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Welcome to the Spring 2019 Newsletter which we have dedicated to celebrating The First 50 Years with Göttingen Minipigs! I am truly excited sharing with you a variety of initiatives that we have planned throughout the year for the benefit of everyone having an interest in or already using Göttingen Minipigs for their biomedical research. Among the initiatives are a number of scientific symposia which will be held at different locations in Europe, Asia and the US, all focusing on sharing research results and knowledge by using Göttingen Minipigs and a number of exciting webinars.

The scientific program for the 13th Minipig Research Forum, 22-24 May 2019, in Vienna is furthermore finalized. Indulge in the comprehensive program with 20 session topics and 3 workshops on page 11 and don’t forget to secure your seat by registering for this great event which also allows time for networking with other Göttingen Minipigs users.

Our Meeting Calendar 2019 at the last page of the Newsletter is updated with dates and locations for our events so mark your calendar and stay updated on invitations at our LinkedIn company page.

In addition, I am proud to announce the planned appointment of Göttingen Minipigs Ambassadors every month throughout our jubilee year in acknowledgement of the Ambassadors’ special efforts and achievements in using and promoting the use of Göttingen Minipigs in their research. I am pleased to report that the first two Ambassadors have accepted the nomination with the pleasure and honour – read more inside the Newsletter.

“We enable development of safer and more effective medicines”

This sentence captures what we do and why we enjoy working at Ellegaard Göttingen Minipigs as well as the meaningfulness of living out our key values: animal welfare, quality, respect and collaboration in our daily operations and interaction with our animals, customers, cooperation partners and colleagues.

I wish you a wonderful spring and hope to see you at one or more of our jubilee events or at a conference during 2019!

Lars Friis Mikkelsen, CEO
Ellegaard Göttingen Minipigs A/S
The 50-years history of Göttingen Minipigs

Lars Friis Mikkelsen, Ellegaard Göttingen Minipigs A/S, Dalmose, Denmark

The early days in the 1960’s
The creation and development of the Göttingen Minipigs started in the 1960’s through an initiative by Prof. Fritz Haring and his co-worker Prof. Ruth Gruhn and later Prof. Peter Glodek at the former Institute of Animal Breeding and Genetics of the Georg-August University Göttingen in Germany. The development of the breed was inspired by the existence of similar miniature pig breeds, like the Minnesota Minipig, in the USA, and was from the beginning aimed at developing a relatively smaller “large animal” model for biomedical research.

The development of the breed started in 1960 with an import of three male and two female Minnesota Minipigs from the Hormel Institute in Austin, Minnesota, USA. The Minnesota Minipig itself is a composite breed, which was developed at the Mayo Clinic in Rochester, Minnesota, by Professor Winters from the Hormel Institute in Austin, Minnesota, USA. The development of the Minnesota Minipig was started in 1949 based on black Guinea hogs from Alabama, feral boars from the Pacific island of Catalina, and Piney Woods “rooters” from Louisiana. In 1957, animals of the Ras-n-Lansa breed from the island of Guam, with strongly expressed dwarfism, were furthermore introduced to reduce size. The Minnesota Minipigs were reciprocally bred with three male and four female Vietnamese potbelly pigs from the Wilhelma Zoo in Stuttgart, Germany. The resulting population was spotted and phenotypically strongly affected by the undesired obese characteristics of the potbelly pigs. To widen the genetic basis four additional Vietnamese female potbelly pigs were imported in 1965 from the Tierpark Friedrichsfelde in East Berlin, leading to a smaller and less colored minipig.

The final creation of the Göttingen Minipigs in 1969
It was soon realized that for many purposes, especially for dermal studies, a leaner and less potbelly-typed minipig with white skin would be desirable. For this purpose, genetics of commercial German Landrace pigs were introduced by artificial insemination during the years 1965 to 1969 – with 1969 being considered the year of the “birth” of today’s Göttingen Minipigs. At that time, separate lines of colored and white minipigs were established. Glodek and Oldigs later reported, that the proportional representation of the three original breeds in the white line in 1969, the year of creation, was 60% Vietnamese potbelly pigs, 33% Minnesota Minipigs and 7% German Landrace.

