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Clean pigs for clear results
I hope everyone has had a relaxed summer break and has now returned with renewed energy. At Ellegaard, we can look back on some hectic months with the opening of our new research barrier, which allows access to a state-of-art minipig housing facility and a surgical suite. This will enhance our business offerings and enable the development, characterisation and validation of new Göttingen Minipig disease models and expand our business offerings into new areas.

Furthermore, we have signed an agreement with the University of Göttingen that enables us to start developing and commercialising transgenic Göttingen Minipigs and to offer these rights to third parties – all for the purpose of ensuring that the Göttingen Minipig will be the preferred minipig for the creation of transgenic animal models. This is an exciting step for our company and a great chance for the scientific community to apply the newest transgenic techniques to the Göttingen Minipig, which has already resulted in several transgenic agreements with external partners aimed at developing transgenic Göttingen Minipigs.

The 10th Minipig Research Forum meeting was held in Copenhagen in May 2016 with record-setting attendance of more than 100 participants. The meeting was very successful with a well-attended welcoming reception followed by an interesting and diverse two-day scientific programme and lots of networking opportunities.

Finally, I would like to welcome our new colleagues: Lena Toft, Management Assistant; Peter Vestbjerg, Head of Business Development; and Kirsten Rosenmay Jacobsen, Laboratory Animal Veterinarian. They will join our existing team of dedicated professionals.

Please feel free to contact any of us for more information about our new initiatives. I hope you enjoy the Newsletter!

Lars Friis Mikkelsen
CEO
Ellegaard Göttingen Minipigs

New Management Assistant at Ellegaard

Lena Toft started as Management Assistant at Ellegaard Göttingen Minipigs on 1 June 2016.

Lena has a BSc in English and German from Copenhagen Business School and has an academy degree in marketing from Copenhagen Business Academy.

Lena has vast international business experience and her previous position was purchase coordinator for Netto, Denmark’s largest retail chain, where she was responsible for the purchase of books and kids’ stationery and worked as coordinator for a group of product managers in the international non-food department.

At Ellegaard, Lena will mainly assist CEO Lars Friis Mikkelsen and the management team. She will be responsible for supporting the cooperation with external business partners, following up on agreements and contracts covering internal and external scientific projects, planning of meetings, following up on actions and several other administrative assignments.

Lena lives in Køge halfway between Dalsnede and Copenhagen with her husband and two teenage sons. She spends most of her spare time with her family, either at home or travelling abroad.

Lena is devoted to her work and looks forward to supporting and guiding you in any administrative matter. You are welcome to contact her on lto@minipigs.dk.

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Follow us on LinkedIn!

You can follow Ellegaard Göttingen Minipigs on LinkedIn! Our Company Page on LinkedIn will keep you updated with useful and interesting information regarding our company and the Göttingen Minipig!
New Head of Business Development at Ellegaard

Peter Vestbjerg started as Head of Business Development for Ellegaard Göttingen Minipigs in July 2016. Peter will be responsible for supporting and overseeing the implementation of our sales strategy. This includes identifying new and developing existing customers and scientific partners, in close collaboration with our Scientific Management, as well as expanding our scientific services by identifying market trends and customer needs and establishing future product and service strategies.

Peter has been working with sales and exports for the last 20 years and has a graduate degree in international business from Copenhagen Business School. For the past 13 years, Peter has been responsible for selling full solutions for Scanbur, which supplies full solutions to animal research facilities.

Peter lives near Køge halfway between Ellegaard and Copenhagen, with his wife and two daughters. Peter enjoys travelling and likes to cook for family and friends in his spare time.

We hope that you will have the opportunity to meet Peter and discuss your future work with Minipigs. You are welcome to contact him on pve@minipigs.dk.

We look forward to introducing you to Peter.

New Veterinarian at Ellegaard

Kirsten Rosenmay Jacobsen started at Ellegaard Göttingen Minipigs as Laboratory Animal Veterinarian on 1 August 2016.

Kirsten graduated as veterinarian in 2009, specialized in biomedicine. In 2012 she received her PhD from the Department of Experimental Medicine, University of Copenhagen, working on refined analgesic treatment and pain assessment of laboratory mice.

Concurrent with her PhD studies, Kirsten received training in non-human primate behaviour, enrichment and welfare at the Michale E. Keeling Center for Comparative Medicine and Research in Texas. In 2013, Kirsten joined the In Vivo Pharmacology group at Translational Medicine Research Centre, MSD in Singapore, before being hired by Scanbur as Scientific Affairs Manager in 2015.

Kirsten has a strong scientific background in the field of animal welfare and looks forward to providing veterinary support and guidance to our customers, as well as keeping Göttingen Minipigs at a high standard in terms of both health and welfare. Together with Anette Blak Grossi, Head of Scientific Management, she will provide scientific support to internal and external projects and collaborations.

