Human Brain Imaging of Alpha-7 nAChR with [18F]ASEM: a New PET Radiotracer for Neuropsychiatry and Determination of Drug Occupancy

Molecular Imaging and Biology

Dean F. Wong[1,2,3,4], Hiroto Kuwabara[1], Martin Pomper[1,2,4], Daniel P. Holt[1], James R. Brasic[1], Noble George[1], Boris Frolov[1], William Willis[1], Yongjun Gao[1], Heather Valentine[1], Ayon Nandi[1], Lorena Gapasin[1], Robert F. Dannals[1,4], and Andrew G. Horti[1].

Departments of [1]Radiology, [2]Psychiatry, [3]Neuroscience, School of Medicine
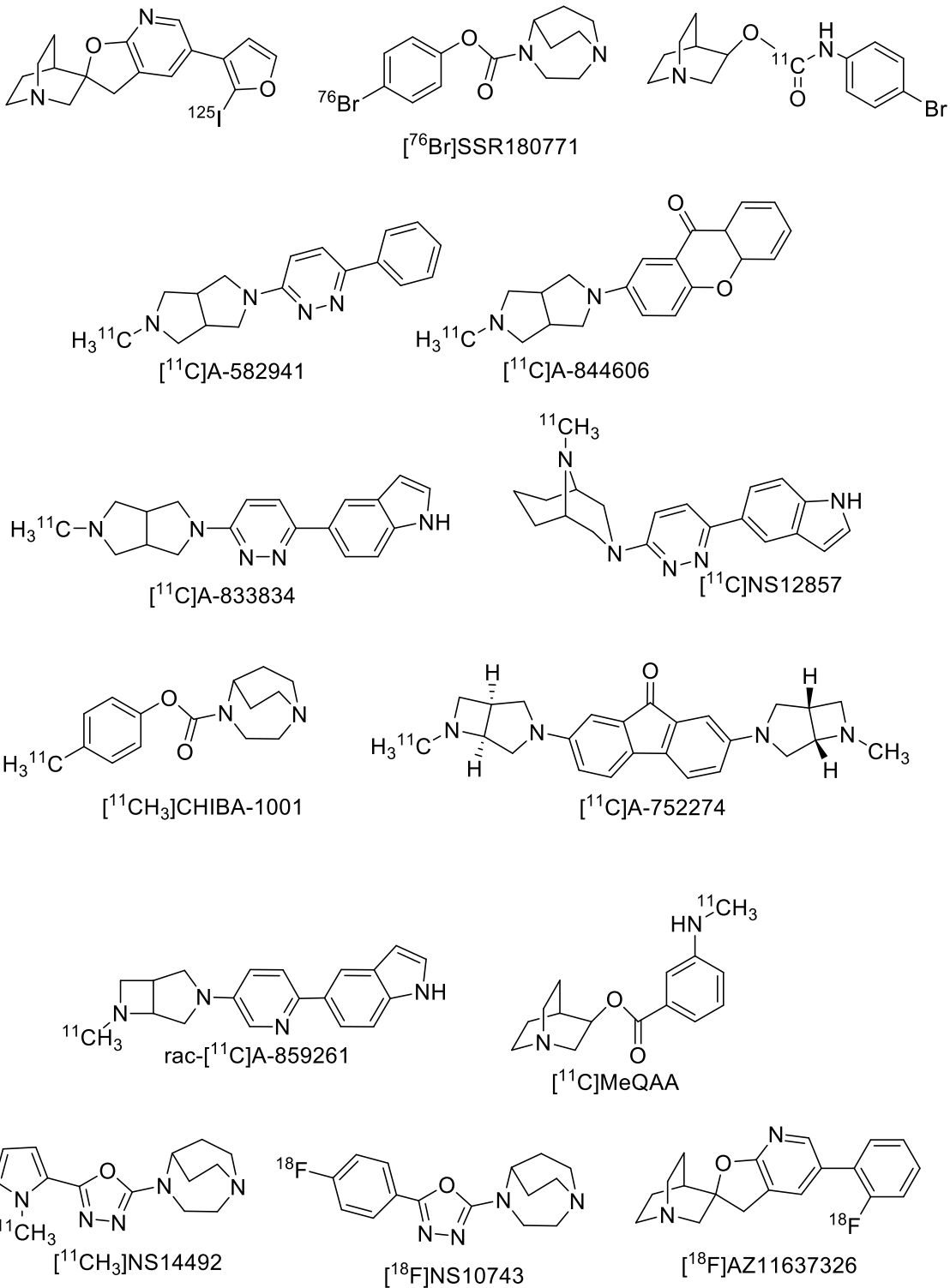**[4]Environmental Health Sciences, Bloomberg School of Public Health**
The Johns Hopkins University, Baltimore, MD.