The resultant and desired small “large animal” model; the Göttingen Minipig is a dwarf breed, characterized by “proportional dwarfism”; all body parts are reduced in size, but the proportions, e.g. relative bone lengths, are comparable to normal-sized pigs, which is in contrast to the achondroplasia type of dwarfism, which is characterized by severe shortness of proximal limbs, increased spinal curvature, and distortion of skull growth and is generally considered as a genetic defect.

In the first years, the Göttingen Minipig breed was developed under “free range” conditions on an experimental farm in Friedland, Germany, which was characterized by a rather low hygienic standard. Although from the very beginning, the breed development is completely documented and all hard-copy paper-based records are still available, most of the phenotypic records at that time, like litter size, weight etc., are difficult to interpret since they are masked by extreme environmental fluctuations. Also, there was a high frequency of losses and poorly developing animals due to infection pressure under the “free range” conditions.

The Relliehausen facility in Germany
In 1970, the experimental farm in Friedland had to be given up, and a new experimental farm was established in Dassel-Relliehausen northwest of Göttingen, Germany. There, with the financial support of the Volkswagen-Foundation, a new minipig housing facility was built which was for the first time suited to keep the population on a reasonable hygienic level in an indoor facility. The facility was stocked by means of caesarian sections done by Prof. Diedrich Smidt with technical support of the commercial pig breeding company Schaumann-Hülseberg.

In the new facility, a closed population with 50 sows was maintained under specific pathogen free (SPF) conditions, composed of nine white and eight colored lines. A line was defined by the paternal strain, i.e. animals of one line had the same sire, grandsire etc., while the maternal origin rotated within the white and colored lines, respectively. This is a well-known pragmatic design to minimize genetic drift in closed populations of small size. Also, the number of matings per animal was limited to keep the family size small.
At that time, animals were sold to various research groups, and in the following decades from 1970 to 1990, Göttingen Minipigs started to become an established and well-known animal model, but still far from the level of standardization and uniformity that is required today.

The establishment at Ellegaard Göttingen Minipigs
The next huge qualitative step in the development of the Göttingen Minipigs was taken in 1992. At that time, Lars Ellegaard from Denmark signaled his interest to set up a high-quality and professional multiplier herd to become the world-exclusive provider of Göttingen Minipigs with a well-defined and high-quality standard regarding population uniformity, health status, recorded breed characteristics etc., than had previously been possible. Based on the interest from Lars Ellegaard, the founder of Ellegaard Göttingen Minipigs, a license agreement between Ellegaard Göttingen Minipigs (EGM) and the University of Göttingen was signed. In accordance with this agreement, EGM built a production facility in Dalmose, Denmark. Caesarian section of 38 pregnant sows imported from the experimental farm in Relliehausen was used to establish the new production facility under full-barrier conditions. From the piglets that were born, 122 breeding sows and 53 breeding boars were used to start the production in Denmark. Once the new production facility in Denmark was implemented and up running, the experimental facility in Relliehausen was emptied, thoroughly cleaned, and restocked with a re-import of breeders from Denmark to obtain the same hygienic standard.

Simultaneous with this genetic bottle neck, it was decided to give up the colored lines and exclusively produce white animals. This was to some extent due to the fact that the colored lines were slightly more variable than the white lines, but primarily the market preferred white animals, especially for dermal studies. Also, the white color is a special and unique feature of the Göttingen Minipig among all commercially available minipig breeds.

Global expansion
The high demand for Göttingen Minipigs led to an increase of the production capacity with the addition of a second production facility at Ellegaard Göttingen Minipigs in Denmark, which was built in 1998 and later increased in capacity in 2004. Seeing a more global demand for Göttingen Minipigs, EGM subcontracted in 2002 the production and sale of Göttingen Minipigs in North America to Marshall Farms, later Marshall BioResources, in the US, who, with the initial support from Jens Ellegaard, the son of Lars Ellegaard, opened their first Göttingen Minipigs production facility in August 2003. In the year 2009, a third production facility was opened at EGM in Denmark, followed by the closure of the first smaller production facility at EGM.

In late 2010 EGM subcontracted the production and sale of Göttingen Minipigs in Japan, and later Taiwan too, to Oriental Yeast Co. in Japan, that successfully initiated the sale of Göttingen Minipigs in 2013 to the growing Japanese market. Recently, in 2014, EGM signed a distribution agreement with Woojung BSC, later WoojungBio, in South Korea to facilitate, distribute and secure access to Göttingen Minipigs in South Korea.

