Characterization of an Emerging Animal Model: Revealing Microcirculation in The Common Marmoset Monkey's Heart via (Fluorescence) Histology

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Background

The common marmoset monkey (*Callithrix jacchus*) is an emerging animal model whose importance for biomedical research has increased in recent years. In many ares, e.g., for multiple sclerosis, infectious diseases or in drug toxicology, the common marmoset is already used as a validated model. Due to its cardiac anatomy and topography, as well as diseases similar to those in humans, there is an increasing interest in this nonhuman primate for cardiovascular research. Additionally, practical reasons such as ease of handling due to its small body size and low zoonotic potential explain the great interest in this model. Although a lot of basic research in this species has already been conducted, a comprehensive characterization of the heart and – especially its (micro)-vascularization – is still lacking. We therefore aimed to further characterize the marmosets heart to support its use in cardiovascular research.

Methods & Results

We successfully established fitting staining protocols and antibodies for the use in left ventricular heart tissue in a cohort of naïve common marmosets of both sexes (N= 11 in total, six for each analysis). Analysis was done using LAS X and ImageJ software. Cells or plathelet endothelial cell adhesion molecule-1 (PECAM-1)/ neuron glia antigen-2 (NG-2) signals, respectively, were counted per field of view. Per animal, five representative image sections were analyzed.

PECAM/NG2: We assessed microcirculatory distribution and maturity performing a PECAM and NG2 doublestaining. Pictures were taken in 63x magnification (corresponding to 211.2 x 211.2 µm per field of view, 44 605 µm²). Per field of view, we calculated an average of 27 PECAM- and 25.6 NG2 signals, resulting in a ratio of 0.98 NG2/PECAM signal which indicates a high rate of mature endothelial cells compared to other animal species.

PECAM/ wheat germ agglutinin (WGA): In addition, we performed a PECAM/WGA doublestaining to set the amount of endothelial cell signals in relation to cardiomyocyte count. Pictures were taken in 40x-magnification (corresponds to 332.64µm x 332.64 µm per field of view, 110 650 µm²). We counted an average of 59.03 PECAM-1 signals per field of view. With an average cell count of 149.53 cells per image section, this results in a ratio of 0.4 PECAM-1 signals per cell.

Fibrosis: For analysis of perivascular fibrosis, a Masson Goldner Trichrome staining in heart slices of six animals was conducted. The average ratios of fibrotic area to vessel tissue from five representative myocardial arteries per animal ranged between around 1.5 and 8 with higher values in older animals, indicating age-related changes and structural adaptations with advanced age.

Conclusion & Outlook

Our findings serve as a basis for the formation of reference values regarding capillary density, maturity and fibrosis distribution in the common marmoset's heart. Prospective comparisons to commonly used animal models as well as extending analyses of sex and age-related differences will uncover the benefits of this promising small human primate and help to establish it as a human-relevant animal model for cardiovascular research.