Oral Presentation Award Winner

β3 Adrenergic Receptors in the Sinoatrial Node for Heart Rate Regulation

Shu Nakao,[1,2] Kazuki Yanagisawa,[1] Tomoe Ueyama,[1] Koji Hasegawa[2] and Teruhisa Kawamura[1,2]

1. Ritsumeikan University, Kusatsu, Japan; 2. Kyoto Medical Center, Kyoto, Fushimi-ku, Japan

Citation: *European Cardiology Review* 2021;16:e58. **DOI:** https://doi.org/10.15420/ecr.2021.16.PO2

Objectives: β1-adrenergic receptor (AR) signalling has a positive chronotropic effect in the heart. However, the role of β3-AR, a minor cardiac β-AR isoform, in heart rate regulation remains unknown. β3-ARs are highly expressed in adipose tissue, and promote energy expenditure. We here investigated whether β3-ARs are expressed in the sinoatrial node (SAN), the primary pacemaking site, and regulate heart rate in mice.

Materials and methods: Adult C57BL/6 male mice were used for electrocardiogram recording under mild anaesthesia with isoflurane inhalation with or without β-AR inhibitors. The right atrial wall including the SAN region was dissected and subjected to electrophysiological recording, immunolabelling and gene expression analysis.

Results: mRNA expression analysis revealed that β3-AR transcripts were detected at a modest level in the SAN region. Immunolabelling revealed that β3-ARs were expressed at low levels in SAN myocytes and at high levels in adipocytes and nerve fibres. In electrocardiogram recordings *in vivo*, the heart rate was decreased by a β1-AR inhibitor. A subsequent injection of a specific β3-AR inhibitor further reduced the heart rate and prolonged PR intervals. In electrophysiological experiment *in vitro*, SAN-driving intrinsic heart rate was significantly increased by a specific β3-AR agonist.

Conclusion: There may be direct and indirect mechanisms linking β3-ARs to impulse generation and propagation. This mechanism possibly presents in SAN myocytes as well as the adjacent adipose tissue, which may provide energy for action potential firing. ❑