Docket #: S19-295

Antibody-Based Delivery of Imaging Probe or Small Molecule Drug to Cardiac Conduction System

Heart rhythm disorders are difficult to treat with conventional drug therapy and intraoperative injury to the cardiac conduction system (CCS) complicates heart-related surgeries and is a major cause of morbidity and mortality. A theranostic approach to visualize and target the CCS would help to mitigate damage during surgical or catheter procedures, as well as offer a general platform for drug delivery. Antibodies targeting CCS-specific surface proteins can be conjugated with near-infrared or contrast imaging probes as well as small molecule drugs for either imaging or treating afflicted CCS tissue. By detailed profiling of surface proteins expressed specifically in cardiac conduction cells such as the sinoatrial node (SAN), atrial-ventricular node (AVN), His bundle and Purkinje fibers, a suite of antibodies that bind to the surface proteins of these unique structures have been developed to enable molecular targeting of the CCS.

Applications

- Visualizing the CCS for surgical pre-planning or during heart surgery or transvenous procedures (catheterizations, electrophysiologic studies) to prevent procedural damage to the CCS
    - Methods include near-infrared, MRI, or CT imaging
- Deliver drugs to CCS to help slow heart rate (rhythm or rate control) in patients with cardiac arrhythmias (such as atrial fibrillation, automatic or reentrant atrial tachycardias, junctional ectopic tachycardias, and/or ventricular tachycardias) or speed up heart rate in patients with heart block or sick sinus syndrome
- **Identification and sorting of CCS cells** derived from dissociated heart muscle tissue, induced pluripotent stem cells (iPSCs) or embryonic stem cells (ESCs)

    - High-throughput drug screening to evaluate potency and toxicity

Advantages

- Novel approach to molecularly target CCS cells
    - Synthetic antibodies binding to CCS-specific surface markers
    - Covalently conjugate imaging and therapeutic agents
- No other known CCS-visualization approaches

Publications

- Goodyer, WR., et al. Transcriptomic Profiling of the Developing Cardiac Conduction System at Single-Cell Resolution. *Circulation Research* 2019; 125(4): 379-397.

Patents

- Published Application: WO2021007193
- Published Application: 20220323616
- Published Application: 20260348982
- Issued: 12,625,147 (USA)

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