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Göttingen Minipigs
MAGAZINE

ELLEGAARD
GÖTTINGEN MINIPIGS

Göttingen Minipigs Magazine | 60 | 2021

Dear reader

Our daily life has significantly changed over the last year. Many people, regions, countries, and continents are still in the middle of the COVID-19 pandemic and what used to be “normality” will never be the same again. But despite lots of tragedies, this unusual situation has also taught us a lot and emphasised the need for collaboration and high-quality preclinical research.

Two of our four corporate values, quality and collaboration, are expressed in the two exciting papers in this Magazine discussing the use of jacketed telemetry in juvenile minipigs and the use of juvenile and neonatal (mini)pigs in drug discovery and drug development. Both papers are in addition highlighting our aim to enable the development of safer and more effective medicines, and not only to the adult population, but also to children.

The use of blood products and biological material for in vitro purposes is a big part of our business. We are not just a breeder and provider of Göttingen Minipigs, but also a provider of high-quality blood and biological material in support of basic research and early drug discovery.

In compliance with our two remaining corporate values, respect and animal welfare, you can read about how you can optimize your blood sampling procedures and techniques and how Göttingen Minipigs organs can support the understanding of complex organ systems and facilitate drug development.

Please enjoy reading the Göttingen Minipigs Magazine and remember that unity and collaboration is the way towards reestablishing a normality as close as possible to what we used to know.

Lars Friis Mikkelsen, CEO
Ellegaard Göttingen Minipigs A/S

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Sustainable development in spite of COVID-19

The UN launched the 17 Global Goals initiative in 2015, an agreement between world leaders on how to create a more sustainable world by 2030 embracing topics such as poverty, inequality, and climate change. Then, in 2020, COVID-19 happened.

One year ago, organisations around the world had started scrutinising their routines, production, and emission trying to find out how to contribute to the UN Global Goals and create a better and more sustainable world. And one year ago, country after country faced lockdowns of the entire society to limit the outbreak of the COVID-19 pandemic. Immediately focus shifted, climate change was no longer at the top of the agenda, and all organisations were forced to initiate (or perhaps even create) contingency plans to handle the new reality.

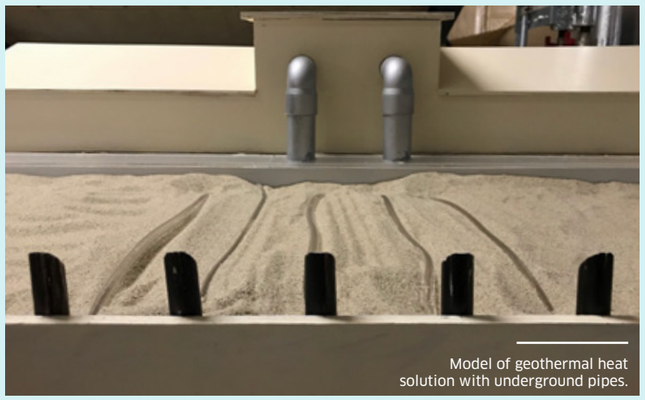
The pandemic still exists, and so does the severe climate changes even though we travel less, work from home, and overall has become much more digital almost overnight. "Though the situation is challenging, we must try to utilize time and grasp the opportunity to develop and implement climate changing solutions", says CEO at Ellegaard Göttingen Minipigs A/S, Lars Friis Mikkelsen. "A virtual working set-up and being restricted from travelling allow us time to focus our energy and presence on how to improve our business and be part of a more sustainable future. We must make the most of the situation and not forget the challenges and tasks we faced before the pandemic. The severity of the climate changes will not diminish just because we face a global healthcare emergency", he says.

Supporting words with action, Ellegaard Göttingen Minipigs has kept working with the UN Global Goals throughout 2020. "During our internal workshops, everyone has shown great engagement and we now have a very diverse list of suggestions with both quick-wins and long-term investments," says Søren Vangsgaard, Production Manager at Ellegaard Göttingen Minipigs A/S. Some initiatives have already been implemented and some are work in progress.

When expanding the facility over the years, sustainable and energy-saving solutions have always been a priority. Søren Vangsgaard gives a few examples: "The temperature in our breeding barriers are regulated through geothermal heat. Through approx. 30 km of underground pipes the ventilated air in the barriers is heated during winter and cooled in the summer. Two meters underground there is a constant temperature of 8 °C, meaning we use no electricity on air-conditioning systems. Of course, 8 °C is too cold in the winter, but instead of using fuel oil we have a straw-fired boiler to heat our entire facility, both breeding barriers and office buildings, and heat our water. This solution saves at least 70,000 litres of fuel oil every year and classifies our heating solution as carbon neutral."

Adding to this, Ellegaard Göttingen Minipigs is currently in the process of replacing all light bulbs and fluorescent lamps with LED solutions. "The new extension to the office building is equipped with LED, and as part of renovating the attic in one of the barriers all light installations here are replaced with LED solutions as well" Søren Vangsgaard explains.

To further investigate sustainable implementations Ellegaard Göttingen Minipigs has entered into dialogue with a consultant on energy saving, and likewise considers initiatives that further support biodiversity and the health and welfare of both employees and animals.



Model of geothermal heat solution with underground pipes.

Straw-fired boiler at Ellegaard Göttingen Minipigs A/S.

Implemented quick-wins

Not all changes have to be expensive, long-term investments. Often there are many overlooked low-hanging fruits that can contribute to the complete picture.

The following serves as inspiration and can be applied by companies of all sizes. The lists are not complete, and everyone is encouraged to add their own initiatives and ideas, just as Ellegaard Göttingen Minipigs constantly reviews consumption, waste, and emission.

Good luck!

Health and welfare

- New company lunch program offering healthier food choices
- Employees are encouraged to bring home leftovers from lunch to minimize food waste
- Company sports as an open invitation to all employees
- Opportunity to work from home
- Every year Ellegaard Göttingen Minipigs sponsor selected charities. As of 2020, employees vote on how to distribute the sponsorships. Everyone is granted the same amount of money and choose who should receive their donation from a preselected list of charities.

Sustainable consumption and production

- New digital routines to limit printing and the use of paper
- New domestic appliances installed with good energy labels
- Göttingen Minipigs Magazine (previously the Newsletter) is distributed per e-mail instead of mail
- Stopped purchasing bottled water, only tap water is served
- Printing on both pages and in black/white as default setting
- Limit use of printed sales and marketing material
- Printed sales materials that are still needed, are produced at a printing house marked with The Nordic Eco-label
- Purchase of office supplies is accumulated to limit transport emissions

Climate and biodiversity

- Use only environmentally friendly cleaning detergents
- Emloyees are encouraged to car-pool to limit fuel consumption and emission (careful/limited approach during COVID-19 pandemic)
- Inlcude company values in company climate goals (quality, respect, collaboration, animal welfare) as these are infused in all corporate activities

Implementation of non-invasive cardiorespiratory and activity assessment in the juvenile minipig using the Decro® jacket system

By L. Penard[1] and T. Flenet[2]

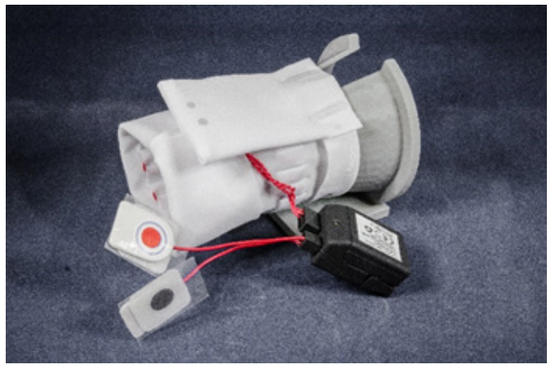
[1]Charles River Laboratories, Lyon, France | [2]Etisense SAS, Lyon, France

In nonclinical research, animal welfare is the cornerstone of relevant, high-quality data. As invasive technologies that affect an animal's well-being can compromise research results, we have worked to develop alternative methods for collecting data that address both ethical and scientific concerns.

Introduction

Etisense, a biomedical engineering firm based in Lyon, France, has developed a solution for the collection of nonclinical cardiorespiratory data on animal models using the DECRO® system (Picture 1), a noninvasive jacket that uses Bluetooth Low Energy® technology for signal transmission. Looking to expand its applications beyond rats, Etisense has partnered with Charles River scientists to develop a solution that allows the monitoring of cardiorespiratory signals and activity levels of juvenile minipigs.

Göttingen Minipigs have now become widely accepted as a non-rodent species for safety testing, including juvenile animal studies, due to the availability of the purpose bred specific pathogen free breed in both the US and Europe and its physiological similarities with human. The minipig has many advantages over other usual laboratory species such as a relatively large litter size, rapid growth rate, and rapid achievement of sexual maturity. Moreover, piglets can be used for laboratory procedures from a very early age, even from postnatal day (PND) 1 onwards due to a high degree of autonomy shortly after birth. In the work presented here, a non-invasive cardiorespiratory and activity assessment in the neonate juvenile minipig, using Decro® jacket, from as early as the first week of life is described.



Picture 1
DECRO® jacket system.

Method

One litter of seven newborn Göttingen Minipigs (pregnant sow supplied from Ellegaard Research Foundation) was allocated to 2 groups, one group of untreated animals and the other group receiving baclofen by oral gavage, a reference item known to decrease respiratory rate. Piglets were fitted with the DECRO® jacket on the day before treatment (where applicable) for training / baseline measurements, and up to 20 hours after treatment (where applicable). The jackets were setup to simultaneously record three biosignals, namely electrocardiogram, respiration by inductance plethysmography (RIP bands) and activity levels by accelerometry. Proprietary Etisense software with advanced algorithms was used to automatically detect cardiac and respiratory cycles and calculate standard ECG, respiratory and activity parameters. Recording was performed once weekly from 1 to 4 weeks of age.