Genetic management
For hygienic reasons and the potential risk of cross-contamination, all subpopulations are kept completely isolated after the separation. There is no genetic flow between populations, neither through the exchange of animals nor through biotechnological means such as the use of artificial insemination or embryo transfer. The maintenance of separated subpopulations in three countries on three continents is considered as a safeguard against the complete loss of the minipig populations as a consequence of a disease outbreak and/or veterinary interventions. The genetic management of the entire breeding population of the Göttingen Minipig is uniformly provided by the Animal Breeding and Genetics Group at the Georg-August University Göttingen, since 2001 under the responsibility of Prof. H. Simianer.

In general, the genetic management of the Göttingen Minipig population has the objectives to maintain the genetic integrity of the population by avoiding, as far as possible, inbreeding and genetic drift, to maintain the genetic uniformity of the subpopulations, to balance adverse effects of inbreeding, e.g. reduced fertility, increased susceptibility to diseases, monitoring and selection against genetic defects, and to pursue desired breeding objectives, like smaller size and smoother temperament.

It is not a trivial problem to achieve these objectives simultaneously, since some of these objectives are antagonistic. However, up-to-date breeding methodology provides tools to pursue this much more efficiently than it was possible in the past. The
genetic management has since the creation of the Göttingen Minipigs, and apart from the small size and white color, being one of the desired strengths of the breed.

**Summary**
Today, Göttingen Minipigs are available almost all over the world. The successful collaboration with Georg-August Universität Göttingen, Germany has ensured both a globally standardized genetic- and phenotypic uniformity, and the collaboration with Marshall BioResources in the US, Oriental Yeast Co. in Japan and WoojungBio in South Korea and the recent expansion of Ellegaard Göttingen Minipigs activities into both China and India have ensured that high-quality, well-defined Göttingen Minipigs now are available and can be used for biomedical research on a global scale.

**Acknowledgements**
My sincere acknowledgement to Prof. Henner Simianer, Georg-August Universität Göttingen, Germany for providing information in relation to the historical development of the Göttingen Minipigs, as major parts of the first sections of this paper are cited from the paper “Genetic management of the Göttingen Minipig population” by Henner Simianer and Friederike Kohn, which was published in the Journal of Pharmacological and Toxicological Methods in 2010. Furthermore, I am thankful to Prof. Henner Simianer for his ongoing support in maintaining the global genetic uniformity of the Göttingen Minipigs.
The translation potential of porcine biomedical models from an immunological perspective

François Meurens & Nicolas Bertho, BIOEPAR, INRA, Oniris, Université Bretagne Loire, Nantes, France


Introduction

Many characteristics make the pig a very interesting biomedical animal model (see table). In this short communication we specifically focus on the translation potential of the porcine biomedical model from an immunological perspective.

Pig model, pros & cons

- Similar size to humans
- Omnivorous like humans
- Large litter size (24-36 animals/year)
- Relatively short gestation (115 days)
- Short generation interval (12 months)
- All season breeding species
- Placenta does not allow the transfer of passive immunity during pregnancy which is an advantage for developmental immunology
- Lifespan allowing the study of degenerative diseases and vaccine development in elders
- Various surgical procedures can be performed and many samples can be collected serially
- High genome and protein sequence homologies with humans
- Cheaper and ethically more acceptable than primates
- Availability of outbred animals and various breeds
- Closely resemble humans for >80% of immune parameters analyzed (versus <10% for mice)
- Breeding conditions are very standardized
- IL8 has been identified in pigs, not in mice
- Pigs have economic value for themselves
- Species particularities can also be seen as advantages and used to answer specific immune questions
- Several zoonotic diseases are naturally present in pigs (influenza, Nipah, hepatitis E)
- Required bigger and more expensive facilities than mouse
- More expensive than mice
- Less tools than mice
- Genome still not fully annotated
- Less close to humans than monkeys
- Ethically less accepted than mice
- Still limited access to inbred animals for basic research
- Pig research community smaller than its mouse counterpart
- Also clear differences with humans in terms of anatomy, immunology, and physiology (double positive T cells, no alpha-defensin, and large proportions of γδ T cells for instance)

Why the pig?

