**Background:**

Long QT syndrome is a heart rhythm disorder where the cardiac muscles exhibit a delay in cardiac repolarization, which can lead to serious arrhythmias (Mayo Clinic). This abnormality may be congenital or acquired due to an underlying medical condition, or response to certain medications. Recently, researchers from the Washington University in St. Louis, identified a novel therapeutic approach to treat these cardiac arrhythmias.

**Technology Description:**

This therapeutic target was identified and validated by Dr. Jianmin Cui, an accomplished researcher in the Department of Biomedical Engineering, and his research team. The identified drug candidate is a novel gate opener for the $I_{ks}$ channel; a macromolecular complex comprised of the KCNQ1 alpha subunit and KCNE1 beta subunit which is critical for cardiac repolarization, and therefore a prime target for antiarrhythmic drug development.

Previously, they demonstrated that PIP2 is essential for activating potassium channels, KCNQ1 and $I_{ks}$, as it triggers the pore gate domain to open, (Zaydman et al., PNAS 2013). Using the previously identified PIP2 binding site, they performed a robust in silico screening of chemical compounds and identified a small molecule, CP1, as a novel $I_{ks}$ opener. Preliminary experiments using Guinea-Pug ventricular myocytes and computer simulations demonstrated the CP1 compound mediates the activation of $I_{ks}$ channels. Therefore, CP1 is potential therapeutic for arrhythmic conditions such as long QT syndrome. This target may also be useful for other conditions such as epilepsy where potassium gated channels are implicated in the disorder. The key features for this novel therapeutic approach include:

**Key Advantages:**

- **Novel:** CP1 is a novel target for anti-arrhythmic drug development.
- **Specificity:** High throughput screening indicates binding is specific and therefore will decrease the chance of side effects.
- **Validated:** Studies in oocytes and mammalian ventricular myocytes coupled with computer simulations of canine ventricular action potential demonstrates CP1 interacts with $I_{ks}$ channels.

**Patent Number:** A patent has been filed.

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**Application Space**
Therapeutic, Cardiology

**WUSTL Case#**
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