-specific binding; TB, Total Binding.