Selective GRK5 Inhibitors for Heart Failure and Cancer

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Categories:
- Chemistry and Chemical Analysis
- Pharmaceuticals

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- Biochemistry
- Breast Cancer
- Cancer
- Cancer Drug
- cardio-metabolic disorders
- Cardiovascular Disease
- Chemical Synthesis
- Chemistry and Chemical Analysis
- Drug Conjugates
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- Inhibitors
- Kinases
- Medicinal Chemistry
- Pharmaceutical Analysis
- Pharmaceutical Development
- Pharmaceutical Research
- Pharmaceuticals
- Pharmacology
- potent
- Selective
- small molecules

Researchers at Purdue University have developed selective small molecule inhibitors of G protein-coupled receptor kinase 5 (GRK5) for preventing heart failure and treating breast cancer. GRK5 is a signaling protein prevalent in the lungs and heart and is an attractive target for disease including heart failure and cancers. Purdue researchers designed a series of selective, irreversible GRK5 inhibitors. Mass spectrometry analysis supports the hypothesis that the best of these compounds interacts with a flexible loop on GRK5 containing a non-conserved cysteine, suggesting high potency and selectivity. This new pharmaceutical development promises to improve patient care by allowing for lower dosing and minimized side effects compared to current treatments of heart related conditions. Further, the new small molecule drug candidates show promise to treat hyperproliferative diseases including breast cancer. A top

compound has a nanomolar half maximal inhibitory concentration and over 1000 times selectivity for GRK5 over GRK2.

Advantages:
-Can Minimize Side Effects and Enables Lower Therapeutic Dosing for Treating Heart Related Conditions and Breast Cancer
-Highly Potent
-Highly Selective to GRK5

Potential Applications:
-Prevention of Heart Failure
-Treatment of Breast Cancer
-Pharmaceutical Research and Development

Technology Validation: A top compound has a nanomolar half maximal inhibitory concentration and over 1000 times selectivity for GRK5 over GRK2.

People:

- Tesmer, John (Project leader)
- Rowlands, Rachel
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Intellectual Property:

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