Rodents, primarily the mouse, and non-human primates (NHPs) have been the most used and the most relevant animal models for decades. Mice are very easy to handle and cheap. Moreover, several inbreed strains allowing cell transfer from one animal to another are available and an enormous choice of transgenic strains, associated with an extensive toolbox make mice the indispensable as well as the most frequently used animal model in biomedical research. While these advantages are useful, anatomical, physiological, and immunological differences between humans and mice may require preclinical studies using other animal models. Because of these limitations of the mouse model, most vaccine candidates are assessed in a second, biologically more relevant animal model before entering clinical phases. Regarding NHPs, their evolutionary proximity to humans enables the collect of biological data highly relevant. The downside is that the use of NHPs is controversial due to their high ethical burden. Experimentation in NHPs is heavily regulated, very expensive, and the availability of NHPs becomes a pressing concern. These limitations of rodent and NHP experimental models has led to an increasing demand for alternative, accessible, affordable, and biologically relevant animal models. Surprisingly and despite a more distant evolutionary separation, the pig presents many convergent similarities with humans regarding their size, anatomy, genetic, immunology, and physiology. For instance, pigs are omnivorous animals, with low hairiness, and thanks to their long standing cohabitation with human being, they are susceptible to a range of pathogens shared with men. There are also widely available, have manageable size and a behavior that allows smooth handling and quite easy experimental interventions. Moreover, pigs are still accepted as experimental animals by the general public, which is not the case for animals such as cats, dogs, and NHPs.

How similar to the human immune system is the porcine immune system?

Lymphoid tissue organization and other anatomical considerations

Overall, the porcine immune organs such as the thymus, the spleen, and the tonsils are organized similarly to other mammalian species and present the same essential functions, although pigs harbour palate and lingual tonsils in close contact with the oral cavity. However, some differences have been identified. For instance, in pigs, lymph nodes are histologically unique. Indeed, in mouse and human, free antigens and dendritic cells (DCs) migrating from the peripheral tissues enter the lymph node (LN) through the afferent lymphatic vessels into the
external capsular sinus. Naïve lymphocytes enter the LN from the blood through the high endothelial venules (HEV). Upon activation, T and B lymphocytes mature and exit the LN through the medullary sinus and the efferent lymphatic vessel. Thus, mice and humans, possess LN with a centripetal lymphatic motion. In pig, lymph presents a centrifuged motion. The afferent lymphatic vessels enter the capsule at one site and penetrate deep into the area occupied by the B follicles (see figure, Bordet, submitted) and the T cells. Then, they filter into the subcapsular sinus from which efferent vessels originate. Moreover, in pig, activated lymphocytes exit directly in the blood through the same HEV they entered. Thus, efferent lymph is composed of lymphatic fluid devoid of immune cells. So far, this inverted LN structure has never been linked to any response peculiarity of the porcine immune system.

Also with an important impact on the pig immune system is the porcine epitheliochorial placentation. This type of placentation does not allow transplacental transfer of antibodies or larger molecules during gestation. Consequently, newborn piglets rely on passively transferred immunity via colostrum and milk.

**Innate immune system**

For the most part, all the immune cell populations and the immune mediators identified in humans and mice are present in pigs. Invariant NK T (iNKT) cells are present in pigs, with a very similar phenotype and functions as in human and mice, although, conversely to human and mouse porcine iNKT cells do not contain cluster of differentiation 4+ (CD4+) population. Interestingly, iNKT cells can be mobilized in order to ameliorate vaccine response, and the porcine model is indeed used for testing new anti-influenza vaccines harnessing the iNKT cells.

Pig is also a γδ T cells high species, presenting large amount of γδ T cells in the peripheral blood, a feature usually associated to young animals.

We observed that porcine neutrophils release neutrophil serine protease that get associated with neutrophil extracellular traps, similarly to human. It is known that mouse macrophages respond preferentially to lipopolysaccharide (LPS) by an arginine metabolism upregulation leading to nitric oxide (NO) production. By contrast, human and porcine macrophages seem to be less prone at responding to LPS by producing NO, but would instead preferentially metabolize tryptophan via indoleamine-pyrrole 2,3-dioxygenase.

