

SIGMA-1 TARGETED PET TRACERS

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Technology Description

Researchers at Washington University in St. Louis and their colleagues have developed positron emission tomography (PET) tracers with high affinity for sigma-1 receptors. Sigma receptors have two subtypes, sigma-1 and sigma-2. Sigma-1 has high expression in the limbic and motor structures in the brain. As such, it is an important target for drug development to treat neurological disorders and neuropsychiatric diseases. In addition, imaging sigma-1 receptors in the brain could be used to diagnose disorders of the central nervous system (CNS), monitor disease progression and assess therapeutic efficacy in treating these diseases. PET could be used for such imaging, but sigma-1 specific tracers are lacking. To help meet this need the inventors have developed this technology. It provides compounds that have high affinity and high selectivity for sigma-1 and can be used as PET tracers. This technology can be used to diagnose and monitor CNS disorders and serve as a tool to assess treatment efficacy.

Stage of Research

In vivo validation studies using animal models have shown that these compounds can be used as PET radiotracers.

Applications

- PET imaging for sigma-1 associated conditions, including CNS disorders
 - Track disease progression
 - Assess therapeutic efficacy
- Potential for therapeutic development

Key Advantages

- Provides effective sigma-1 targeted PET tracers
- High affinity for sigma-1
- High selectivity for sigma-1 versus sigma-2
- High specific binding of sigma-1 in the brain
- Good clearance rates from the brain

Publications

- Wang W, Cui J, Lu X, Padakanti PK, Xu J, Parsons SM, Luedtke RR, Rath NP, Tu Z. [Synthesis and in vitro biological evaluation of carbonyl group-containing analogues for \$\sigma_1\$ receptors](#). J Med Chem.

- 2011 Aug 11;54(15):5362-72. doi: 10.1021/jm200203f. Epub 2011 Jul 20.
- Ikome HN, Ntie-Kang F, Ngemenya MN, Tu Z, Mach RH, Efang SM. [4-arylpiperidines and 4-\(\$\alpha\$ -hydroxyphenyl\)piperidines as selective sigma-1 receptor ligands: synthesis, preliminary pharmacological evaluation and computational studies](#). Chem Cent J. 2016 Aug 23;10(1):53. doi: 10.1186/s13065-016-0200-1. eCollection 2016.
 - Yue X, Jin H, Luo Z, Liu H, Zhang X, McSpadden ED, Tian L, Flores HP, Perlmutter JS, Parsons SM, Tu Z. [Chiral resolution of serial potent and selective \$\sigma_1\$ ligands and biological evaluation of \(-\)-\[\$^{18}\$ F\]TZ3108 in rodent and the nonhuman primate brain](#). Bioorg Med Chem. 2017 Feb 15;25(4):1533-1542. doi: 10.1016/j.bmc.2017.01.017. Epub 2017 Jan 16.

Patents

- Issued US Patent. [Compounds comprising 4-benzoylpiperidine as a sigma-1-selective ligand](#). Patent number US 8,658,131

Related Web Links

- [Dr. Tu profile](#)