Kirsten lives in Menstrup with her husband and daughter. She spends most of her spare time with the family, working on their small farm or travelling abroad.

We hope that you will have the opportunity to meet Kirsten and discuss your work with Minipigs. You are welcome to contact her (veterinary@minipigs.dk) if you have any veterinary questions or challenges regarding the use of our Minipigs.

Scientific publications on the Göttingen Minipig

Ellegaard Göttingen Minipigs A/S gives high priority to collaborative projects that aim to better characterise and validate the Göttingen Minipig as a translational animal model and which facilitate and refine the use of the Minipig in research projects and safety testing. Below is a list of some of the articles which report the results of collaborative projects between Ellegaard Göttingen Minipigs A/S and universities, the pharmaceutical industry and/or contract research laboratories.

Toxicologic Pathology, Volume 44, Number 3 (2016), Swine in Translational Research and Drug Development. The special newly-published issue of Toxicologic Pathology, Volume 44, Number 3, 2016, addresses the latest developments in the utilisation of swine in biomedical and translational research with an emphasis on toxicological pathology and nonclinical safety testing in the Minipig. It provides an assessment of the current status of swine in research and the increasing use of the Minipig in toxicology studies, as well as potential future strategies for the use of the Minipig as a replacement for other non-rodent animal models.

Adrian Zeltner contributed to the article “Sexual Maturation in the Female Göttingen Minipig” and Anette Blak Grossi contributed to the article “Vehicle Systems and Excipients Used in Minipig Drug Development Studies”.

Bilateral congenital cataract in a young male Göttingen Minipig – a case report

Ruth Williams¹, Bob Greenhill¹, Ann Williams¹ and Ann-Sofie Cæcilie Søndergaard²

¹GSK - ²Ellegaard Göttingen Minipigs A/S

Introduction

Congenital cataracts (which may only become apparent at a later age), are relatively rare in the Minipig. None were seen in a survey of 18 young and 49 older Göttingen Minipigs¹. In a survey of the histopathology of 417 male and 418 female Göttingen Minipigs, focal, slight, lenticular degeneration was observed in only two animals². Clinicians working with this species confirm the low incidence: only 2 or 3 true cataracts were diagnosed after examining approximately a thousand Minipigs³ and only one has been reported in the UK⁴. Incidentally two further male Minipigs with bilateral cataracts were reported back to Ellegaard Göttingen Minipigs at around the same time as this case report⁵.

Clinical examination and ocular findings

A routine general veterinary examination was performed on a 3 months old male Minipig (*16.02.2015, body weight 10.9 kg). It was clinically unremarkable and haematology and clinical chemistry parameters were within the normal reference range for this species.

Ocular examination using diffuse illumination (torch pen) and subsequently a slit lamp, revealed a bilateral cataract with a clearly visible anterior Y suture line (Figures 1 and 2). Pupillary light reflex was present, menace reflex was absent. The Minipigs’ behaviour was not indicative of blindness.

Histopathology

Microscopically, the right and left eye showed moderate lenticular degeneration characterised by swollen fibres in the posterior lens from the pole to the equator but also persistent lens fibre nuclei at the posterior surface (Figure 3 - 5).

Discussion

In most species the lens becomes transparent during late gestational stages when the organelles and nuclei of the primary fibres degrade (denucleation); only a monolayer of nucleated epithelial cells remain at the anterior surface up to the lens equator (Figures 4 and 6). Disturbances in the process of de-nucleation can result in congenital cataract in both humans and animal models⁶. In this case, the presence of persistent nuclei at the posterior surface of both eyes suggests that these were congenital cataracts. The aetiology of congenital cataracts can be idiopathic, inherited, infectious, toxic or metabolic and could not be established in this case.

Conclusions

Göttingen Minipigs are frequently used in preclinical safety studies and cataracts can result from xenobiotic induced toxicity in the eye.

This case report highlights the importance of performing routine ocular examinations prior to the start of the study to ensure ocular lesions - such as cataracts - are detected and differentiated from possible compound induced toxicity.

Ethical statement

All animal studies were ethically reviewed and carried out in accordance with Animals (Scientific Procedures) Act 1986 and the GSK Policy on the Care, Welfare and Treatment of Animals.
Acknowledgements
Photos taken by Debbie Ridley, GSK

Figure 3: Histology of the left lens.

Figure 4: Lens showing anterior epithelial cell nuclei at the equator (#), normal (+) and swollen (Ø) fibres.

Figure 5: Posterior pole of the lens showing degenerate swollen fibres (#), acidophilic globular debris (+) and persistent nuclei (Ø).

Figure 6: Schematic diagram of the arrangements of lens fibres to a “Y” on the anterior and an inverted “Y” on the posterior lens surface. Note the absence of lens fibre nuclei on the posterior surface of the lens.