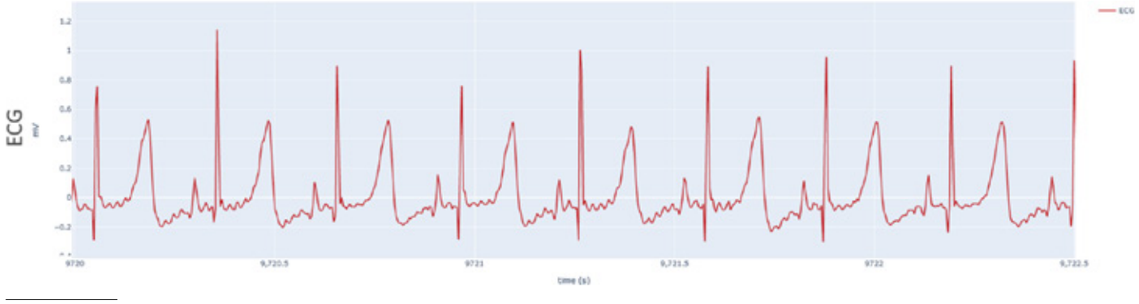


Figure 1
ECG waves in the first week of life, recorded at rest

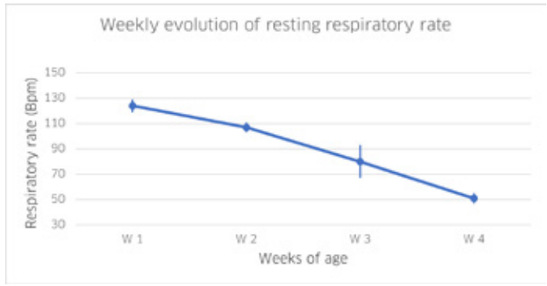


Figure 2
Weekly evolution of resting respiratory rate. Over the first four weeks of life, mean respiratory rates decreased with age.

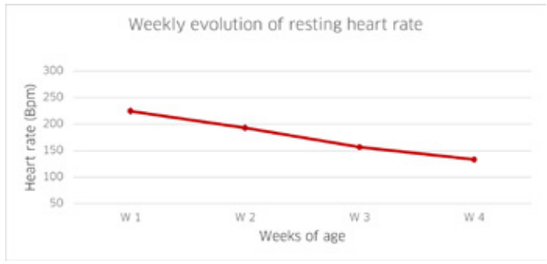


Figure 3
Weekly evolution of resting heart rate. Over the first four weeks of life, mean heart rates decreased with age.

Results

Baclofen-related effect

Based on preliminary internal data and literature, baclofen was tested at 2, 3 or 4 mg/kg, depending on the animals' age and reaction to previous doses. At these doses, piglets showed either reversible clinical signs (labored breathing and decreased activity) or no signs at all, depending on the age at the time of dosing. Baclofen-related effect on cardiorespiratory and activity parameters was only noted at high doses when marked clinical signs were observed (low activity levels and low heart rate and respiratory rate values).

Jacket tolerance and integrity

The minipig-designed jacket induced skin lesions / abrasions in the axillary and cervical areas of all animals. Topical care (ointment application) was applied and the jacket was subsequently modified to ensure better protection by the addition of foam and reshaping of the collar. Despite any potential discomfort generated by wearing the jacket for approximately two days per week for four weeks, no impact on growth (body weights) was noted.

The jackets remained in place for the majority of piglets aged one week and RIP bands embedded into jackets remained operational. The ECG electrodes were occasionally re-positioned but in most instances, the biosignals were recorded as scheduled. From two weeks of age, the biosignals were recorded for all animals but the jackets remained in place and RIB bands operational during the entire recording period for approximately half of them.

Cardiorespiratory and activity analysis

In the first week of age, a clear correlation was found between high activity levels and elevated heart rate (HR) and respiratory rate (RR) values. On average, animals spent approximately 20% of the time resting (defined as activity level < 50mG).

Overall, 90% of ECG signals were of good quality, with well-defined waveforms and low noise, allowing for a proper detection of ECG complexes and corresponding waves (Figure 1). Optimal fitting of the jackets embedding the RIP bands provided good respiratory signals suitable for analysis. At two weeks of age, respiratory rate (90-135 breaths/min) and heart rate (181-252 beats/min) values were comparable with those obtained in a previous juvenile minipig study with animals restrained in adapted slings. Over the first four weeks of life, respiratory and heart rates decreased with age (Figure 2 and Figure 3).

Conclusion

In conclusion, simultaneous non-invasive recording of quality electrocardiographic, respiratory and activity signals and subsequent analyses were achieved in the juvenile Göttingen Minipig using the jacketed Decro® system from the first week of life. Fitting juvenile animals with this device at different post-natal ages had no impact on their growth and behavior. Cardiorespiratory parameters obtained using the Decro® jacket were comparable with results obtained from restrained animals in previous studies (snapshot ECG and visual assessment of respiratory rate). Improvements in both the robustness and comfort of the jacket and recording system are currently ongoing to ensure that uninterrupted data can be obtained from the fast-growing juvenile minipigs through to an age when traditional methodology can be applied.

MORE INFORMATION

ETISENSE website:
etisense.com
The DECRO® jacket:
decro.fr

This study is supported by the Ellegaard Göttingen Minipigs Research Foundation.

New publication regarding recommended nomenclature for reporting of histopathological findings in minipigs used in non-clinical safety studies

By Nanna Grand[1] and Gitte Jeppesen[1]

[1]Scantox A/S, Lille Skensved, Denmark

The INHAND (International Harmonization of Nomenclature and Diagnostic Criteria for Lesions) Project (www.toxpath.org/inhand.asp) is a joint initiative of the Societies of Toxicologic Pathology from Europe (ESTP), Great Britain (BSTP), Japan (JSTP), and North America (STP) to develop an internationally accepted nomenclature for proliferative and nonproliferative histopathological lesions in laboratory animals.

In January 2021, the INHAND publication "International Harmonization of Nomenclature and Diagnostic Criteria (INHAND): Nonproliferative and Proliferative Lesions of the Minipig" was made public in the "Journal of Toxicologic Pathology". The authors of this publication included experienced toxicopathologists from pharmaceutical companies, academia and CROs, including a senior toxicopathologist at Scantox A/S.

The purpose of this publication is to provide a standardized nomenclature for classifying microscopic lesions observed in most tissues and organs from the minipig used in nonclinical safety studies. Some of the lesions are illustrated by color photomicrographs. The standardized nomenclature presented in the document is also available electronically on the internet (www.goreni.org). Content includes spontaneous lesions as well as lesions induced by exposure to test materials.

A widely accepted and utilized international harmonization of nomenclature for lesions in minipigs will provide a common language among regulatory and scientific research organizations in different countries and increase and enrich international exchanges of information among toxicologists and pathologists.

This is a major advancement in the use of the minipig as a commonly accepted non-rodent species in pre-clinical toxicity testing. At Scantox we have implemented this nomenclature as our standard glossary used in histopathologic reporting of minipig studies conducted at our site. This offers an advantage to our customers not the least at regulatory submissions, as histopathology reports from Scantox provide a clear and concise communication of findings using this internationally accepted terminology.

Picture 1
Frontpage of the Toxicologic Pathology volume 49 publishing the INHAND publication in January 2021.

The use of neonatal and juvenile (mini)pigs in drug discovery and drug development

By Miriam Ayuso and Steven Van Cruchten[1]

[1]Comparative Perinatal Development (CoPeD), Department of Veterinary Sciences, University of Antwerp, Belgium

Drug therapy in paediatric patients is challenging in view of the maturation of organ systems and processes that affect pharmacokinetics (PK) and pharmacodynamics. Especially for the youngest age groups and for paediatric-only indications, neonatal and juvenile animal models can be useful to assess drug safety and to better understand the mechanisms of diseases or conditions. In this respect, the use of neonatal and juvenile pigs in the field of paediatric drug discovery and drug development is promising, although still limited at this point.

We summarized the comparative postnatal development of pigs and humans and discussed the advantages of the neonatal and juvenile pig in view of developmental pharmacology, paediatric diseases, drug discovery and drug safety testing in the following review paper: Ayuso, M.; Buyssens, L.; Stroe, M.; Valenzuela, A.; Allegaert, K.; Smits, A.; Annaert, P.; Mulder, A.; Carpentier, S.; Van Ginneken, C.; Van Cruchten, S. The Neonatal and Juvenile Pig in Pediatric Drug Discovery and Development. Pharmaceutics 2021, 13, 44. https://doi.org/10.3390/pharmaceutics13010044 [1]. For a complete overview, we refer to this open access paper. In the following paragraphs, we will only discuss the highlights.

Nonclinical *in vivo* models, like the neonatal and juvenile pig are of increasing interest in paediatric drug development from two perspectives. First, to investigate and consequently better understand the mechanism of a disease, particularly when it is unique to paediatric patients. Second, the model may also provide important safety data for the paediatric population when performing juvenile toxicity studies. The choice of species and the design of juvenile toxicity studies are therefore the result of a series of complex considerations, including the therapeutic use of the drug, the age at which children will be treated, the duration of treatment, and potential age- or species-specific differences in efficacy, PK, or toxicity observed in adult animals.

