ESC European Society of Cardiology
European Heart Journal (2020) **41**, 2036
doi:10.1093/eurheartj/ehaa251

DISCUSSION FORUM

Animals in cardiovascular research: important role of rabbit models in cardiac electrophysiology

Katja E. Odening [1,2]*, Istvan Baczko [3], and Michael Brunner [1,4]

[1]Department of Cardiology and Angiology I, Heart Center, University of Freiburg, Faculty of Medicine, Hugstetter Str. 55, 79106 Freiburg, Germany; [2]Translational Cardiology, Department of Cardiology, Inselspital, Bern University Hospital, Institute of Physiology, Buehlplatz 4, University of Bern, 3012 Bern, Switzerland; [3]Department of Pharmacology and Pharmacotherapy, Dóm tér 12, University of Szeged, 6721 Szeged, Hungary; and [4]Department of Cardiology and Medical Intensive Care, St. Josefskrankenhaus, Sautierstrasse 1, 79104 Freiburg, Germany

Online publish-ahead-of-print 15 May 2020

This commentary refers to 'Animals in cardiovascular research: Clinical relevance and translational limitations of animal models in cardiovascular research', by N. Cesarovic *et al.*, 2020;41:200–203.

With great interest we have read the comprehensive review by Cesarovic *et al.*[1] on animal models in cardiovascular research. While the important role of several species for different cardiovascular disease entities has been highlighted, one important species, which is highly relevant for disease-models of inherited 'electrical' cardiac disorders, and for safety pharmacology for detection of potential pro-arrhythmia, has been omitted: the rabbit.

In contrast to rodents, the rabbit mimics human cardiac electrophysiology surprisingly well. Key electrical features show pronounced similarities in the two species, such as the shape of action potential, the biophysical properties of the underlying cardiac ion channels/currents, and the responses to electrophysiologically relevant pharmacological interventions.

Many of the recent advances in our understanding of inherited arrhythmia disorders stems from transgenic rabbits models for long-QT and short-QT syndrome that mimic the human disease phenotypes on multiple levels of complexity with alterations of cardiac repolarization on cellular, whole heart and *in vivo* levels, spontaneous atrial and ventricular arrhythmias and sudden arrhythmogenic cardiac death.[2–4] These rabbit models have been instrumental in increasing our understanding of mechanisms initiating and sustaining ventricular arrhythmias,[2,5] to study mechanisms underlying hormonal influences on the disease phenotype (as seen in humans), mechanical consequences of electrical alterations, and beneficial pharmacological interventions to rescue the phenotype (reviewed in Ref.[5]). Further insights into risk stratification and mechanism-based therapies are likely to be obtained with these (and future) rabbit models for inherited arrhythmia disorders.

Conflict of interest: none declared.

References

1. Cesarovic N, Lipiski M, Falk V, Emmert MY. Animals in cardiovascular research: clinical relevance and translational limitations of animal models in cardiovascular research. *Eur Heart J* 2020;**41**:200–203.
2. Brunner M, Peng X, Liu GX, Ren XQ, Ziv O, Choi BR, Mathur R, Hajjiri M, Odening KE, Steinberg E, Folco EJ, Pringa E, Centracchio J, Macharzina RR, Donahay T, Schofield L, Rana N, Kirk M, Mitchell GF, Poppas A, Zehender M, Koren G. Mechanisms of cardiac arrhythmias and sudden death in transgenic rabbits with long QT syndrome. *J Clin Invest* 2008;**118**:2246–2259.
3. Major P, Baczkó I, Hiripi L, Odening KE, Juhász V, Kohajda Z, Horváth A, Seprényi G, Kovács M, Virág L, Jost N, Prorok J, Ördög B, Doleschall Z, Nattel S, Varró A, Bősze Z. A novel transgenic rabbit model with reduced repolarization reserve: long QT syndrome caused by a dominant-negative mutation of the KCNE1 gene. *Br J Pharmacol* 2016;**173**:2046–2061.
4. Odening KE, Bodi I, Franke G, Rieke R, Ryan de Medeiros A, Perez-Feliz S, Fürniss H, Mettke L, Michaelides K, Lang CN, Steinfurt J, Pantulu ND, Ziupa D, Menza M, Zehender M, Bugger H, Peyronnet R, Behrends JC, Doleschall Z, Zur Hausen A, Bode C, Jolivet G, Brunner M. Transgenic short-QT syndrome 1 rabbits mimic the human disease phenotype with QT/action potential duration shortening in the atria and ventricles and increased ventricular tachycardia/ventricular fibrillation inducibility. *Eur Heart J* 2019;**40**:842–853.
5. Lang CN, Koren G, Odening KE. Transgenic rabbit models to investigate the cardiac ion channel disease long QT syndrome. *Prog Biophys Mol Biol* 2016;**121**:142–156.

*Corresponding author. Tel: +49 76127034010, Email: katja.odening@uniklinik-freiburg.de; katja.odening@insel.ch