Mice and humans who belong to the Laurasiatheria superorder, mainly clear blood borne particles by their liver macrophages known as Kupfer cells. Conversely, pigs, sheep, goat, and bovines, from the Euarchontoglires superorder, clear blood borne particles mostly through lung associated macrophages bounded to the lung endothelial wall named pulmonary intravascular macrophages (PIMs). We recently phenotyped these cells using modern tools and observed that PIMs were very similar to alveolar macrophages. It is worth to highlight here that the presence of PIMs in porcine lungs might be responsible for their high sensitivity to endotoxin-induced acute lung injury and to blood particles induced lung hypertension. Interestingly, induced PIMs have been described in rats and humans in the case of liver injury, thus pigs might be a good model of medical conditions related to liver injuries.

Interspecies transcriptomic comparisons of DCs from blood and skin demonstrated that in pig as in mouse and human, different DC populations could be defined that belong to the mouse-defined conventional DC1 (cDC1), cDC2, monocyte-derived DC (moDC), plasmacytoid DC (pDC), monocyte-derived...
macrophages (moMΦ), and Langerhans cells (21). These DC populations have been first defined in mouse for their differential response to pathogens as well as for their different capacities in activating immune responses (22). Interestingly, porcine cDC2 appear closer to human than to mouse cDC2 in skin (20), blood (19), and lung (23) for their expression, as human cDC2, of Langerin and of the IgE receptor FcεRIα. Moreover, in human and swine lung, cDC2 are localized in a subepithelial localization similar to the human cDC2 (23). In mouse cDC1 expressed Langerin and are in a subepithelial location, whereas inflammatory moDC expressed FcεRIα. Thus, porcine cDC2 expression of FcεRIα and subepithelial positioning are in agreement with pig being a better respiratory allergic model than mouse. In swine pDC, it has been observed a high expression of CD36 and CLEC12A, which are more broadly expressed in human DC subsets and macrophages. Moreover, in pig, pDC are the only subset expressing complement-related genes (C2, C3, C5, and CD93), whereas these are expressed in several human DC subsets. This would suggest a more prominent role of the porcine pDCs in complement biology compared with other species (19).

Interestingly, mouse TLR sequences have strongly diverged from human and swine (24), which lead to important functional differences, such as the TLR8 response difference between mouse and man (25). Indeed, mice use TLR7 to detect single strand RNA, whereas human and swine use TLR8. Again for the sake of vaccination, it has been shown that in human and swine TLR8 act as a ‘vitapamp’ that discriminate life from dead pathogen and give to attenuated vaccines their powerful capacity to trigger the differentiation of follicular helper T cells (Tfh) and of high affinity neutralizing antibodies (25,26). However, the different TLR expressions are restricted to various cell types according to the species, what can potentially lead to important differences in response to pathogens. For instance, it has been shown that in porcine blood, conversely to mouse and man, the expression of TLR7 and TLR9 are less stringently restricted to pDC and can be found on cDC1, whereas TRM3 is mostly expressed on pDC in pig but on cDC1 in mouse and man (19).

Adaptive immune system

As far as the T helper responses have been studied, it seems that Th1, Th2, Th17, and Treg responses are very similar in swine, mouse, and human (25,27). However, two exceptions can be highlighted: i) Memory and activated CD4 T cells express the homodimer CD8αα (28); ii) In pig, conversely to human and mouse, IL4 is not essential in B cell development and Th2 responses (29). Indeed, IL13 appears more consistently expressed during a Th2 response while IL4 remain undetectable (17,23). Thus, in pig, as in mouse and human, Th1 response can be characterized by IFNγ secretion and Tbet expression, Th2 by IL13 secretion and GATA3 expression, Th17 by IL17 secretion and RORyT expression, and Treg cells by Foxp3 expression. Most of the cytokines and more generally most of the proteins of the immune system share structural and functional similarities with their human counterparts.

Conventional DC1, cDC2, and moDC capacities to activate and orientate the differentiation of CD4 and CD8 T lymphocytes are similar to humans and mice as observed using skin (20) and lung (17,23) DC allogeneic stimulations. Namely, cDC1 are better to activate CD8 T cells and to induce Th1 responses whereas according to tissue and stimulus cDC2 and moDC better induce Th2 and/or Th17 responses. Although even in mouse and human these capacities are variable according to the tissue of origin of the DC and the pathogen studied.