The utility of a 'leverage concept' for dose determination and drug development programs in neonates has recently been described [2]. The following scenarios can be distinguished:

- Paediatric disease similar to that in adults and/or older paediatric patients where dosing is known for adult and/or older paediatric patients = extrapolation of efficacy from adults to paediatric patients is permitted, and even supported.
- Paediatric disease related but not similar to that in adults and/or older paediatric patients where dosing is known for adult and/or older paediatric patients = additional information can be leveraged from either in vitro or *in vivo* models to guide initial dosing.
- Paediatric disease unique to a given (sub)population within paediatrics, where these drugs are not utilized for these specific diseases in adults.

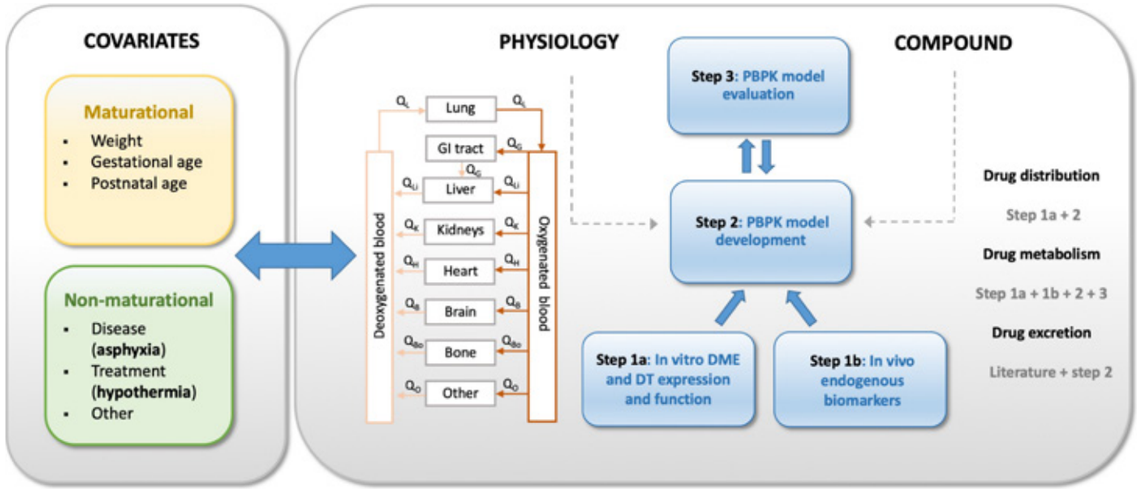


Figure 1
Strategy for a neonatal hypothermia physiology based pharmacokinetic (PBPK) framework development. DME: drug metabolizing enzymes; DT: drug transporters. Adapted from [8].

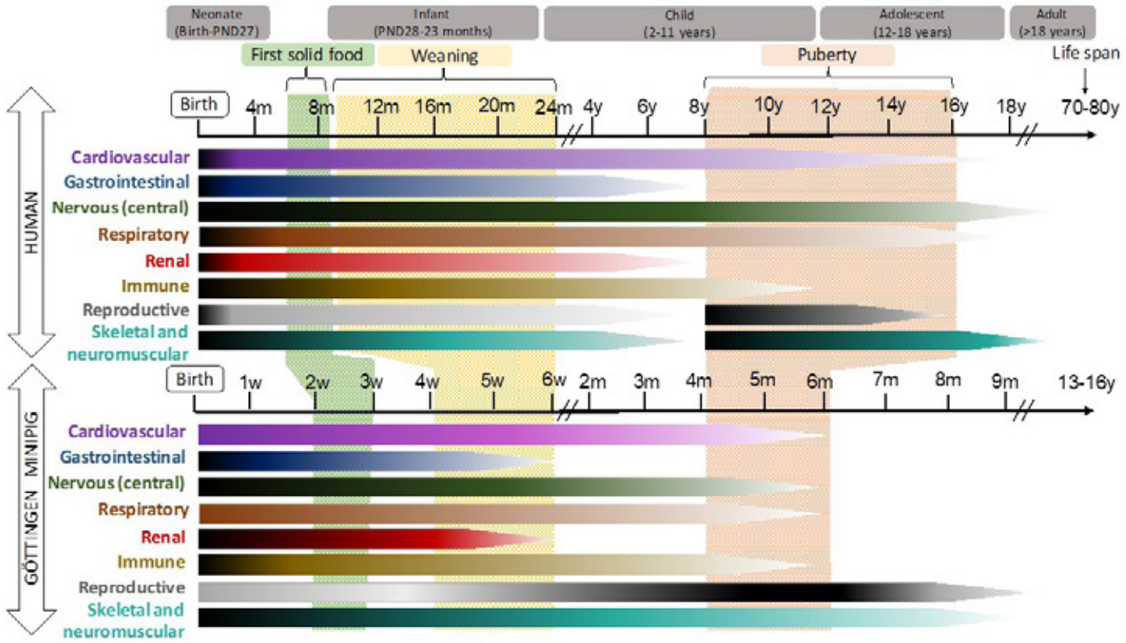


Figure 2
Schematic representation of the postnatal development of different organ systems in human (top) and Göttingen Minipig [1]. In the horizontal bars, the intensity of the maturation process is represented by dark (more intense) and light (less intense) tones. The time bar represents weeks (w), months (m) or years (y) of life.

Even in the setting of similarity, additional research in juvenile animals may still be warranted when concerns related to developmental toxicology (like growth, neurodevelopment, kidney, or cardiovascular system) should be addressed. Only about 10% of the 400 products (almost exclusive new drug approvals) of which the labels were reviewed between 1998–2009 by the FDA contained information on juvenile animals [3]. In a recent survey on European Paediatric Investigation Plan (PIP) decisions (2007–2017, 229 drugs) with juvenile animal requests, general toxicological studies were the most applicable study designs, with infectious diseases, endocrinology, neurology, and cardiovascular diseases being the most common therapeutic areas. As anticipated, about 80% of these studies were in rats, while studies in pigs were limited (4.2%) [4]. Interestingly, a recent European Medicines Agency (EMA) analysis on juvenile animal studies in the field of anticancer drug research documented that juvenile models also generated evidence regarding new target organ toxicity (kidney, central and peripheral nervous system, impaired learning or memory, cardiac system) or increased severity of toxicity (including mortality rate) [5]. At the other end of the spectrum, with diseases that are unique to a given subpopulation within paediatrics, pig models can be instrumental in drug discovery and development for accurate mechanistic understanding of the disease or condition. Specific to neonates, this has been described for, e.g., necrotizing enterocolitis (NEC), resuscitation practices, or perinatal asphyxia. Studies in pigs have established the essential roles of prematurity, microbial colonization, and enteral nutrition in the pathogenesis of NEC [6]. The (juvenile) pig is also an important animal model in research on human resuscitation [7]. In addition, *in vivo* data generated in neonatal animals—including (mini)pig—facilitate the development of a neonatal physiology-based PK (PBPK) model during therapeutic hypothermia [8] (see Figure 1).

In order to assess the feasibility of the neonatal and juvenile pig as models for paediatric drug development, an in-depth characterization of this model must be carried out in the first place, followed by a comparison of the anatomical, physiological and ADME characteristics in the corresponding paediatric age groups.

Regarding anatomical and physiological characteristics, our group has already reported on the age-related maturation of organ weights in the developing Göttingen Minipigs in an effort to further develop a PBPK model [9], but more data are needed. The implementation of this model would benefit from data on microsomal protein per gram of liver and abundance on drug metabolizing enzymes during development, or from a better understanding of pig orthologues for human cytochrome P450 (CYP) enzymes. For the developing domestic pig, the anatomy, physiology and the absorption, distribution and excretion of drugs have been reviewed by others [10]. As some of the above data are publicly accessible in the ICH S11 guideline

on nonclinical safety testing in support of the development of paediatric pharmaceuticals [11], we will only highlight some key points. The EMA has established different age categories within the paediatric population, and many similarities between human and Göttingen Minipigs organ development (as the reference breed used in the pharmaceutical industry) were reported in the ICH S11 guideline. In general, pigs and humans share many developmental milestones: The patterns of development of the gastrointestinal tract (GIT), the cardiovascular, the CNS systems and the eye are quite similar in both species, while renal, immune, and reproductive development occur slightly earlier and more quickly in humans than in pigs. These data are illustrated in Figure 2.

