

10th European Organic Chemistry Congress

March 21-22, 2019 | Rome, Italy

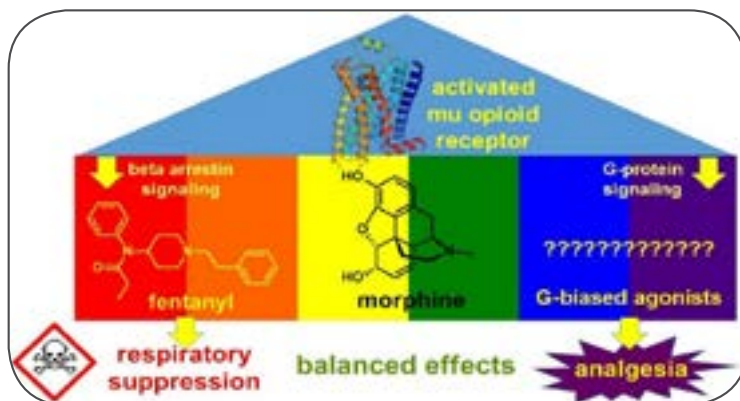


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Addressing the opioid crisis with safer opioid pain relievers: Is it possible?

Compounds that activate opioid receptors, especially the mu opioid receptor (MOR), have been used extensively since antiquity for pain relief and euphoria. Unfortunately poppy-derived compounds (e.g. morphine) as well as their modern synthetic functional mimics (e.g., fentanyl) also can elicit a host of unwanted side effects, include life-threatening respiratory suppression. In fact, the ongoing worldwide opioid crisis has made the dangers of opioid abuse quite clear. In our studies we have made probe molecules and potential drugs to untangle the mechanistic details of MOR signaling and its pharmacological effects. A wide respiratory safety window appears to require robust G-protein-mediated MOR signaling with almost no measurable beta arrestin involvement. We have identified functionally biased and drug-like MOR agonists with this specific profile. Further, we have found them to be robust pain relievers in mice, with greatly improved respiratory safety relative to currently available opioid drugs.



Recent Publications

1. Kennedy N M, Schmid C L, Lovell K M, Yue Z, Chen Y-T, Cameron M D, Bohn L M and Bannister T D (2018) Optimization of a series of Mu opioid receptor (MOR) agonists with high G protein signaling bias. *Journal of Medicinal Chemistry* 61(19):8895-8907.
2. Schmid C L, Kennedy N M, Ross N C, Lovell K M, Yue Z, Morgenweck J, Cameron M D, Bannister T D and Bohn

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- L M (2017) Bias factor and therapeutic window correlate to predict safer opioid analgesics. *Cell* 171(5):1165-1175.
3. Pan X, Yang C, Cleveland J L and Bannister T D (2016) Synthesis and cytotoxicity of sempervirine and analogues. *Journal of Organic Chemistry* 81(5):2194-2200.
 4. Nair R N, Mishra J K, Li F, Tortosa M, Yang C, Doherty J R, Cameron C, Cleveland J L, Roush W R and Bannister T D (2016) Exploiting the co-reliance of tumors upon transport of amino acids and lactate: Gln and Tyr conjugates of MCT1 inhibitors. *Med. Chem. Commun.* 7(5):900-905.
 5. Wang H and Bannister T D (2014) Synthesis and structure-activity relationships of pteridine dione and trione monocarboxylate transporter 1 inhibitors. *Journal of Medicinal Chemistry* 57(17):7317-7324.

Biography

Thomas Bannister is a Senior Scientific Director of Molecular Medicine at Scripps Research in Jupiter, Florida, world leader in nonprofit biomedical research. He received his scientific training at Wabash College, Yale University, and Indiana University. AT, IU he studied under Professor William R Roush. He then worked in the pharmaceutical industry as a Drug Discovery Medicinal Chemist for 14 years. He came to Scripps Florida in 2005 to actively collaborate on project teams seeking breakthrough therapies for various cancers, neurological disorders, and pain.

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