Understanding vascular regulation in Göttingen Minipigs

ABOUT STUDY INSIGHTS: Göttingen Minipigs are increasingly selected for all aspects of pharmaceutical research and are fully recognized as a reliable and established animal model by all regulatory authorities worldwide. This section aims at providing an insight into the wide use of Göttingen Minipigs within biological research. If you know of an interesting study, you are welcome to reach out.

Insight provided by:
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What is the study about?
Gaining a better understanding of vascular regulation in Göttingen Minipigs.

What is the purpose of the study?
To characterize regulation of vascular tone in Göttingen Minipigs by using selected agonists for sympathetic, parasympathetic, sensory and endothelial pathways and to compare vasomotor responses of coronary, cerebral and peripheral arteries using myographs.

Through this basic characterization, we will qualify the selection of the Göttingen Minipigs model:

- for development of new drugs within cardiovascular and neurovascular diseases (e.g. stroke, myocardial infarct, migraine)
- for mechanistic understanding of side-effects of drugs that have already entered the marked, and of new potential drug candidates.

Why is it important?
Pigs are superior animal models for human health and diseases because their anatomy and physiology are similar to humans and because the porcine genome is three times closer than the rodent genome to that of the human.

Rodent models of neurovascular and endothelial regulation of vascular tone has been thoroughly studied in vivo and ex vivo and does not always offer good translation to sparse human vascular biopsies available from surgery and biopsies. The size of Göttingen Minipigs allows us to dissect sufficient artery segments for thorough characterization, pairing and comparison using a very limited number of animals (3Rs: Replacement, Reduction and Refinement).

The Göttingen Minipigs heart anatomy and its regulation is much closer to the human physiology than is the case in rodents. As Göttingen Minipigs is the current best validated model for heart disease, a thorough characterization will improve the translational value of the research.

Clinical or pathological biopsies are often stored for many hours before experimentation and the effect of long-term storage is not known. Here we can mimic the journey of clinical samples and comparison of the fresh and stored tissue samples from Göttingen Minipigs will help us understand the impact of storing vascular tissue.

Pharmacological characterization is often taking place in arteries isolated from only one anatomical origin. Here we have the chance to compare vascular segments isolated from 3 different anatomical regions in one animal.

What makes this study particularly interesting?
Currently, only limited and sporadic functional studies of Göttingen Minipigs vasculature exists. As an example, endogenous vasoprotective CGRP pathways have previously been shown to be absent. Our study concludes that the endogenous CGRP vasoprotective pathway is indeed present.

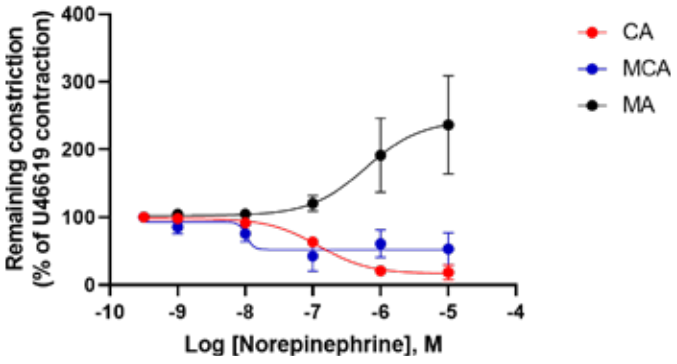

Figure 1
Effect of norepinephrine on isolated segments of Göttingen Minipigs coronary artery (CA), middle cerebral artery (MCA) and mesenteric artery (MA). Data are given as mean ± SEM (n = 6). Noradrenalin constricts mesenteric artery whereas it dilates coronary and cerebral artery preconstructed with the thromboxane A2 receptor agonist.

Below we share the different effects of mimicking the sympathetic stimulation with norepinephrine (Fig. 1) and the parasympathetic stimulation with carbachol (Fig. 2) on coronary, cerebral and mesenteric arteries isolated from Göttingen Minipigs.

Which challenges have you met during the study?
This study has been extraordinary free from challenges and our techniques have been directly applicable to Göttingen Minipigs vasculature.

The organs were isolated at Ellegaard Göttingen Minipigs and stored in our buffers during transport to Rigshospitalets Forskerpark. Here we teamed up for the dissection of selected arteries, mounting in myograph organ-baths for studies of fresh arteries and after 24h storage to mimic the clinical journey of arterial grafts. For 3 consecutive days, all our 24 myograph organ-baths were used for 12h daily.

How do you recommend going about species selection?
We selected the Göttingen Minipigs model because it is so well characterized and - to our knowledge – the current best model in neuro- and cardiovascular diseases. We are currently working on new targets that has not yet been studied in Göttingen Minipigs and the basic vascular characterization is important before interpreting future in-vitro and in-vivo studies.

Any learnings you would like to share??
Our collaboration with Ellegaard Göttingen Minipigs has been very fruitful and free of challenges.

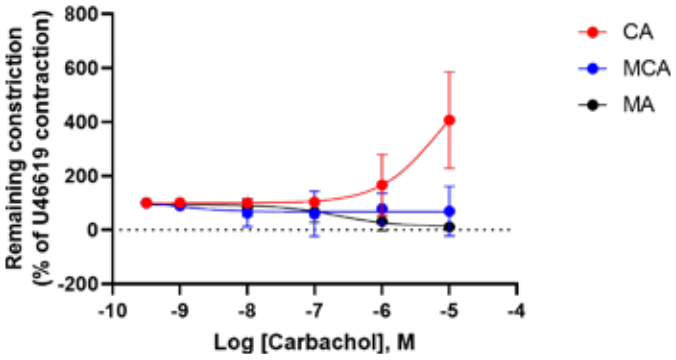

Figure 2
Effect of carbachol on isolated segments of Göttingen Minipigs coronary artery (CA), middle cerebral artery (MCA) and mesenteric artery (MA). Data are given as mean ± SEM (n = 6). Carbachol constricts coronary, dilates mesenteric and show no effect on cerebral artery segments.

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