Regarding ADME characteristics, hepatic Phase I drug metabolism mediated by CYP enzymes has been investigated extensively in adult conventional pig strains and minipig strains over the past 30 years. Knowledge on the ontogeny of these processes in the neonatal and juvenile population is much more limited. Particularly in neonates, it is crucial to predict drug disposition correctly in order to avoid inefficacy due to underdosing or adverse effects caused by overdosing. Recently, CYP activity was determined in neonatal and juvenile conventional pig [12] and Göttingen Minipigs [13] in different age groups using several human CYP450 substrates. As such, substrate specificity was examined and CYP450 activity levels in (mini)pig were compared to those in human. In Göttingen Minipigs, we found that CYP450 enzyme activity increased postnatally. However, differences in onset and speed in development were observed: CYP1A2- and CYP2D6-like activity levels increased fast during the first week of life, whereas CYP2C9- and CYP3A4-like activities matured more slowly, reaching their highest levels in 1-month-old pigs [13], corresponding roughly to a 2-year-old child (see Figure 3). In the conventional pig, similar results were obtained [12]. In addition, no sex-related differences were observed in the neonatal and juvenile age groups regarding the CYP450 ontogeny patterns until puberty [12,13]. With regard to CYP450 protein abundance, some research has already been conducted in the conventional pig [12], and this question is currently being addressed in Göttingen Minipigs by our group. In general, activity and abundance data correlate

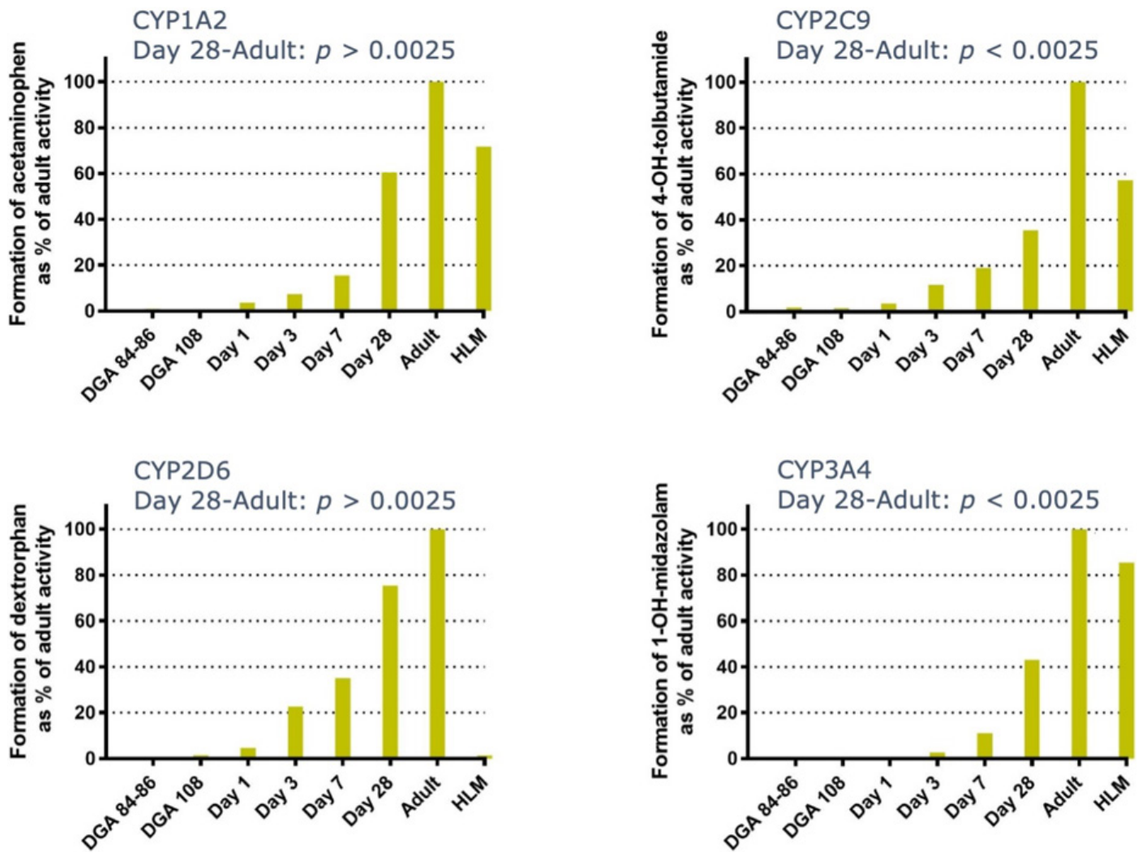


Figure 3
CYP activity profiles in liver microsomes of foetal, neonatal, juvenile, and adult Göttingen Minipigs. DGA: days of gestation; HLM: adult human liver microsomes

well, although CYP isoform-specific differences have been reported [12]. Regarding Phase 2 metabolism, data are scarce. A recent study on 1-day and 2-, 5-, 10- and 20-week old male Camborough-29 pigs showed that in vitro UDP Glucuronosyltransferase (UGT) enzyme activity increased from day 1 until week 10, followed by a decline at around week 20 [14]. An *in vivo* study with ibuprofen in 1-, 4-, and 8-week old, and 6–7-month old, mixed breed pigs also showed UGT activity already in neonatal pigs [15]. In our group, UGT activity was investigated in Göttingen Minipigs with age groups ranging from the late foetal stage until postnatal day 28, and adults [13]. From PND 7 onward, UGT activity increased without sex-related differences and reached adult levels at PND 28. In the youngest age groups (gestational day age (GDA) 84–86, GDA 108, postnatal (PND) day 1 and 3), activities were below the lower detection limit when using a luminescence-based assay. However, immunohistochemical analysis showed that even in the late foetal stages, UGT1A could be detected. In accordance with the activity results, UGT1A detection increased with age [13]. In general, it can be concluded that UGT enzymes are expressed from an early age, but further characterization of the different isoforms is needed in order to better predict drug disposition in this animal model. With regard to drug transport (often referred to as Phase 0 for uptake transporters and Phase III for efflux transporters), the data in the pig are even more scarce. For Göttingen Minipigs, we performed a semiquantitative assessment of P-glycoprotein (P-gp, encoded by the Multidrug Resistance Gene, MDR) in the liver of neonatal and juvenile pigs and foetuses using immunohistochemistry. No difference was observed in P-gp expression between livers from GDA84 to adult animals (1.5–3 years of age) [16].

When comparing the above data with the ontogeny profiles of the drug disposition processes in human, which have been reviewed extensively elsewhere [17-19], remarkable similarities are present. For UGT and P-gp, the ontogeny profile on protein and activity level, if assessed, is very similar. With regard to the CYP activity, the interpretation is more complex. The slow maturation profile of CYP2C9 and CYP3A4 activity in (mini)pigs corresponds well with the paediatric population. For CYP1A2 and CYP2D6, there appears to be an earlier onset of activity in the pig than in human, and CYP2D6 activity in general appears to be much higher than in human. Still, when comparing the pig with man, one needs to be very cautious, as studies may use different substrates or other testing conditions, which may confound the results and, as such, species comparisons. This said, even when not directly translatable to human, in vitro and *in vivo* drug metabolism data in juvenile animals are critical, as they may explain differences in efficacy or toxicity with the human population, and they can be used in PBPK models to better predict exposure, especially in the very young age groups, as further discussed in our review paper.

In conclusion, the physiology and development of several organ systems and conditions associated with (preterm) birth are very similar in pigs and humans. Despite this fact, the use of neonatal and juvenile Göttingen Minipigs, the reference breed in the pharmaceutical industry, in paediatric drug development programs is still very limited. One of the

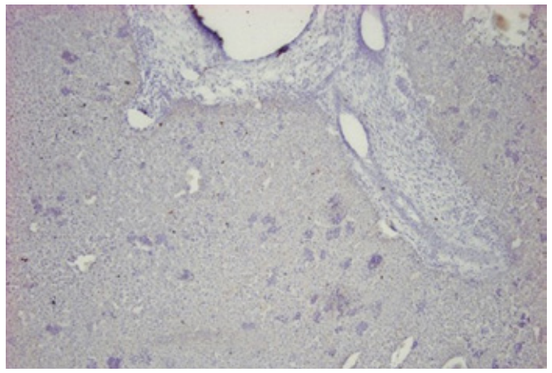


Figure 4a
Immunohistochemical detection of UGT1A in the liver of a Göttingen Minipig fetus at 84-86 days of gestation. A mild staining among all hepatocytes is present. Scale bar 200 µm.

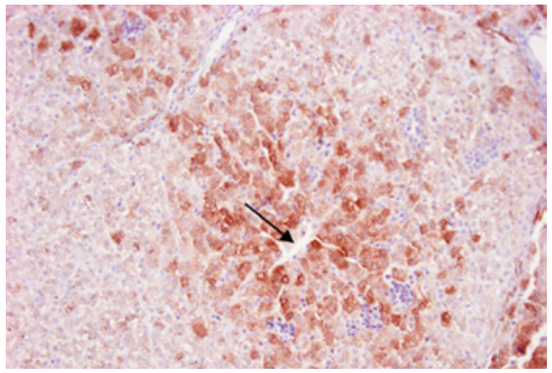


Figure 4b
Immunohistochemical detection of UGT1A in the liver of a 7-day-old Göttingen Minipig. Small groups of more intensively stained hepatocytes appear close to the central vein of each lobule, though not generalized. The black arrow indicates the central vein. Scale bar 200 µm.

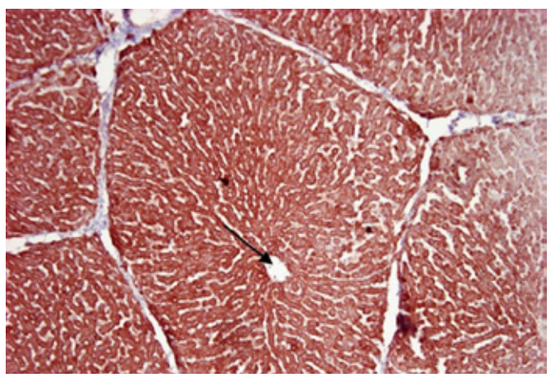


Figure 4c
Immunohistochemical detection of UGT1A in the liver of an adult male Göttingen Minipig. The hepatocytes of the entire liver lobules are intensely stained. The black arrow indicates the central vein. Scale bar 200 µm.

main reasons is the fact that paediatric regulatory guidelines recommend using the same (preferably rodent) species and strain in juvenile animal studies as in adult repeated dose toxicity studies. As regulatory guidelines for adult repeated dose toxicity studies currently do not define species selection in a detailed manner, there is no consistent approach and pharmaceutical companies often base their decision for species selection on experience and data with rats and dogs over the years. As such, Göttingen Minipigs are not considered in their species selection process. In our opinion, including more detailed species selection criteria in the regulatory guidelines for adult repeated dose toxicity studies would increase the use of Göttingen Minipigs in drug safety testing for indications in the adult and paediatric population. For paediatric-only indications, especially in the youngest age groups in which extensive clinical and nonclinical studies in adults are, in general, not performed, pharmaceutical companies should consider by default neonatal and juvenile Göttingen Minipigs for their nonclinical program, as it often represents a better translational model than rat and dog pups. We anticipate that current efforts to fully characterize the model, including ADME processes, and the development of juvenile pig PBPK models will promote the use of the juvenile pig model in paediatric drug safety studies.