References:
3. Personal communication Sofiène Mhedhbi
4. What You Can See In the Eye of a Minipig (The ophthalmic examination in the Ellegaard Göttingen Minipig) Helmut Ehall
5. Personal communication Adlego Biomedical (JH)
Advanced Imaging of Atherosclerosis in Göttingen Minipigs

Trine Pagh Ludvigsen¹, Berit Østergaard Christoffersen¹ and Henrik Duelund Pedersen²
¹Novo Nordisk A/S  -  ²BioAdvice A/S

Background
Cardiovascular disease is the leading cause of death worldwide, and atherosclerosis is the major underlying cause. In atherosclerosis, plaques composed by cholesterol, cellular waste products and inflammatory cells build up in the inner walls of the blood vessels. Plaques are initially stable, but more advanced plaques become inflamed and unstable, and when a plaque breaks and some of its contents are released, or when a thrombus forms on the plaque’s surface, a heart attack or stroke may result. Several pig models of atherosclerosis have been described, and pigs are increasingly being used to study the pathogenesis of the disease as well as the therapeutic effect of novel treatments. The utility of the pig in atherosclerosis research is supported by several similarities to the human situation; amongst others the disease in pigs mimics all stages of human atherosclerosis; pigs have a size allowing translational in vivo end-points to be used and pig models have been shown to be predictive for effects of several classes of therapeutics. We recently showed that it is possible to induce advanced atherosclerosis in castrated Göttingen Minipigs by feeding them a high-fat diet rich in cholesterol.¹ As in humans, severe lesions were found in both the coronary arteries and the aorta (Fig 1 and Fig 2).

In clinical trials with patients suffering from atherosclerosis, advanced imaging is used to obtain an early reading of the effect of a given compound. Intravascular ultrasound (IVUS) is the gold standard for measuring coronary plaque burden and 18-fluorodeoxyglucose (¹⁸F-FDG) positron emission tomography (PET) is used in many trials to assess plaque inflammation as a surrogate measure of plaque instability. In a recently completed study, we evaluated the feasibility of these two techniques in Göttingen Minipigs with atherosclerosis. Here, we present a short description of these two methods and their feasibility.

IVUS
In brief, the principle behind IVUS is to advance (via a peripheral artery) a <2 mm diameter high-frequency ultrasound transducer (45 MHz) into diseased vessels such as the coronary arteries. The arterial wall is then visualized during motorized pullback of the transducer, allowing evaluation of plaque distribution and volume (Fig 3).

Figure 1. Aortae opened longitudinally (en face view) from a lean control (A) and an obese dyslipidemic Minipig (B). Stained with Sudan IV (lipophilic staining).

Figure 2. Coronary arteries from a lean control (A) and an obese dyslipidemic Minipig (B). Verhoeff-van Giessons staining.

Figure 3. Tip of the intravascular ultrasound (IVUS) catheter used in the study (Revolution®, 45 MHz, Volcano Cooperation, San Diego, CA, USA) (A). Intravascular ultrasound (IVUS) image of abdominal aorta with atheromatous plaque (the lumen is delineated with light blue, vessel wall marked by dark blue arrow) in obese, dyslipidemic Minipig (B).
In our experience, it was feasible to perform the procedure repeatedly in the Minipigs included in the study. It was necessary with an intravenous infusion of lidocaine during the procedure to prevent lethal arrhythmias, and the Minipigs also received anticoagulant treatment. The technique is difficult and requires some practice, and access to perform fluoroscopy (real-time projection X-ray) from different angles. During two procedures out of 35 the animals were lost directly due to procedure-related causes; one as a consequence of lethal arrhythmias that could not be reversed and one due to damage to the right coronary artery. With increased training, the frequency of procedure-related deaths will likely decrease.

**PET/MR**

The principle behind ¹⁸F-FDG PET is that a radioisotope-labelled glucose analogue is taken up by metabolically active cells with high glucose consumption, e.g. macrophages in the plaque. As this glucose analogue is non-metabolisable, radioactive molecules build up in active cells in advanced and inflamed plaques. By combining the technique with a morphological scan such as magnetic resonance or computerized tomography imaging (MRI or CT), the plaque can be identified and delineated and the glucose uptake in the plaque quantified by signal intensity. Prior to the procedure, Minipigs with significant plaque were selected by performing 2D vascular ultrasonography of the caudal aorta. The PET scanning required that the Minipigs were anaesthetised for 5-6 hours, and that they were fitted with a transcutaneous bladder catheter to avoid interference from accumulated tracer in the bladder. The pictures below show the setup in the scanner and a representative PET/MR image (Fig 4).

**Perspectives**

Advanced imaging of atherosclerotic plaques is a rapidly developing field. With regard to IVUS, novel approaches including optical coherence tomography and intravascular photo acoustic imaging are promising with regard to enabling measurement of not only the plaque volume, but also the fibrous cap and the lipid core of unstable plaques. With regard to PET, the novel tracer ⁶⁴Cu-DOTATATE is promising in terms of specific imaging of activated macrophages in plaques.² We recently presented data indicating that this tracer can also be used in the Göttingen Minipig model (Poster by Pedersen SF et al. presented at the recent Arteriosclerosis, Thrombosis and Vascular Biology conference and the recent Minipig Research Forum).

