Cardiac Transplanted in Pharmocology

Ion channels have long been targets for cardiac safety testing. However, other proteins involved in the transport of ions across membrane barriers are also relevant for pharmacological safety.

To explore the progress in pharmacological investigation of cardiac transplanted, we have evaluated new methodologies for both desired and unwanted effects of compounds on several cardiac proteins. Based on solid supported membrane (SSM) and impedance technology, recording from either 1 or 16 wells simultaneously. As protein containing samples we have used HEK293 cell lines, mitochondrial inner membrane vesicles from pig heart as well as PSC-derived cardiomyocytes on automated systems.

We have focused on two transporters which emerged as targets in pharmacological safety and testing. First we investigated the Sodium-Calcium-Exchange (NCX), which plays an important role in the cardiac cell calcium homeostasis under physiological and pathological conditions.

**Literature**


**Human iPSC derived cardiomyocytes show NCX currents and inhibition of NCX increases the beat rate**

**Development of a screening tool for NCX**

**NaK-ATPase in different cells**

A Sensor Based Technique for Pharmacological Safety Testing of Cardiac Transport Proteins NCX, NaKATPase and Respiratory Chain Complexes

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NaK-ATPase and Respiratory Chain Complexes

**SSM-based electrophysiology: A method to resolve electric events generated by transmitters**

Solid Supported Membrane (SSM)-based electrophysiology is a method, which allows the resolution of low amplitude electric events in biological membranes. In this work, we have investigated the advantages of electrophysiology to the transport of ions. It enables real-time activity measurement of electronegative SLC-transports, MS-transports and ion pumps, localized in a defined site and in different sites. Unlike in-cellular electrophysiology, which requires sensitive sensor coated with a high amount of membrane vesicles or proteoliposomes used. In this way, any process that generates an electrical potential can be registered with high amplification. The method was established in the 90's and has recently been improved up to a 16-well format.

**Direct measurement of respiratory chain complex activity in mitochondrial membranes**

**Sample preparation**

A mitochondrial preparation is obtained, followed by the isolation of the mitochondria. The inner mitochondrial membrane is isolated and resuspended. At the end of the experiment, the signal from a mitochondrial preparation is determined in an electrochemical cell under oxygen.

**The activity of individual respiratory chain complexes recorded with SSM-based electrophysiology**

**NaK-ATPase inhibitor in HEK293 cells**

A NaK-ATPase was purified from HEK293 cell and used for a screening of NaK-ATPase activity in different cells. The NaK-ATPase activity in different cells can be measured under control condition. Differences in the NaK-ATPase activity in different cells depend on the presence of NaK-ATPase activity in different cells. In this way, NaK-ATPase activity in different cells is assessed in a single cell.

**Direct measurement of NCX activity with SSM-based electrophysiology.**

SEA Inhibitors increase the beat rate of PSC derived CMs. Cardiomyocytes were dispersed in the control group. After the cell density was fixed, the carbamates were added to the cultured media. The activity was measured directly by the change in calcium amplitudes. The conclusion was that the NaK-ATPase activity in different cells is assessed in a single cell.