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Blood sampling from Göttingen Minipigs

By Carina Christoffersen[1] and Kirsten Rosenmay Jacobsen[1]

[1]Ellegaard Göttingen Minipigs A/S, Dalmose, Denmark

Collecting blood samples from Göttingen Minipigs is a process that has been refined and evaluated continously over the years, as it is important to reduce the level of stress imposed on the animals, both due to animal welfare, staff experience, and ensuring high quality blood samples to enable research results of as high validity as possible.

Background

Up until 2019, V-benches were mainly used when collecting blood samples from Göttingen Minipigs, which required the presence of four staff members. The process was to lift the minipig and place it on its back. Up to three staff members would restrain the minipig: One for the hind legs, one for the front legs, and one for the head. Once the minipig was calm the sample could be collected.

This involved a certain stress factor for the minipig, as being placed on its back and restrained in this position is unnatural to the minipigs but was necessary to access the blood vessels in the throat. Therefore, most pigs struggle to get back on their feet, and the more the pig struggle, the harder it is for the staff to restrain it. This is also why it could be difficult to collect blood samples from older and larger pigs without sedation.

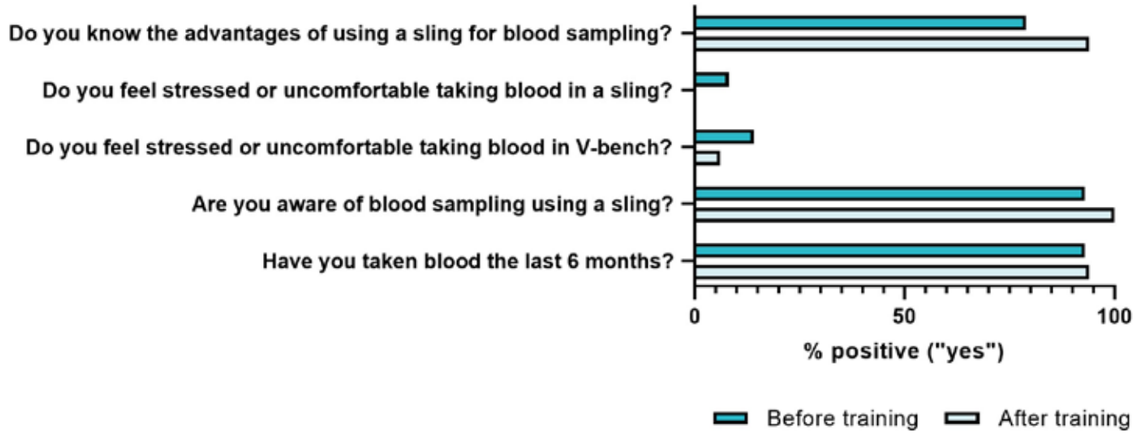
Refined method

An alternative to blood sampling in V-bench is sampling from a sling. The minipig is lifted and placed in a sling, which looks like a suspended hammock with holes for the legs. When placed in the sling they therefore hang in a belly-down position, as if simply elevated from the floor, which is much more natural for them. The sling also has a hole at the neck position from where the blood sample is collected. For this process only two staff members are needed: One for lifting, placing, holding the front legs if needed and calming the minipig, and one for collecting the blood sample. This method also enables blood sampling from larger animals, and successful collection of blood samples from animals up to 24 months of age has been performed, only here you need two staff members to do the lifting.

The vast majority of the minipigs are completely calm when placed in the sling which creates a much more stress-free environment and positive experience for both minipigs and staff members.

Staff training

As part of our continuous focus on the 3Rs, we decided to refine our standard blood sampling procedure. The aim was to further reduce the level of stress imposed on the animals, by not only considering the physical placement of the minipigs during sampling, but also assessing the experience inflicted by the staff members.



Graph 1
Extract from questionaire to 19 staff members conducted before and after training.
Note: Not all questions were answered by all participants, so the results is a calculation in percentages. The questions have been rephrased for the purpose of visual presentation.

Practicing blood sampling in the sling with the animal caretakers at Ellegaard Göttingen Minipigs started in January 2020. Before training commenced, the animal caretakers answered a survey about their experience with blood sampling (graph 1). The purpose was to follow up with the same survey after training, to be able to measure the output of the training program.

The animal caretakers were trained using the sling in pairs. Animal welfare was discussed and the caretakers were trained in lifting the minipigs to create as stress-free an experience as possible. Taking animal welfare into account, blood sampling was first trained on sedated minipigs. The caretakers needed to gain the basic blood sampling skills before practicing on un-sedated animals, to avoid stressing the minipig in the training situation.

After completing the training, the survey was filled out again to see if the experience with blood sampling had changed (graph 1). It showed a significant increase in using the sling when collecting blood samples on minipigs weighing over 10 kg (graph 2).




Picture 1-4
How to place Göttingen Minipigs in a sling.

Challenges and retention of new method

When introducing a new method, it is important to present all the advantages before training commences. It must be explained why the new method is better and remove any insecurity that the new method might induce. In this training process the staff has been very welcoming to the changes, as they experience a significant improvement of animal welfare and quickly discovered the many advantages of this new procedure.

The biggest challenge was not the training itself, but rather performing the blood sampling for a real project. Here it has proven important to ensure a successful experience resulting in the confidence to continue. If insecurity occurs, it is easy to go back to the old method which has been performed time and time over, or withdraw from the assignment completely. The level of training or support needed is very individual, and must be taken into account.

Another challenge has been to maintain the training, so blood samples can be performed by all staff members and not be reduced to a selected few over time.

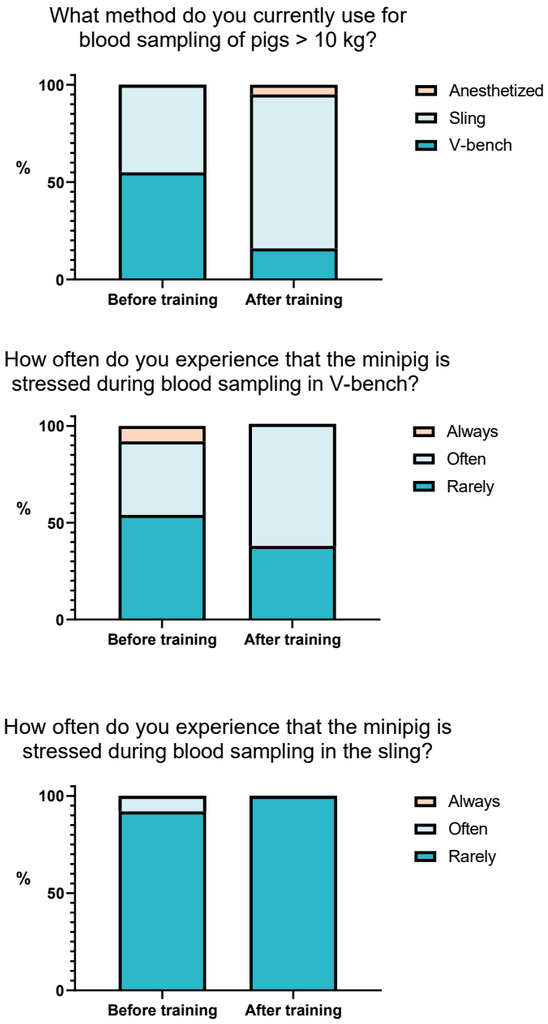
The method of collecting blood samples from a sling demands a continous focus and ongoing training. This includes new staff members, who must be introduced to and trained in this way of collecting blood samples. It is important that they build up the same confidence to perform this process, so we can retain a high level of animal welfare and a good and stress-free environment for all parties.

Refinement and reduction

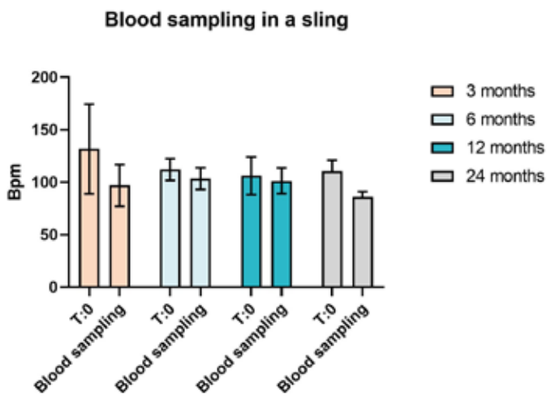
There is no doubt that by implementing blood sampling in a sling the procedure has been improved significantly. Using the sling makes it possible to collect samples from larger animals and thereby collect larger batches. This way the number of animals used can be reduced.