**Collaborators and acknowledgements**

The IVUS studies were performed in collaboration with Professor Michael Sturek, Indiana University, Lisbeth Høier Olsen, University of Copenhagen and Lisette Okkels Jensen and Mikkel Hougaard, Odense University hospital and the PET/MR studies were performed together with researchers from Copenhagen University Hospital (Rigshospitalet), especially Sune Folke Pedersen, Rasmus Sejersten Ripa, Helle Hjorth Johannesen, Adam Espe Hansen, Liselotte Hojgaard and Andreas Kjær.

Technicians from the Obesity & Diabetes Pharmacology department at Novo Nordisk A/S and Copenhagen University Hospital are acknowledged for excellent technical assistance during the procedures.

**References:**


**Figure 4.** Obese Minipig positioned for the positron emission tomography and magnetic resonance imaging (PET/MRI) (A). Example of ¹⁸F-flourodeoxyglucose (FDG) uptake in an atheromateous abdominal aorta vessel wall (light blue arrow), as visualized by PET/MRI (B).
The 5th Porcine Biomedical Models meeting
3rd of November, 2016

Metabolic syndrome and associated sequelae in pig models: Focus on nephropathy, NAFLD/NASH and atherosclerosis

Preliminary programme

Participation in the seminar is free of charge. (please note maximum 100 participants)
Registration online latest by 28 October 2016:

Contact secretariat: Helle Lohmann Schøler, hlsc@sund.ku.dk

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<thead>
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<td>8.30-9.00: Registration and coffee</td>
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<td>9.00-9.05: Welcome</td>
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<tr>
<td>9.05-9.50: Non-alcoholic fatty liver disease in human patients: Pathogenesis and liver changes (Professor Mogens Vyberg, Aalborg University, Denmark)</td>
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<td>9.50-10.00: Discussion</td>
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<td>10.00-10.45: Non-alcoholic fatty liver disease in the Ossabaw Minipig Model of Metabolic Syndrome (Professor Michael Sturek, Indiana University, USA)</td>
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<td>10.45-11.00: Discussion</td>
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<td>11.00-11.30: Coffee, tea and posters</td>
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<td>11.30-12.15: The Pig as a Model of Metabolic Syndrome and the Associated Nephropathy (Professor Lilach O. Lerman, Mayo Clinic, USA)</td>
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<td>12.15-12.30: Discussion</td>
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<td>12.30-13.00: Lunch break and posters</td>
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<td>13.00-14.15: A Translational Model for Diet-related Atherosclerosis: Effect of Statins on Hypercholesterolemia and Atherosclerosis in the LDL-receptor Knock Out Minipig (Dr. Dale Mais, MPI Research, USA)</td>
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<td>14.15-14.30: Discussion</td>
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<tr>
<td>14.30-15.15: Molecular imaging of atherosclerosis in clinical and translational medicine (Dr Trine Pagh Ludvigsen, Novo Nordisk A/S and senior researcher Sune Folke Pedersen, University of Copenhagen, Denmark)</td>
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<tr>
<td>15.15-15.30: Discussion</td>
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<td>15.30-16.00: Coffee, tea and posters</td>
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<td>16.00-16.30: Short abstract presentations:</td>
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<td>TBD (PhD student Camilla Schumacher-Petersen, University of Copenhagen)</td>
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<td>TBD (PhD student Simone Krog, University of Copenhagen)</td>
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Registration and further details on the program: http://ivs.ku.dk/english/calender/2016/5th-porcine-meeting/
Manoeuvre track and mental driving techniques

By Cristina Kragh Thomsen, Order Manager, Ellegaard Göttingen Minipigs A/S

At Ellegaard Göttingen Minipigs we make sure that our drivers’ driving skills are kept up to date and that they receive the latest information on how to drive safely when delivering all over Europe.

Our drivers spent a day on the manoeuvre track in the town of Sørø, not far from our facility, to maintain their driving techniques and acquire new knowledge.

The drivers started out with one hour of theory provided by an experienced instructor who had many anecdotes to tell. After this, the instructor guided our drivers around the manoeuvre track.

As you can see from the pictures, all our vans were out in the field and drove on the slippery track, performed evasive manoeuvres and braking exercises, among other things.

Our drivers also attended a “mental driving technique” course conducted by a former police officer. The course content was “influencing attitudes, learning driving techniques, enhancing traffic knowledge and preventing injury and damage”.

Attending this course was a very interesting experience for our drivers, and the knowledge and practical techniques they learned can primarily be used for driving on the job but also in their personal driving, as well.
On 17 June 2016, we had the grand opening of our new Research Barrier B5, which allows access to a state-of-art minipig housing facility and a surgical suite, which will enable the development, characterization and validation of new Gottingen Minipig disease models and expand our business offerings into new areas.

