Supporting Information

Radiosynthesis and *in vivo* evaluation of a novel σ_1 selective PET ligand

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Contents of Supporting Information

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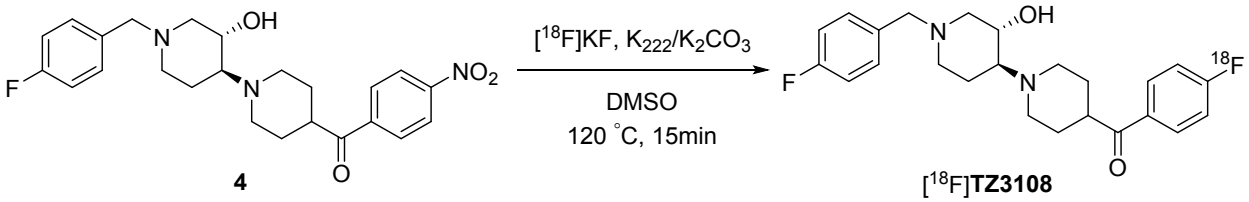
1. Optimization of Radiolabeling [^{18}F]**TZ3108**



Scheme S1. Radiosynthesis of [^{18}F]**TZ3108.**

The radiosynthesis of [^{18}F]**TZ3108** was accomplished by a direct NO_2^-/[^{18}F]F$^-$nucleophilic displacement on an aromatic ring activated by an electron withdrawing carbonyl group at the para-position. Aqueous [^{18}F$^-$]/fluoride was azeotropically dried by co-evaporation with anhydrous acetonitrile in the presence of potassium carbonate as a base and Kryptofix 222 as a phase transfer chelator. The dried mixture was then dissolved in dimethylsulfoxide (DMSO) and reacted with nitro precursor **4** (1.0 ~ 2.0 mg). Carrying out the reaction at 120 °C for 15 min afforded [^{18}F]**TZ3108** in good yield. During the method development, we optimized radiolabeling conditions including: reaction temperature (100, 120 and 140 °C); heating time (5, 10, 15 and 20 min), solvent (DMF vs. DMSO), and the quantity of base (3 vs. 6 equivalent) to improve the radiolabeling yield of [^{18}F]**TZ3108**. At the lower temperature (100 °C), kinetics were slow; a lower yield was observed; whereas at higher temperature, decomposition of reagents occurred which also resulted in a lower yield. 120 °C was chosen for radiolabeling [^{18}F]**TZ3108**. Regarding to the heating time, we found that heating 15 min gave higher yield than heating 5 and 10 min, while extending to 20 min did not increase the yield. Interestingly, using DMSO as solvent gave higher yield than using DMF. In addition, the base amount was noted to affect the yield significantly. Three equivalents of base were sufficient to give good yield; in contrast, when six equivalents of base were used, the excess base caused significant decomposition of the precursor which afforded lower yield of [^{18}F]**TZ3108**. It was noted that starting quantity of precursor (either 1.0 mg or 2.0 mg) had no significant impact on RCY. The purification and the formulation of the final dose are described in the manuscript.

Table S1. Optimization of the temperature for radiolabeling [^{18}F]TZ3108

Temperature (°C)	Heating Time (min)	Base amount	RCY (%)*
100	15	3 eq.	10 ± 3%
120	15	3 eq.	21 ± 3%
140	15	3 eq.	4 ± 2%
* Decay corrected to end of synthesis			

Table S2. Optimization of the heating time for radiolabeling [^{18}F]TZ3108

Temperature (°C)	Heating Time (min)	Base amount	RCY (%)*
120	5	3 eq.	8 ± 2%
120	10	3 eq.	15 ± 3%
120	15	3 eq.	21 ± 3%
120	20	3 eq.	17 ± 3%
* Decay corrected to end of synthesis			