Also, the minipigs are exposed to less stress, which is an important measure for our animal welfare but also ensures high quality blood samples. Heart rate was measured immediately after the minipig was placed in the sling (time 0) and during blood sampling. Blood was sampled once the minipig was calm and within 0-3 minutes after placed in the sling. Minipigs at age 3 months (n=13) had received 6 training sessions prior to sampling (placed in the sling and rewarded afterwards), minipigs aged 6 (n=-10) and 12 (n=10) months had received 2 training sessions, and minipigs aged 24 month (n=5) had not been trained.

The younger minipigs received more training as these were part of a specific project. Also, younger minipigs benefit from more sling training as they are a bit more restless in the sling compared to older animals. As the figure shows, all minipigs were relaxed within 3 minutes (by evaluation of their pulse) after being placed in the sling (graph 3).



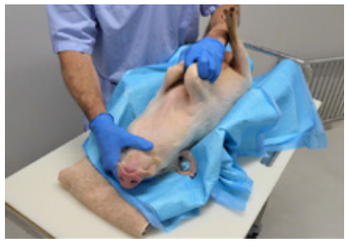
Graph 2
Extract from questionaire to staff members conducted before and after training.
The questions have been rephrased for the purpose of visual presentation.



Graph 3
Heart rate: Mean with SD.

Taking Blood from Göttingen Minipigs while placed in a sling

Adrian Zeltner, Ellegaard Göttingen Minipigs A/S Carina Christoffersen

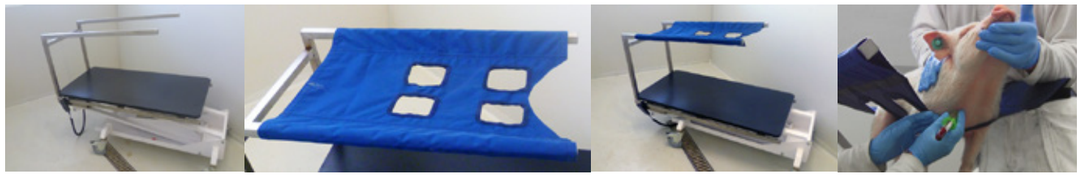


Abstract

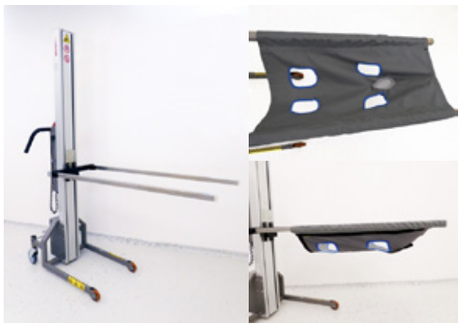
Traditionally Minipigs are restrained in dorsal recumbency to have access to the blood vessels in the neck. (picture on the left) Minipigs, like any other animal, do not particularly like to be restrained and being turned on their back with their belly exposed. With increasing age and weight this method creates also some physical challenges to the technicians. The force needed to control a resisting Minipig can be considerable. Lifting and turning a larger Minipig on its back could also infringe some occupational health regulations. The sling has been proven to be a valuable restraint for various procedures with the Minipig. This study showed that with slight modification the sling can be used to restrain Minipigs for blood sampling and thus reduce strain on animals and personnel.

Materials and Methods

The aim of this study was to test whether the sling could be used as a restraint in various blood sampling situations. A standard sling was modified and several options explored to find the most satisfying design.

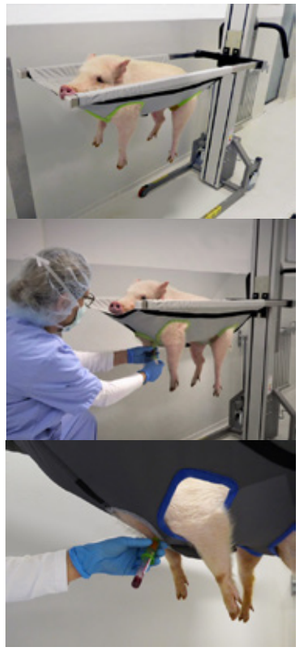


As there was an electric, height adjustable table in the facility a frame was custom made to fit this device. The actual sling is quite stretched in the frame and a cut out was made at the head end, to such a degree that the manubrium sterni of the Minipig is exposed when it hangs in the sling. Once the Minipig is placed in the sling, the head is supported by an assistant and the table can be raised to give easy access to the lower neck. The Minipig head is lifted so the neck is nicely stretched and exposed. Sitting in a low chair the technician can now obtain a blood sample.



To have an alternative we fitted an industrial lift with forks that can carry the slings. The forks can be lowered to the ground to have the option to train the Göttingen Minipigs to step into he sling by itself and to be raised to a comfortable working position.

The sling was modified that the head is lifted and an extra hole was placed centrally, halfway between the openings for the front legs. The raised head makes it easier to palpate the anatomy of the neck trough the central opening and find the right site for puncture. The hole was fitted wit a flap that covers the opening while placing the Minipig. This helps preventing the Minipig to put its snout trough the hole. When the flap is opened, the site for sampling is exposed.



Results, Conclusion and Discussion

We could come up with two methods that work flawlessly in most cases if the Minipigs are properly acclimatized. The Minipigs are calm, do not appear to be stressed and no vocalization was observed. Less manpower than usual was required and we were able to take a sample every 2 minutes with time to spare.

The systems were tested on males and females ranging from 5 to 35 kg. It proved to be particularly successful in the range >10kg, however after a certain size it is advised that two persons lift and place the Minipig in the sling.

Minipigs in the low weight range are generally a bit more nervous or unsettled and might be restrained by a sitting technician (picture on the left) or in the traditional method on the V-bench.

Göttingen Minipigs adapt very well to the sling and require minimal training for that procedure. However it is imperative to take your time when placing the Minipig in the sling. You need to give this procedure the outmost attention when you do it the first time with the Minipig because the outcome of this first attempt will define the character of all the subsequent sling placements.

The technique of the actual sampling needs to be adapted to the new position. Practice has shown that technicians adapt quickly to the new angle of view and even not so experienced technicians have no problems obtaining a blood sample with this type of restrain. The feedback from the technicians is positive throughout, they experience less stressed animals and need less manhours.

Over all it is a true contribution to animal welfare and is a refinement in the sense of the three R's.

To download this poster please scan here:

For more information and help in design of the devices please contact the author at: az@minipigs.dk

Göttingen Minipigs Magazine | 60 | 2021

Working with Göttingen Minipigs

Why did you choose a career within biomedical research, specifically pharmacology?
I had wanted to become a veterinarian ever since I was a child, as animals and helping animals was my passion. Also, biology was one of my favourite classes in school, so veterinary school was the obvious choice. After working as a veterinarian for 2-3 years a casual conversation with a professor of pharmacology at the University of Copenhagen presented the opportunity of writing a PhD in a collaboration with Novo Nordisk A/S.

Do you regret changing direction for your career?
Though pharmacology and biomedical research was not my initial goal, I have never regretted following this path. Fortunately, the veterinary education offers various opportunities of changing path as it is quite broad, so though I fully enjoyed realising my childhood dream of becoming a veterinarian, changing to pharmacology is the best coincidental change I ever made.

How/when were you introduced to minipigs as a large animal species?
Until I started my PhD, I did not know about minipigs for biomedical research. The PhD was about gender differences in obesity in Göttingen Minipigs and looking into why the female minipigs tend to be particularly prone to obesity. Obesity was an area of increasing interest to Novo Nordisk due to the close relation to development of type 2 diabetes and other metabolic diseases.

Explain the value you believe Göttingen Minipigs bring to biomedical research.
At Novo Nordisk we use minipigs as our preferred non-rodent animal model for several reasons. Pigs in general have many anatomical and physiological similarities with humans, e.g. their skin is very similar to that of humans making them useful for pharmacokinetic studies. Also, their metabolism is overall quite similar to human metabolism making them an interesting model for metabolic diseases. Göttingen Minipigs are extremely well characterised both from a pharmacological and toxicological perspective, and due to their small size they are preferred in medium to long-term pharmacological studies, where the size of domestic pigs would quickly become a challenge. In addition, they are attractive for their availability, they are easy to handle, and easy to train for many different procedures. Lastly, the use of minipigs as non-rodent animal model comply with EU legislation for species selection.

What fascinates you the most about Göttingen Minipigs?
That will have to be their healthy phenotype. As part of our studies in obesity, diabetes, and diabetic complications, we have been feeding various unhealthy diets to the minipigs to incite human-like symptoms on the organs. It is amazing that even though they become extremely overweight, weighing more than double of a lean age-matched minipig, they still maintain an incredible healthy phenotype and do not easily develop the typical metabolic complications to obesity.

You have worked a lot with diet-induced models. How did Göttingen Minipigs fit this purpose?
It depends on the disease in question. We have been working with diet-induced, obesity, metabolic syndrome, and atherosclerosis, and have characterised those models. In addition, we have been looking into various diets in combination with chemically induced diabetes to further accelerate e.g. the development of diabetic kidney disease. We test many of our anti-obesity compounds in minipigs, and the results have been very interesting although the translation to the effect in humans remains to be seen for some of the compounds currently in clinical trials. For several of our diet-induced models we have outsourced the initial feeding period to the research facility at Ellegaard Göttingen Minipigs which has worked extremely well and saved us room for other studies in our own animal facility. The level of communication in such a collaboration is essential, and we now have a very well-functioning set-up that we can use going forward.

