Rapid High-Throughput GPCR Screen for IBS-C Drug Discovery (#8330)

Permits rapid screening of pharmaceutical libraries for drug discovery

Georgia Tech researchers have developed a rapid high-throughput assay that can be used to screen pharmaceutical libraries to identify novel treatments for irritable bowel syndrome with constipation (IBS-C). Georgia Tech's luciferase-based 5-HTR_{4b} assay achieves a screening throughput of one compound per second, with an overall assay time of 2.5 hours. A major challenge in identifying novel treatments for IBS-C is a lack of serotonin receptor 4b (5-HTR_{4b}) high-throughput assays to rapidly assess large libraries of chemicals. Currently, a 2-day culture time is required to test colon cell motility, which is time-prohibitive for a primary screen tool.

Using their G-protein coupled receptors (GPCR) assay, researchers screened more than 1,000 natural products and anti-infection agents and identified five previously unidentified 5-HTR_{4b} ligands. The team validated three of the five ligands (hordenine, halofuginone, and revaprazon) as 5-HTR_{4b} agonists, as they increase motility or wound healing in colon epithelial cells. Significantly, the increased assay signal of the luciferase reporter should enable the generation of other high-throughput GPCR-based assays.

Benefits/Advantages

- **Powerful**: Permits the rapid screening of pharmaceutical libraries to identify 5-HTR_{4b} agonists as therapeutic candidates for IBS-C
- **Efficient**: Achieves a screening throughput of one compound per second
- **Innovative**: Enables screening of gut microbiota metabolites to further understand the link between the host and gut microbiome

Potential Commercial Applications

- Drug discovery

Background/Context for This Invention

In humans, 95 percent of 5-HT is found in the gastrointestinal tract, where its release and reception transmit information from the gut lumen to gut nerve cells and smooth muscles. Of the seven 5-HT receptor families, 5-HTR_4 is broadly expressed in the gut—for example on neurons that control muscle contraction and relaxation—and has been implicated in IBS-C, which affects 15 percent of the world population. Agonists of 5-HTR_4 are used for treatment of IBS, relieving constipation, abdominal pain, and bloating.

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More Information

U.S. Number: 62/930,194

Publications

Identification of Three Antimicrobials Activating Serotonin Receptor 4 in Colon Cells, ACS Synthetic Biology, 2019-11-12

For more information about this technology, please visit:
https://licensing.research.gatech.edu/technology/rapid-high-throughput-gpcr-screen-ibs-c-drug-discovery

Images:

The automated sequential delivery of multiple fluids. A varying number of delay gates imprinted in the branches are shown in the figure.

COVID-19 and flu saliva test on paper: (A) The automatic sequential delivery of multiple reagents required for virus test; (B) Water pouring into the device triggers the virus assay, allowing the presence of SARS-CoV-2 and influenza A & B viruses to be visually identified by the color changes in the corresponding detection spot