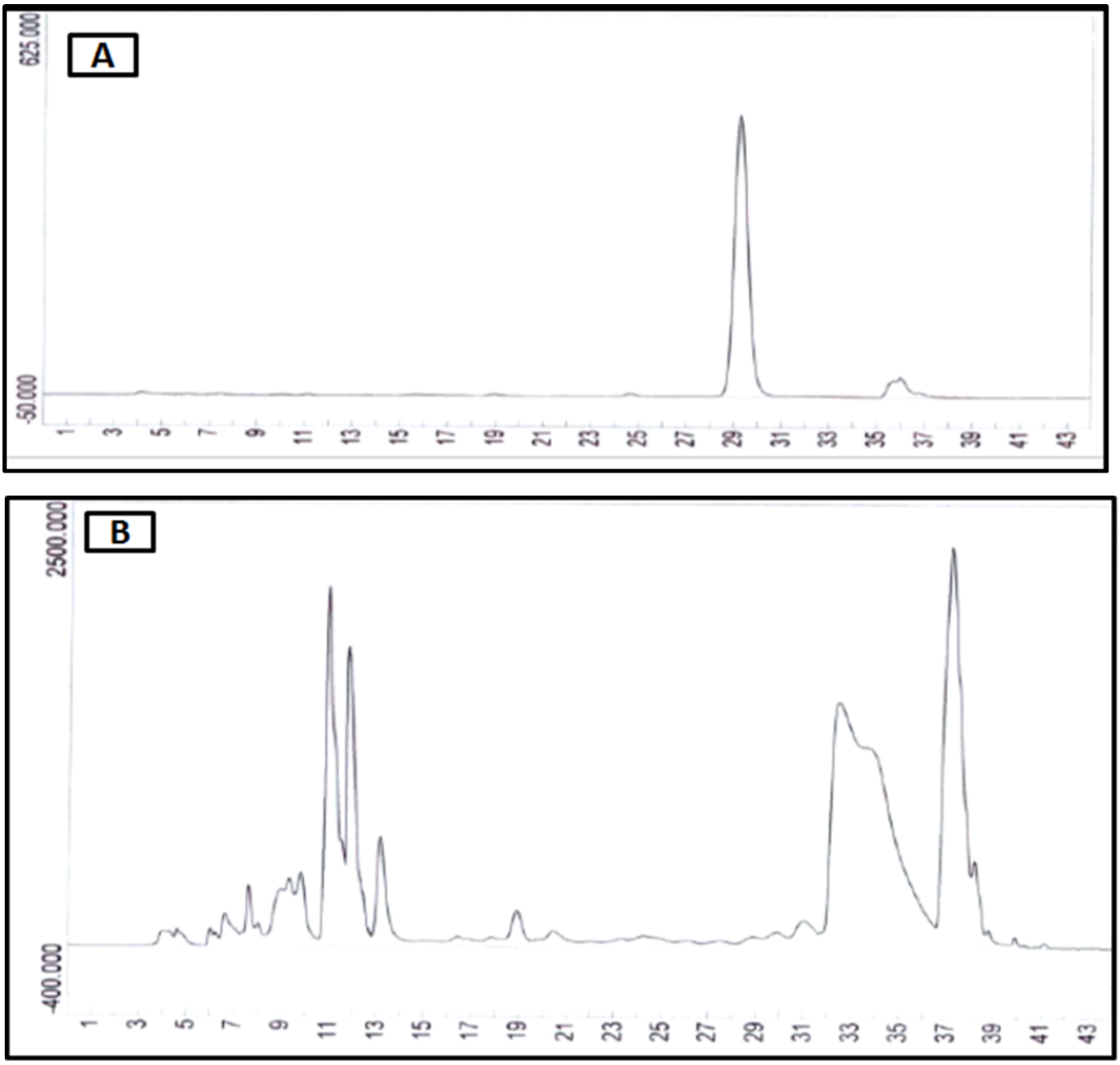


Figure S1. [^{18}F]**TZ3108** was purified by semi-preparative HPLC system (A. Radioactivity; B. UV;)

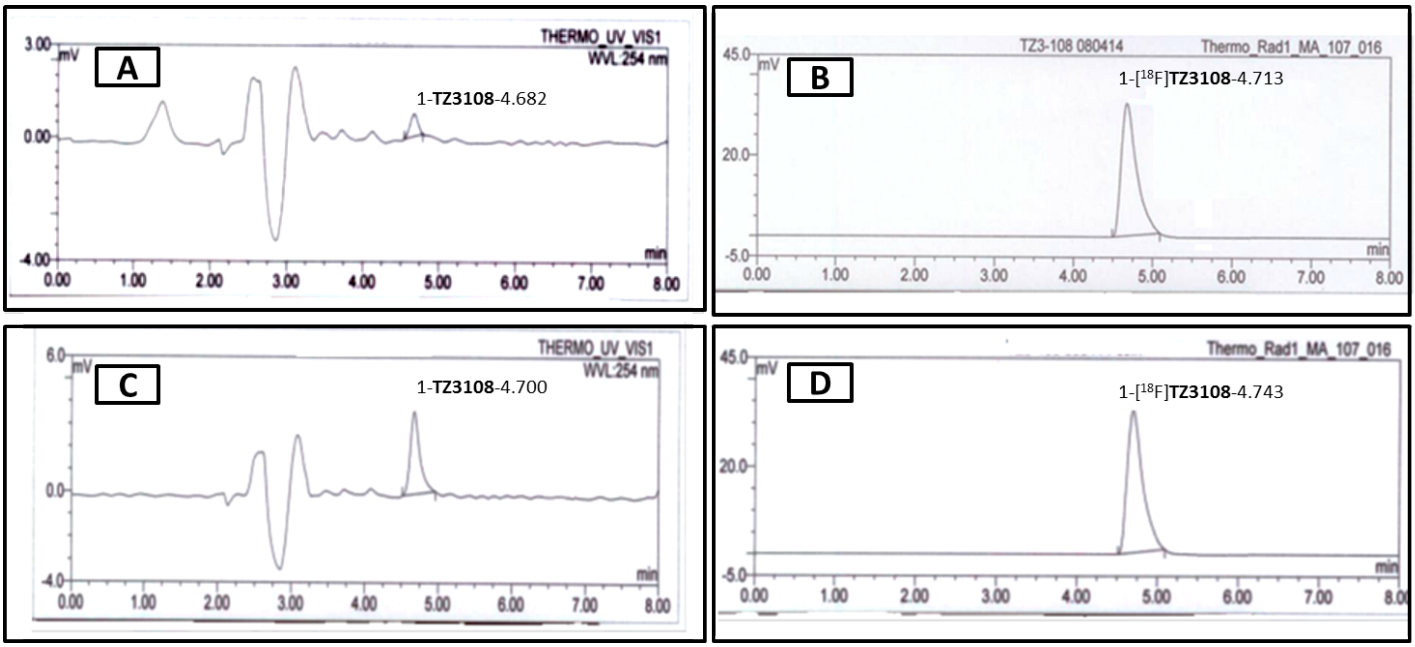


Figure S2. QC of the [^{18}F]**TZ3108** (A. UV; B. Radioactivity) and QC co-injection of the [^{18}F]**TZ3108** + cold standard (C. UV; D. Radioactivity)