After lots of brainstorming and planning and not least months of hectic activity involving a huge number of local builders and Ellegaard staff, we finally managed to re-open our oldest breeding barrier, formerly known as barrier B1. The totally renovated and updated barrier facility includes several flexible housing rooms, rooms for examination, blood sampling and smaller procedures plus a large top-modern surgical suite for advanced surgical procedures and a post-operative recovery room.

With our increased focus on scientific branding and scientific collaboration to further characterize and validate the Gottingen Minipigs as a suitable translational animal model, and the development of disease models based on the Gottingen Minipigs, it has for a while been a huge wish for us to offer long-term housing of animals of various diets to develop and provide diet-induced animal models, and to offer and provide surgically based animal models or animals with e.g. permanent catheters or other devices. We can now offer these opportunities to our customers incl. CROs, pharmaceutical companies and universities, and are open for other customer-based request for developing various disease models in the Gottingen Minipigs.

Furthermore, as having signed an agreement with the University of Gottingen that enables us to start developing and commercializing transgenic Gottingen Minipigs and to offer these rights to third parties – all for the purpose of ensuring, that the Gottingen Minipig will be the preferred minipig for the creation of transgenic animal models, we also aim at offering to breed transgenic animal in the Research Barrier B5 depending on customer interest and request.

This new business offering is a step-stone for Ellegaard Gottingen Minipigs and has only been possible due to a huge effort from many dedicated colleagues and support from collaborators.
trusting, that our decade-long experience of housing, handling and managing Göttingen Minipigs also will be valuable for the developing, characterizing and validating of new exiting Göttingen Minipig based disease models.

With all these new initiatives, we believe, that we can save valuable time for our customers by providing prepared animals for the actual scientific procedures or “ready-to-go” diet-induced or surgically prepared disease models.

Please feel free to contact us at ellegaard@minipigs.dk to learn more about these exciting new opportunities for acquiring “ready-to-go” animals or disease models or access to the development, breeding and commercialisation of transgenic Göttingen Minipigs.
The utility of the Minipig as an animal model in evaluation of an artificial sphincter

By Pomme Boissier, Study Director, Aginko Research, Switzerland

Urinary incontinence is a devastating physical disability [1] affecting more than 15 million people only in the USA. Current treatments of severe stress urinary incontinency include pharmacological therapy [3], bulking agents [4], surgical approaches [5], and cellular therapy [6-8]. All these modalities have limitations, and many innovative approaches have been proposed experimentally to improve treatment success. Aginko supports the development of an innovative medical device. Several acute studies have been previously performed in different animal models (dog, sheep and farm pig). All these models have several limitations. It has previously been established that the Minipig urethra is a suitable model for in vitro study [9] and that urodynamic measure can be performed in the Minipig [10].

In the experiment performed at Ellegaard Gottingen Minipigs we reviewed the value and utility of the Minipig as an animal model in evaluation of an artificial sphincter.

Two female Minipigs (12 and 24 months) were used in the study. Minipigs were anesthesied and a rigid urethral catheter of 9 CH was introduced (Figure 1). Due to the anatomy of the Minipig, the catherization was easier than in farm pig, an important point for the urodynamic measurement.

Different surgical approaches were tested to determine the less invasive procedure to access to the bladder and the urethra.

Numerous blood vessels and umbilical artery are located in the pelvic area, surgery should be performed with caution and a cautery instrument.

Whereas the bladder is smaller and the length of urethra shorter, the diameter of the urethra in the Minipigs seems similar to the diameter of the urethra in farm pigs. Farm pigs and Minipigs have an urethra diameter in the range of the human one, which makes good models to evaluate artificial sphincter. However, the urethra of the Minipig is located deep below the pubis, which makes its access really difficult.

Bladder and urethra were isolated (Figure 2) and artificial device was placed around the urethra. Different measures of elasticity were performed using a dynanometer (Figure 3). Urethra of the Minipigs seems to have a higher elasticity compared to the farm pig, however, anesthesia used during the experiment can influence the results.

In conclusion, due to its anatomy, the Minipig can be easily catheterized compared to the farm pig, which required a considerable time for catherization. A 9 CH catheter can be introduced in the urethra of the Minipig with a small speculum. Whereas the bladder size is smaller and the urethra length shorter than in farm pigs, the Minipigs urethra diameter is matching the one of the farm pig. As such, the Minipig is a usable model.
Artificial sphincter can be closed around the urethra of the Mini-pig. However, the access to the urethra is difficult due to the fact that it is located deep below the pubis. Surgical approach should be adapted to place the cuff in this model.

Pull Force Test showed that urethra of the Minipigs is more compliant than the one of farm pigs. It is also worth noting that while the urethra response to a compression force seemed linear on the farm pigs, this does not seem to be that obvious with the Minipigs where the behaviour would be best described as exponential. This can be due to the deep anaesthesia performed on the Minipig. Anaesthesia using propofol should therefore be used to compare urethra elasticity between farm pig and Minipig.