Contact information:

Dean F. Wong, Johns Hopkins Medical Institutions., JHOC Bldg room 3245, 601 N. Caroline St., Baltimore MD 21287.

410-955-8433 (voice); 410-955-0696 (fax), email:dfwong@jhmi.edu

Supplemental Material

[76Br]SSR180771

[11C]A-582941

[11C]A-844606

[11C]A-833834

[11C]NS12857

[11CH3]CHIBA-1001

[11C]A-752274

rac-[11C]A-859261

[11C]MeQAA

[11CH3]NS14492

[18F]NS10743

[18F]AZ11637326

Supplemental Figure 1. Previous representative PET and SPECT radioligands for imaging α7-nAChR

Inclusion Criteria for Human Volunteers for PET Iimaging:

1. Healthy non-smoking males and females, as determined by medical history, physical examination, vital signs, clinical laboratory tests, and an electrocardiogram.
2. Between 18-65 years old, inclusive.
3. BMI between 18-30 kg/m^2 inclusive.
4. Have clinical laboratory test results within normal reference ranges for the population or investigator site or results with acceptable deviations that are judged not considered by the investigator to be clinically significant.
5. All subjects and their partners of childbearing potential must commit to use two methods of contraception, one of which must be a barrier method, from the time of screening and throughout the study and until follow-up.
6. Less than 195 cm (6 feet and 5 inches) tall in order to accommodate the whole body scanning. (Part II)
7. Have sufficient arterial or venous access.
8. Willing to give written informed consent and to comply with the study restrictions.

Exclusion Criteria:

1. Current or prior smoker.
2. Are currently enrolled in or discontinued within the last 30 days from a clinical trial involving an investigational drug or device (other than the study drug) or are currently enrolled in any other type of medical research.
3. Are currently experiencing neuropsychiatric illness or severe systemic disease based on history and physical exam.
4. Have participated in other research protocols in the last year such that radiation exposure would exceed the annual limits.
5. Pregnant or nursing women.
6. History of head trauma with prolonged loss of consciousness (>10 min.) or any neurological condition including stroke or seizure (excluding childhood febrile seizure) or history of migraine headache.
7. History of any clinically relevant hematological, hepatic, respiratory, cardiovascular, renal or CNS disease or other medical condition that is capable of constituting a risk factor when taking the study drug.
8. Suffer from claustrophobia and would be unable to undergo MRI or PET scanning.
9. Any confirmed significant allergic reactions against any drug, or multiple allergies.
10. Clinically significant abnormal MRI.(Part I & Part II only)
11. Subject has implanted or embedded metal objects, prostheses, or fragments in the head or body that would present a risk during the MRI scanning procedure, or have worked with ferrous metals either as a vocation or hobby (for example, as a sheet metal worker, welder, or machinist) in such a way that might have led to unknown, indwelling metal fragments that could cause injury if they moved in response to placement in the magnetic field. (Part I & Part II only)
12. Currently uses any medications (prescription drugs, over-the-counter drugs or herbal remedies such as St. Johns Wort) which cannot be discontinued 14 days (or < 5 half-lives, whichever is longer) prior to the PET scan and throughout the study. Exceptions include daily multiple vitamins., including any prior use of cholinesterase inhibitors
13. Currently a user (including "recreational use") of any illicit drugs of drug or alcohol abuse, or has a positive drug screen.