How do you see the minipig as a model for lifestyle diseases in general?
They have many advantages, for example their metabolism is quite comparable to human metabolism, they are prone to developing obesity, and their organs - especially the cardiovascular system - is very similar to that of humans. However, from an obesity research perspective, ideally the minipigs should have been less healthy when overweight to better resemble human physiology. For example, they are not disposed to developing diabetes.

How do you see the future perspective of an animal model for lifestyle diseases and sequela?
There is great potential in genetically altering the minipigs, so they have an increased tendency to develop human lifestyle diseases. Many of the diseases we work with, such as diabetic kidney diseases and diabetic cardiovascular diseases, develop over a period of 10-15 years in humans. In the minipigs, we would like to obtain this over a period of only 6-12 months, which is a challenge. Genetically modified animal models may be a valid solution as this can help accelerate the development of disease.

Over the years, have any of the projects that you have been involved in had a special impact on you?
Our GLP-1 (glucagon-like peptide 1) projects constitute one of our main business areas. In the beginning the GLP-1 analogues were developed as treatment of diabetes, but later it was discovered that they also have a positive effect on obesity, cardiovascular diseases, NASH, and possibly even Alzheimer's disease. We have done a lot of testing in minipigs in these projects, and the anti-obesity effects have translated very well to humans where we see very positive effects. This has certainly made an impression on me - to see the positive effects observed in animal models translate into positive effects in the patients. Far from all new treatments make it to clinical development, so when you succeed you are very excited and proud, even though your own work only constitutes a small part of the entire process.

In focus

Name Berit Østergaard Christoffersen
Function Principal Scientist at Novo Nordisk A/S

Education
DVM, PhD

Background
After graduating, Berit worked a couple of years as a veterinarian at an animal hospital. After a few years she started a PhD which was a collaboration between the University of Copenhagen and Novo Nordisk A/S. This opened the door to a new chapter in her career.

Engagements
Berit specializes in metabolic diseases and has contributed with several papers and articles on the topic. In 2019 she was appointed Göttingen Minipigs Ambassador for her high-level knowledge dissemination and promotion of Göttingen Minipigs in biomedical research, and for her characterization, validation, and development of Göttingen Minipigs disease models.

About Novo Nordisk A/S
Novo Nordisk A/S is a global healthcare company located outside Copenhagen in Denmark. With research and development centres in 5 countries and production sites in 9 countries around the world, the company employs more than 45,000 people and market their products in 169 countries.

Novo Nordisk develops and produces treatments for some of the most common chronic diseases: Diabetes, obesity, haemophilia and growth disorders. The company was founded in 1923 to start the production of the new drug insulin, and today they produce 50% of the world's insulin supply.

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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:
Anette Sams, Senior Scientist; Kristian Agmund Haanes, Senior Scientist; and Lars Edvinsson, Professor at Lund University | Clinical Experimental Research, Rigshospitalet, Denmark.
Majid Sheykhzade, Associate Professor | Molecular and Cellular Pharmacology, University of Copenhagen, Denmark.

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.

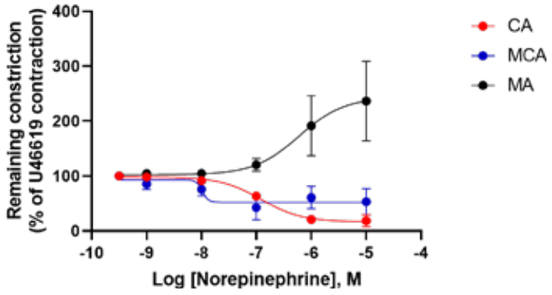


Figure 1
Effect of norepinephrine on isolated segments of Göttingen Minipigs coronary artery (CA), middle cerebral artery (MCA) and mesenteric artery (MA). Data are given as mean ± SEM (n = 6). Noradrenalin constricts mesenteric artery whereas it dilates coronary and cerebral artery preconstructed with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

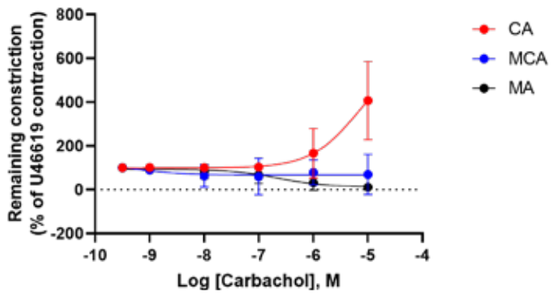


Figure 2
Effect of carbachol on isolated segments of Göttingen Minipigs coronary artery (CA), middle cerebral artery (MCA) and mesenteric artery (MA). Data are given as mean ± SEM (n = 6). Carbachol constricts coronary, dilates mesenteric and show no effect on cerebral artery segments.

This study is supported by the Ellegaard Göttingen Minipigs Research Foundation.

Spotlights

Publications

New papers on Göttingen Minipigs worth noticing

Genetically altered Göttingen Minipigs play a central role in a new important paper studying cellular mechanisms of age-related neurodegenerative diseases such as Alzheimer's disease. Read the paper here: bit.ly/GottingenMinipigsMAPT-APP

Another new publication evaluates the effects of steroids and antibiotics on the biological activity of TSO (Trichuris suis ova) in Göttingen Minipigs. The paper highlights the use of Göttingen Minipigs as a translational animal model for inflammatory bowel disease (BD).
Read the paper here: bit.ly/GottingenMinipigsTSO

Göttingen Minipigs biological material

Biological material from Göttingen Minipigs is a unique ressource for the early study of cause, prevention and treatment of diseases.

When using biological materials from Göttingen Minipigs, you are ensured samples from healthy, genetically standardized, and barrier-bred animals, supporting your research and enabling useful and valid research data. Because biological materials derive from the same colony of animals used in In Vivo studies, results achieved in In Vitro research can be transferred to In Vivo studies without compromising data validity.

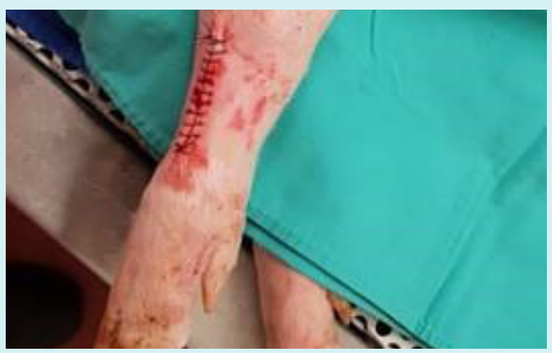
Find more information here: bit.ly/GottingenMinipigs-BioMat

Publication

Validation of a Göttingen Minipig Model of Post-Operative Incisional Pain

New publication confirms the use of Göttingen Minipigs as an ideal translational animal model for evaluating new therapies to treat post-operative pain (POP). Similarities between human and animal model are key to be able to successfully translate preclinical studies, and in this case, for example, similar skin innervation to humans, make Göttingen Minipigs an ideal translational animal model for this study.

Read the paper here (open access): bit.ly/GottingenMinipigsPOP



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Blood samples from Göttingen Minipigs

Göttingen Minipigs is a well established large animal model for biological studies within all areas of biomedical research, and are fully recognized as a large animal model by regulatory authorities worldwide. Therefore, it is important that blood samples are available to facilitate and support the importance of In Vitro testing.

All blood products derive from the established Göttingen Minipigs herds and therefore ensure the same high quality and standards for which Göttingen Minipigs are known:

- A stable genetic background ensured through careful genetic selection and breeding
- Well-defined health status through isolated barrier-breeding
- Similarities to humans and availability in large uniform groups
- Availability of comprehensive background data

Find more information here: bit.ly/GottingenMinipigs-blood

Health Monitoring Report: December 2020

In August 2020, FELASA published their new guidelines "Federation of European Laboratory Animal Science Associations recommendations of best practices for the health management of ruminants and pigs used for scientific and educational purposes".

Highlights in the new HMR include:

- Past results are now reported as the cumulated results from the previous 3 HMRs for the individual agent
- To expand HMR transparency, sample material is now reported along with test method
- Some agent replacements as well as changes in test frequency in our newest HMR have been made. Agents tested and test frequencies are based on risk assessments (depending on e.g. prevalence and risk of interference with research, zoonotic risks, and customer request).
- An exclusion list alongside our HMR is reported, to give a quick overview on which agents prompt either authority notification or further diagnostic or corrective action

"We are very pleased to confirm, that there are no changes in the overall health status at our facility as documented in the HMR from December 2020. The updates are in accordance with the new FELASA guidelines and ensure a continued comprehensive and relevant health management and monitoring programme", says Maja Ramløse, Laboratory Animal Veterinarian at Ellegaard Göttingen Minipigs.

Download the full report from minipigs.dk/goettingen-minipigs/health-status.

