Automated radiosynthesis of the ^{18}F-fluoropropylsulfonyl derivative of TAK875, a FFA1-binding PET radiotracer for *β*-cell mass imaging.

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Objectives Type 2 diabetes mellitus (T2D) is marked by a depletion of *β*-cell functional mass. As current understanding of *β*-cell dysfunction in T2D has largely come from post-mortem autopsy data, there is an unmet need for a non-invasive method to monitor *β*-cells. The fatty-acid receptor FFA1 is highly expressed in *β*-cells and is a promising target for pharmacological agents and radiotracers. Recently the synthesis of the ^{18}F-fluoropropylsulfonyl derivative of the synthetic FFA1 agonist TAK875 has been reported [1]. This tracer has potential for quantitative *in vivo* imaging PET studies of *β*-cell functional mass. Herein, we report the fully automated radiosynthesis of the ^{18}F-TAK875 derivative in high specific activity.

Methods An IBA Synthera® Chemistry synthesizer was programed to perform ^{18}F-labeling of the tosylate precursor 1 followed by ester hydrolysis, purification and reformulation. [^{18}F]Fluoride (IBA Cyclone® 18 MeV) was eluted with K_{222}/K_2CO_3/acetonitrile from a QMA cartridge into the reactor. After azeotropic drying, the tosylate precursor 1 (3 mg) in acetonitrile was added and the reaction heated to 100 °C for 2.5 min. NaOH was added for hydrolysis. The solution was quenched and then purified with a C_{18} cartridge and by HPLC. The fraction containing the radiotracer was transferred to a second Synthera® Chemistry synthesizer to perform cartridge-based reformulation.

Results The ^{18}F-fluoropropylsulfonyl derivative of TAK875 was produced, purified and reformulated in the module in under 60 minutes with a RCY of 17.0 ± 4.7 % (n = 3). Analytical HPLC revealed the radiochemical purity >98 % with a high specific activity of 163-322 GBq/μmol (4403 – 8706 mCi/μmol) at EOS. Stability, reactivity and optimization studies of the synthetic route are currently underway to reduce production of an elimination byproduct and to increase overall yield and chemical purity.

Conclusions An automated method for high purity and high specific activity radiochemical production of the ^{18}F-TAK875 derivative has been developed using the Synthera® platform

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References [1] R. Bertrand et al. *J. Label. Compd. Radiopharm.* **2016**, (In press).

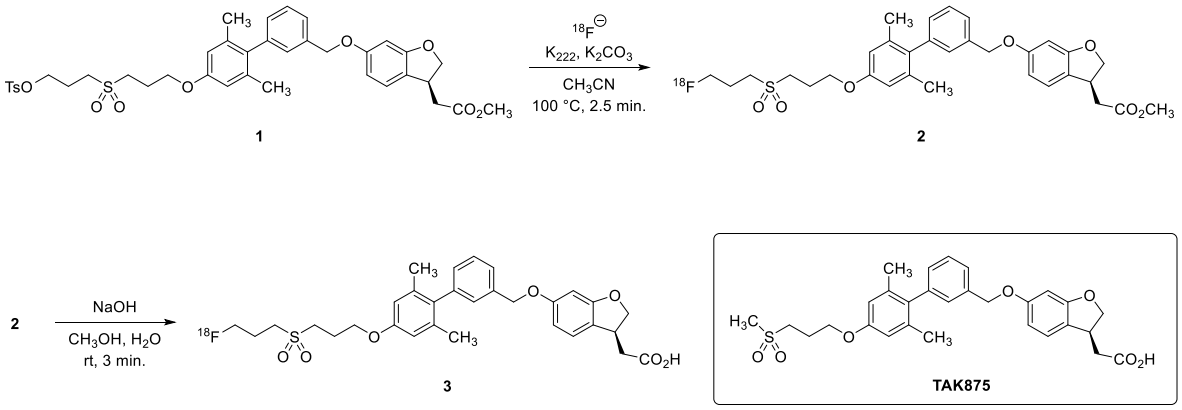

Figure 1. Radiosynthesis of the ^{18}F-fluoropropylsulfonyl derivative of TAK875.