The Minipig is a suitable model for GLP biocompatibility studies.

<table>
<thead>
<tr>
<th>Catheterization</th>
<th>Farm pig</th>
<th>Minipig</th>
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<tbody>
<tr>
<td>Catheter size</td>
<td>12-9 CH</td>
<td>9-7 CH</td>
</tr>
<tr>
<td>Urethra diameter</td>
<td>~10-15 mm</td>
<td>~10-12 mm</td>
</tr>
<tr>
<td>Access to urethra</td>
<td>Easy</td>
<td>Difficult</td>
</tr>
<tr>
<td>Handling</td>
<td>Difficult</td>
<td>Easy</td>
</tr>
</tbody>
</table>

Table 1: Comparison of farm pig and Minipig model.

References:
[1] Walters MD. Mechanisms of continence and voiding, with international continence society classification of dysfunc-
Gynecol. 2004; 104:607-20
S11: S3-S11
Social housing during telemetry studies – an industry survey

Helen Prior, PhD. Programme Manager, National Centre for the Replacement, Refinement & Reduction of Animals in Research (NC3Rs), London, UK.

The NC3Rs and Safety Pharmacology Society (SPS) recently published the paper ‘Social housing of non-rodents during cardiovascular recordings in safety pharmacology and toxicology studies’. The open access report, available in the Journal of Pharmacological and Toxicological Methods, summarises a survey on current practices in the field of telemetry (remote recording of cardiac parameters) and identifies opportunities to improve animal welfare during the studies.

Most new medicines are assessed for their potential to affect the cardiovascular system in non-rodents before they enter first-in-human clinical trials. These studies are usually carried out in dogs, Minipigs or non-human primates, and are designed to better understand the potential of drugs to affect parameters including blood pressure, heart rate and electrocardiogram (ECG). These tests are commonly performed during either a standalone safety pharmacology study (with the animals implanted with a telemetry device) or as part of the repeat dose toxicity study (using telemetry recordings from animals wearing jackets containing the recording equipment). Using telemetry enables researchers to remotely monitor and collect large amounts of data from animals without restraint or disturbance.

The number of respondents housing their animals socially or individually, on recording or non-recording days within a safety pharmacology telemetry study. The numbers within the bars give the actual number of respondents, for ease of reading. Legend definitions are as follows: Social housing: an animal is housed with at least one pen/cage mate for 24 hours a day (apart from veterinary reasons for single housing); Partial social housing: an animal is housed with at least one pen/cage mate for the majority of the day, apart from during study procedures (e.g., separation for recording of food consumption or clinical sign observations immediately post-dose); Individual housing: an animal is housed alone in the pen/cage (note, the animal may or may not have contact with other animals through the bars or adjoining pens/cages).
It is general practice for the animals to be housed in social groups when they are not being studied. However, the majority of the pharmaceutical industry will separate animals from these groups on the telemetry data collection days. This is usually due to limitations in the current technology which cannot collect data from multiple devices simultaneously. Although these periods of isolation may be short, this practice can introduce additional stress to the animals, which could be avoided if updated telemetry systems (allowing recordings from socially housed animals) were adopted.

In 2015 a working group led by the NC3Rs, in collaboration with the SPS, carried out a survey to collect information on current practices for housing of non-rodents during the collection of this data. The aim was to share experiences and canvas opinions on study procedures and designs that could be used for socially housing animals during telemetry recording periods, and discover the barriers which currently exist to prevent this. The report shares the output of the survey which was completed by 39 sites across 12 countries (51% from Europe, 41% from USA) either running studies (pharmaceutical companies or Contract Research Organisations, CROs) and/or outsourcing work. This article summarises the Minipig results and the reader is directed to the full report for details of the other non-rodent species.

**Use of Minipigs in safety pharmacology studies**

Twenty different sites provided information on Minipig safety pharmacology telemetry studies; twelve of these were CROs, six were pharmaceutical companies outsourcing work, one was a pharmaceutical company running studies in-house and one was a pharmaceutical company running some studies in-house and outsourcing others.

Figure 1 shows the housing conditions employed on non-recording and recording days. In common with the other non-rodent species, Minipigs tend to be socially housed on non-recording days (67% of respondents) however on recording days only 20% of respondents socially house their Minipigs. The main barriers for social housing of Minipigs were limitations of the recording equipment, study design, size/number of available pens and temperament of individual animals.