We enable development of safer and more effective medicines

At Ellegaard Göttingen Minipigs we are all for sharing and believe that openness creates trust, enriches and clears the path for new opportunities. ***We share knowledge*** *about Göttingen Minipigs for biomedical research, both our own knowledge but also learnings from scientists around the world.* ***We create fora*** *for networking and knowledge sharing amongst scientists.* ***We support scientific research*** *through our Research Foundation.* ***We educate*** *through webinars and practical courses.*

Subscribe to news and invitations

Receive invitations to webinars and scientific meetings, new Göttingen Minipigs Magazine publications and other news directly in your inbox, by subscribing to news from Ellegaard Göttingen Minipigs: minipigs.dk/sign-up-for-news

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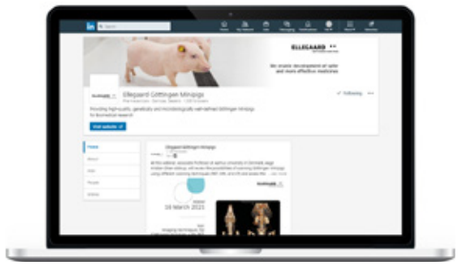
- Health status incl. Health Monitoring Reports, health screenings, accreditations etc.
- Project call-outs from Ellegaard Göttingen Minipigs Research Foundation



Attend webinars

If you are interested in specific topics, or you would like to share your knowledge or experience with Göttingen Minipigs in one of our webinars, please contact us on events@minipigs.dk

Topic	Date	Guest speaker	Register
Induction of prediabetes and diabetes in adult obese Göttingen Minipigs	15 April 2021 10 am CEST*	Sietse-Jan Koopmans | Wageningen University & Research, The Netherlands	bit.ly/EGMweb210415
The use of Minipigs in juvenile toxicity testing	28 April 2021 10 am CEST*	Bianca Feyen | Janssen, Belgium	bit.ly/EGMweb-210428
Inhalation therapy for heart failure with reduced ejection fraction in Göttingen Minipigs	10 June 2021 10 am CEST*	Alessio Alogna | Charité Universitätsmedizin Berlin, Germany	bit.ly/EGMweb210610
Pig models for human nutrition research	29 June 2021 10 am CEST*	Knud Erik Bach Knudsenm Helle Nygaard Lærke and Yetong Xu | Aarhus University, Denmark	bit.ly/EGMweb210629

** Central European Summer Time*
*** Central European Time*

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mrf research forum

The 14th Minipig Research Forum


Facility of Ellegaard Göttingen Minipigs A/S

Dates and venue | Mark your calendar:

29 September - 1 October 2021 at Ellegaard Göttingen Minipigs A/S in Dalmose, Denmark

REMIND ME, WHAT IS MRF ABOUT?

The Minipig Research Forum is a unique opportunity for Göttingen Minipigs users to meet, discuss and share knowledge and experiences within all areas of minipig use related to biomedical research. Mark your calendar for this 3-day conference packed with scientific lectures, poster presentations and the opportunity of networking with minipig users from all over the world.

ABOUT THE CHOICE OF DATE

The MRF meeting will be held in continuation of EUROTOX 2021, that will be held in the city centre of Copenhagen, thus potentially enabling you to participate in both events with less traveling activity. In addition to this obvious time and cost reduction, you will also leave a significantly smaller carbon footprint. Of course, you are welcome to attend the MRF without attending EUROTOX 2021, as the two events in no ways are co-hosted or directly linked.

NOTICE

The MRF Stearing Committee monitors the development of the COVID-19 situation, and hopes to be able to conduct the physical meeting as planned.

Stay updated on the full scientific program and for registration opening at the MRF website and the LinkedIn group.

ABOUT THE LOCATION

The event will be hosted in Ellegaard Göttingen Minipigs' brand new conference room at their site, located only 1½ hour outside the city of Copenhagen and Copenhagen Airport, in the beautiful Danish countryside. During the MRF you will get a unique opportunity to visit the breeding and research facilities of Ellegaard Göttingen Minipigs. Of course, as usual during an MRF meeting, you will be able to network with minipig users from all over the world; a highly valued part of the meeting and a very important reason why we refrain from arranging a virtual MRF meeting.

The MRF is a non-profit organization with more than 500 members worldwide working with minipigs in industry, academia and regulatory bodies. Participation in the annual MRF conference requires membership (free of charge). Read more and apply for membership at www.minipigresearchforum.org

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New publications on Göttingen Minipigs

Ellegaard Göttingen Minipigs gives high priority to collaborative projects that aim to better characterize and validate Göttingen Minipigs as a translational animal model and which facilitate and refine the use of Göttingen Minipigs in research projects and safety testing. Do you have an idea for such a collaborative project? Please contact ellegaard@minipigs.dk.

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Pre-clinical evaluation of the effect of co-medication with antibiotics and oral steroids in Göttingen Minipigs on the biological activity of the probiotic medicinal product TSO (Trichuris suis ova)
Parasitol Res. 2021 Feb;120(2):743-746
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Regul Toxicol Pharmacol. 2021 Mar;120:104861
Doi: 10.1016/j.yrtph.2021.104861
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J Anesth Surg Care. 2021 Jan. Vol 2:101
http://www.jscholaronline.org/articles/JASC/Validation-of-a-Gottingen.pdf

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Directly Reprogrammed Neurons Express MAPT and APP Splice Variants Pertinent to Ageing and Neurodegeneration
Mol Neurobiol. 2021 Jan 7
Doi: 10.1007/s12035-020-02258-w [Epub ahead of print]
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Laboratory Animals. 2021 Feb.
https://pure.au.dk/portal/da/publications/hepatic-blood-flow-in-adult-goettingen-minipigs-and-prepubertal-danish-landrace-x-yorkshire-pigs(07ebe9a5-b6f4-4064-b09d-eb17a0566ee3).html

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Lyhne MK, Vegge A, Povlsen GK, et al.
Hyperinsulinaemic hypoglycaemia in non-anaesthetized Göttingen minipigs induces a counter-regulatory endocrine response and electrocardiographic changes
Sci Rep. 2021 Mar 16;11(1):5983
Doi: 10.1038/s41598-021-84758-w
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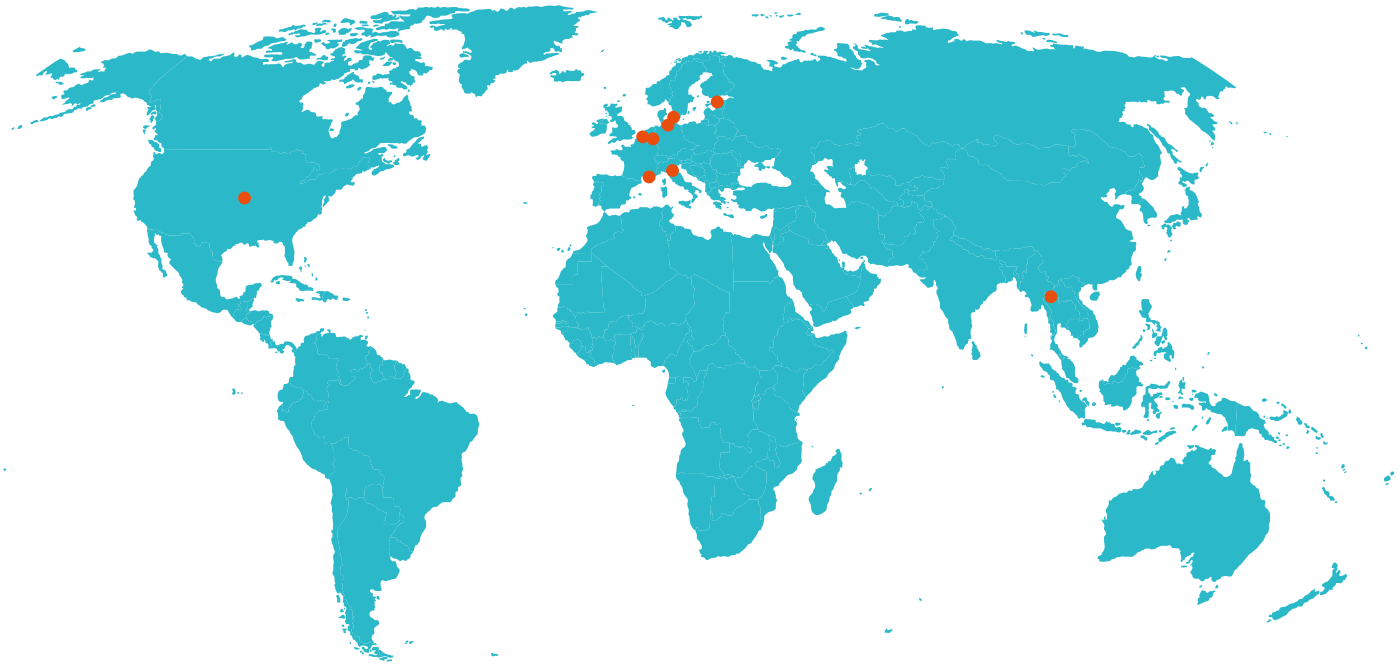
Doi: 10.3389/fimmu.2021.613810
https://www.frontiersin.org/articles/10.3389/fimmu.2021.613810

Where to meet us in 2021



CONGRESS / CONFERENCE	DATE	LOCATION
IAT	9-25 March	*Online event*
SOT and ToxExpo	15-25 March	*Online event*
Tierschutz-Tagung Travemünde	8-9 June	Lübeck, Germany
ESLAV ECLAM	21-24 June	Bologna, Italy
AFLAS	21-27 June	*Cancelled*
SBR	10-14 July	Madison, Wisconsin, USA
World Congress (WC11)	22-26 August	*Online event*
GV-Solas IGTP	22-24 September	*Online event*
EUROTOX	26-29 September	Copenhagen, Denmark
Minipig Research Forum (MRF)	29 September - 1 October	Dalmose, Denmark
SPS	4-8 October	*Online event*
AALAS	16-21 October	Kansas City, Missouri, USA
Scand-LAS	2-4 November	Tallin, Estonia
AFSTAL	30 November - 2 December	Marseille, France
STP-I	TBA	TBA
3R's Research and Progress	TBA	TBA
LASACON	TBA	TBA
CALAS	TBA	TBA

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