

# NORBERT NAGY



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## RESEARCH AREA

The cardiac electrophysiology investigates the electrical changes of the heart, including both the physiological and pathological functions as well as novel pharmacological interventions. The cardiovascular diseases, and especially the arrhythmias are leading cause of mortality. The arrhythmias have a complex underlying mechanism where the intracellular  $\text{Ca}^{2+}$  handling plays a critical role. Therefore, the main aim of our laboratory is the investigation of the physiological function of the cardiac  $\text{Ca}^{2+}$  handling, its role in different arrhythmias, and development of new pharmacological interventions.

A novel antiarrhythmic strategy could be the selective inhibition of the cardiac  $\text{Na}^+/\text{Ca}^{2+}$  exchanger that may decrease the excessive  $\text{Ca}^{2+}$  load of the cell, additionally may have positive inotropic effect.

The sinus-node as a primary rhythm generator of the heart has an extremely complex electrophysiological mechanism, at the same time, it could be involved in several types of arrhythmias. Our further aim is the investigation of the  $\text{Ca}^{2+}$  handling in sinus-node cells under normal as well as during pathological condition (e.g.: metabolic syndrome).

It is well-known that physical activity is healthy and significantly contributes to the normal physiology of the cardiovascular system. Still, several times sudden cardiac death of competitive athletes was observed where organic disease of the heart was not found. The underlying mechanism of sudden death could be the abrupt disturbance of the normal electrophysiological function of heart, however the arrhythmia mechanism is unknown. Therefore, further aim of our Institute is to develop a reliable "athlete's heart" animal model that provides data regarding the electrophysiological changes during physical activity. Our group investigates the alterations of the  $\text{Ca}^{2+}$  handling in the athlete's heart.

## TECHNIQUES AVAILABLE IN THE LAB

Isolation of cardiac myocytes from rabbit and canine heart. Measurement of action potentials from cardiac tissue and isolated cells with standard microelectrode and patch-clamp technique. Combined ionic current and  $\text{Ca}$  movement measurement by patch-clamp technique associated with

fluorescent optical method from isolated ventricular and sinus node cells. Optical mapping of membrane potential and intracellular  $\text{Ca}$  movements in isolated rabbit heart. Analysis and interpretation of the data.

## SELECTED PUBLICATIONS

Tóth, N., Szlovák, J., Kohajda, Z., Bitay, G., Veress, R., Horváth, B., Papp, J.G., Varró, A., **Nagy, N.** (2021) The development of L-type  $\text{Ca}^{2+}$  current mediated alternans does not depend on the restitution slope in canine ventricular myocardium. **Sci Rep 11:** 16652.

Szlovák J., Tomek, J., Zhou, X., Tóth, N., Veress, R., Horváth, B., Szentandrassy, N., Levijoki, J., Papp, J.G., Herring, N., Varró, A., Eisner, D.A., Rodriguez, B., **Nagy, N.** (2021) Blockade of sodium-calcium exchanger via ORM-10962 attenuates cardiac alternans. **J Mol Cell Cardiol 153:** 111-122.

Gazdag, P., Oravec, K., Acsai, K., Demeter-Haludka, V., Ördög, B., Szlovák, J., Kohajda, Z., Polyák, A., Barta, B.A., Oláh, A., Radovits, T., Merkely, B., Papp, J.G., Baczkó, I., Varró, A., **Nagy, N.** & Prorok, J. (2020) Increased  $\text{Ca}^{2+}$  content of the sarcoplasmic reticulum provides arrhythmogenic trigger source in swimming-induced rat athlete's heart model. **Sci Rep 10:** 19596.

Varró, A., Tomek, J., **Nagy, N.**, Virag, L., Passini, E., Rodriguez, B., Baczkó, I. (2020) Cardiac Transmembrane Ion Channels and Action Potentials: Cellular Physiology and Arrhythmogenic Behavior. **Physiol Rev 101:** 1083-1176.

Kohajda Z., Tóth N., Szlovák J., Loewe A., Bitay G., Gazdag P., Prorok, J., Jost, N., Levijoki, J., Pollesello, P., Papp, J.G., Varró, A., **Nagy, N.** (2020) Novel  $\text{Na}^+/\text{Ca}^{2+}$  Exchanger Inhibitor ORM-10962 Supports Coupled Function of Funny-Current and  $\text{Na}^+/\text{Ca}^{2+}$  Exchanger in Pacemaking of Rabbit Sinus Node Tissue. **Front Pharmacol 10:** 1632.