Of the respondents with experience of social housing Minipigs for safety pharmacology studies, all four indicated that the

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**Figure 2: Flow-diagram with decision tree for social-housing on Safety Pharmacology studies**

- **Start**
  - May have to individually house
    - NO
    - Pen/cage size suitable for multiple animals
  - Is the test compound suitable for group housing?
    - YES
    - Consider social housing
    - Consider using a companion animal
    -  **Considerations:**
      - Quality of data
      - Study design
      - Temperament of animals
      - Colony management
  - NO
    - Telemetry hardware suitable to record from multiple animals in the same area?
      - YES
      - Consider social housing
      - Consider using a companion animal
      -  **Considerations:**
        - Site of colony/availability of companion animals
        - Is the companion animal considered ‘on-study’ or ‘stock’?
        - Contamination of the companion
        - Is companion animal a telemetry animal (colony) or nonimplanted?
      - NO
        - Consider social housing
        - Consider using a companion animal
        -  **Considerations:**
          - Site of colony/availability of companion animals
          - Is the companion animal considered ‘on-study’ or ‘stock’?
          - Contamination of the companion
          - Is companion animal a telemetry animal (colony) or nonimplanted?

This flow diagram contains decision points and suggestions for housing options for individual studies within a facility. Definition of companion animal is as follows: an additional animal is housed in the same pen/cage as the recorded animal. This animal may be part of the study (e.g., dosed and recorded on a different day) or may be an undosed animal (e.g., part of the stock colony) provided solely for companionship.
data quality was the same or better than data obtained from individually housed animals.

**Use of Minipigs in toxicology studies**

Thirteen different sites provided information on Minipig toxicology studies; seven of these were CROs, five were pharmaceutical companies outsourcing work and one was a pharmaceutical company running some studies in-house and outsourcing others. In common with the other non-rodent species, Minipigs tend to be socially housed on non-recording days (100% of respondents) however on recording days only 25% of respondents socially house their Minipigs. The main barriers for social housing of Minipigs in toxicology studies were risk of damage to and limitations of the recording equipment, food consumption recording and temperament of individual animals.

Of the respondents with experience of social housing Minipigs for toxicology studies, all three indicated that the data quality was the same or better than data obtained from individually housed animals.

**Concluding Remarks**

Most respondents listed multiple reasons preventing social housing in safety pharmacology and toxicology studies, indicating that although some barriers could potentially be overcome, a number of other aspects also require addressing. The main barriers identified in the survey included the need for capital investment in equipment, potential damage to recording equipment (e.g. jackets), changes to established study designs, food consumption control and changes in animal temperament/activity. Despite these, the survey also highlighted that there is support for socially housing non-rodents throughout the whole study, with many companies already working this way and others actively planning to move towards these refined conditions. The report provides recommendations to facilitate this transition in practice and to encourage more companies to review their practices and consider adoption of this refinement across the industry (see Figure 2).

**References:**

The 43rd Annual Meeting of the Japanese Society of Toxicology (JSOT) was held on June 29 - July 1, 2016 in Nagoya, Japan. Lars Friis Mikkelsen and Anette Blak Grossi from Ellegaard Göttingen Minipigs A/S had joined us for giving talks in the luncheon seminar hosted by Oriental Yeast Co., Ltd.

The titles of presentation are as below:

Lars Friis Mikkelsen: The Göttingen Minipigs – past, present and future global perspectives

Anette Blak Grossi: The use of Göttingen Minipigs in scientific research

The meeting had lots of Minipig focus and over 200 audiences participated in our seminar; it was very successful. Interest in the Minipigs is growing in Japan.

The 50th Annual Meeting of Japanese Association for Experimental Animal Technologists (JAEAT) will take place on September 29 - October 1. OYC is invited to give a talk at the meeting. Naoki Hayashi from Ina MP Breeding Center of OYC will participate in and talk about [How to manage Minipigs; Housing, Handling, Dosing, Socialization, and Training].

Please contact us at fbi@nisshin.com for further details.
Lars Friis Mikkelsen becomes board member of European Animal Research Association

By Sarah Wells, European Animal Research Association

The European Animal Research Association (EARA) was set up in March 2014 with the aim of improving the climate around animal research on a European level. EARA is a membership organisation which currently has around 50 members from both the public and private research sectors across Europe. Ellegaard Göttingen Minipigs has been a member of EARA since its early days in 2014. Since June of this year, EARA is pleased to count Ellegaard’s CEO Lars Friis Mikkelsen as one of its new board members.

By balancing out the public debate around animal research with truthful, evidence-based information, EARA aims to create a supportive climate in which responsible animal research can take place. Our strategy is based on four principal goals. In this newsletter, we would like to tell you about our work in these fields, and how they are benefiting Ellegaard and its clients.

Supply chain
From laboratory animal breeding, to transportation, to cage manufacturing – without the supply chain sector, vital research using animals would be rendered impossible. Therefore the supply chain takes up a key part of EARA’s efforts. EARA leads discussions with transport providers to improve the options for laboratory animal transportation, e.g., EARA gathered policymakers’ support for Air France, the only commercial airline currently transporting non-human primates (NHP’s) for research and helps the airline deal with questions from non-French media sources as to their continued transportation of NHP’s. EARA has previously countered activists’ campaigns against airlines and other transport providers.

