UNIVERSITY OF MINNESOTA
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Unique small molecule modulators of GPCRs

Novel small molecules that bind and modulate G-protein coupled receptors (specifically Sigma 1 and 5-HT7) for therapeutic development.

Applications

- GPCR basic research
- Chemical probes
- Therapeutic development
- COVID-19 drug development

Key Benefits & Differentiators

- **High therapeutic potential:** More than 40 structurally unique heterocyclic phenethylamine derivatives that target therapeutically relevant GPCRs.
- **Selective and specific:** Selective ligands for the 5-HT7 and Sigma 1 receptors were identified, each with low nanomolar binding affinities.
- **Minimal toxicity:** In-vitro assays with the compounds show minimal cytotoxicity to mammalian cells in culture.
- **Modulation of COVID-19 target:** Identified compounds modulate Sigma 1, a recently identified target for COVID-19 therapies.

Targeting GPCRs

G-protein-coupled receptors (GPCRs) are a prominent pharmacological target for the treatment of a wide variety of diseases and disorders. Exemplifying the success of this approach, more than 30% of FDA approved drugs target at least one GPCR and worldwide more than 25% of drug sales come from GPCR modulating compounds. To expand this promising this pharmacological space, Dr. Joseph Topczewski developed structurally novel small molecules that act as GPCR modulators with either agonist or antagonistic effects. Furthermore, some of these compounds target Sigma 1, a recently identified target for COVID-19 therapies.

Unique phenethylamine derivatives

The new molecules are small, rigid derivatives of phenethylamine, a structural motif that is part of several natural GPCR ligands including dopamine and epinephrine, as well as morphine and pseudoephedrine. The GPCR binding affinity of these compounds was assessed through the Psychoactive Drug Screening Program (National Institute of Mental Health). In vitro testing has revealed one of the compounds to have negligible cytotoxicity and to be capable of inhibiting oxidative stress in cultured mammalian cells. These compounds have the potential to be developed for use in a wide variety of indications including COVID-19, migraines, heart disease, alcohol abuse, pain management, psychoses, depression, asthma, and retinal degradation.

Phase of Development

In vitro assessment of compounds has revealed low nanomolar binding affinities of the compounds to select GPCRs and minimal toxicity to mammalian cells in culture.

Researchers

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Technology ID

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Publications

3-Amino-chromanes and Tetrahydroquinolines as Selective 5-HT2B, 5-HT7, or σ1 Receptor Ligands
ACS Med. Chem. Lett. , 2019, 10, 10, 1436–1442

Desired Partnerships

This technology is now available for:

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- Sponsored research
- Co-development

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