Information
By helping create national organisations that communicate about animal research and by organising media campaigns, EARA promotes a balanced public dialogue about animal research. EARA advised on the creation of Pro-Test Deutschland, which aims to provide reliable information about animal research in Germany. To mark World Day for Laboratory Animals 2016, EARA published a statement in support of animal research in Belgium. To gather support for animal research legislation at the EU level, EARA is coordinating a statement, signed by 240 European organisations to date, in support of Directive 2010/63/EU for the protection of animals used for scientific purposes which is currently under review by the European Commission. Next to these pro-active communications activities, EARA also provides comments and reacts to media coverage of animal research where possible.

Supportive climate
To create a supportive climate in which responsible animal research can take place, EARA is actively involved in a great
number of advocacy initiatives. EARA has provided evidence to explain the continued need for responsible use of animals in biomedical science to counter mounting pressure against animal research, for example in the case of the ‘Stop Vivisection’ European Citizens’ Initiative in 2015 and various campaigns against breeders and transport companies. The European Commission has invited EARA as one of the stakeholders to feed into the review of Directive 2010/63/EU which is currently underway. In Italy, EARA co-created Research4Life, an advocacy platform to defend biomedical research. With these and other advocacy initiatives, EARA represents the interests of its members at the European and national levels of policymaking.

Communications advice
EARA provides its members with the communications advice to suit their individual needs. As EARA has a wide variety of members, ranging from universities and public research institutes to animal breeders to large pharmaceutical companies, the communications advice covers a wide range of topics. We have advised members on the development of their animal research website, helping them think about what type of information to include, and how best to structure and present it. We provide workshops to help our members develop a communication strategy and a crisis communications plan, and offer media training. On a more general level, EARA will help key people in member organisations understand the need for and benefits of greater openness surrounding the communication of animal research.

Aside from the advice and other activities which EARA can provide for Ellegaard, membership of EARA allows Ellegaard access to a wide-ranging network of organisations conducting or otherwise relying on animal research. With Lars on the Board, EARA looks forward to working more closely with Ellegaard to ensure the interests of the animal research sector, and animal breeders in particular, will continue to be protected.

If you need further information about EARA please contact Sarah Wells: swells@eara.eu.
10th anniversary of the Minipig Research Forum in 2016

In 2016 the Minipig Research Forum welcomed more than 100 registered participants to its annual meeting in Copenhagen. A group of twenty excellent speakers presented valuable information on the following topics: “Immunology and vaccine testing in the Minipig”, “Minipig ophthalmology” as well as “Juvenile and embryofetal development studies in the Minipig”.

The programme also included various posters and workshops: “Importance of perioperative pain management in Minipigs … All you always wanted to know and never dared to ask”, “Immunotoxicity evaluation in the Minipig” and “Three ways to improve public understanding and acceptance of bio-medical research using animals”, where attendees could share their knowledge and experiences.

Many of the scientific presentations are available by logging on to the Minipig Research Forum website: www.minipigresearchforum.org

The MRF organisers also arranged a guided canal tour through Copenhagen, where we passed some of the city’s attractions by boat. The conference dinner was held at the Royal Theatre and featured delicious seasonal food from Denmark.

Prior to the actual start of the MRF meeting, there was a get-together event with an evening buffet, food and drinks on the top floor of Axelborg, affording great views of the centre of Copenhagen. The dinner and get-together event gave attendees an excellent opportunity to network.

We would like to thank our generous sponsors for supporting this year’s MRF meeting.

Thank you for joining this year’s MRF meeting. If you have any suggestions for interesting topics for the next MRF meetings please contact: info@minipigresearchforum.org.

We look forward to seeing you again next year on 17-19 May in Cambridge, UK.

Paulina Smirnova Valund
On behalf of the Minipig Research Forum Steering Committee

Follow MRF on LinkedIn

The Minipig Research Forum group on LinkedIn is an informative, useful platform where minipig users interact, ask questions and share experiences.

Find the group “Minipig Research Forum” and apply for membership.

You can follow MRF on LinkedIn – to stay connected and be able to contact other minipig users!

Meeting Calendar 2016

<table>
<thead>
<tr>
<th>Name</th>
<th>Date</th>
<th>Location</th>
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<tbody>
<tr>
<td>EuroTox - European Societies of Toxicology</td>
<td>4-7 September</td>
<td>Seville, Spain</td>
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<tr>
<td>SPS - Safety Pharmacology Society Meeting</td>
<td>18-21 September</td>
<td>Vancouver, Canada</td>
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<tr>
<td>AFSTAL</td>
<td>12-14 October</td>
<td>Nantes, France</td>
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<tr>
<td>ACT - American College of Toxicology</td>
<td>6-9 November</td>
<td>Baltimore, USA</td>
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For more information, please visit: www.minipigs.dk