Finally, although porcine B cell lymphogenesis have been thought for long to take place outside of the bone marrow, it has been proven since that it indeed takes place in the bone marrow as it is the case in all other mammalian species and following the classical proB, preB, immature, and naive B cell stages (30,31). Moreover, in a submitted paper (Bordet, submitted) we observed that the affinity maturation steps taking place in the lymph node B cell follicles recapitulate all the steps described in mouse and man B cell follicular maturation.

The porcine toolbox

Major developments took place in the porcine biomedical toolbox during the past ten years leading to significant improvements in the use of this model (for most of the references see 32). In 2012 the reference genome sequence of pigs was first published in Nature (32). More recently the genome sequence of several porcine breeds has been made available inclusive the Gottingen minipig (33). Annotations of the porcine genome is continuously growing and with the establishment of the "DQIL Porcine Translational Research Database" in 2017, researchers got a powerful searchable database at hand. In 2013, Tan et al. used CRISPR/Cas9 to manipulate the genome of livestock species inclusive pigs and in 2017 a CD163 knockout pig was generated, fully resistant to porcine respiratory and reproductive syndrome virus. The manipulation of porcine genome could even further improve the biological relevance of the pig model for studying various biological questions. With the increased annotation coverage of the porcine genome, more immune targets became available for transcriptomic analysis (34). Moreover, multiplexed cytokine and chemokine protein analysis was developed and became commercially available (for more references see 35). In the last years the establishment of polychromatic flow cytometry (pFCM) enabled a better and more detailed understanding of the phenotype, maturation and differentiation of porcine innate immune cells, B cells, NK-cells, and T-cells. Regarding porcine CD8 to identify the different cell populations, a comprehensive review has been published very recently (36). Then, the recent developments in next-generation MHC(SLA)-typing, neural network-based prediction of SLA-binding peptides, and recombinant expression of SLA class 1 molecules for peptide-specific staining of reactive CD8+ T-cells using tetramers, allows for detailed studies of cell-mediated immune response against various stimuli in pig models. The porcine toolbox should further improve in the next years bringing exciting new possibilities.

Conclusion

There are no doubts pigs are not going to replace mice for basic research and to establish all the new proofs of concept in the next years. However, for toxicological studies, preclinical research and all the other aspects of research directly asking for a high predictive validity they can be extremely useful and with the recent developments in porcine immunology taking advantages of all the newly developed tools it will certainly continue.
References


Invitation to join

THE 13TH MINIPIG RESEARCH FORUM
22-24 MAY 2019 IN VIENNA, AUSTRIA

Read the full scientific program with speakers on next page
The program also features poster presentations and time for networking with minipig users from all around the world. We accept posters with technical (e.g. tips & tricks) and/or scientific (including data) content. View the poster guidelines at www.minipigresearchforum.org and send your poster as pdf to contact@minipigresearchforum.org.

REGISTER BEFORE 1 MAY 2019: FEE € 350 (Later registration fee: € 400)
The registration fee covers welcome lecture, five scientific sessions, one workshop of choice, get-together evening with food, drinks & networking (Wednesday at the venue hotel, 18:30-21:30 hrs.), social event with dinner & networking (Thursday evening), lunches, coffee breaks and conference material.

DURATION, VENUE & ACCOMODATION
Duration: From 22 May 2019 at 14:00 hrs. CEST (registration desk opens at 13:00 hrs.) to 24 May 2019 at 13:00 hrs. CEST.
Venue: Novotel Wien Hauptbahnhof (15 min. from Vienna Airport by direct train)
Accommodation is also available at Ibis Wien Hauptbahnhof (situated next to the venue hotel).
Log-in to the member section of our website to get the hotel booking form for rooms at special conference rates at Novotel or Ibis and book your room before 10 April 2019.
Not a member? Apply for free membership at www.minipigresearchforum.org.
WE LOOK FORWARD TO SEEING YOU IN VIENNA!
The Minipig Research Forum Steering Committee

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

MAIN SCIENTIFIC TOPICS:
- Toxicology
- Animal training & welfare
- Better understanding of the Göttingen Minipig
- Transgenic models
- Immune system

WORKSHOPS:
- Species selection in regulatory toxicology
- Designing regulatory toxicology studies
- Identifying disease model gaps

Feedback from participants 2018:
“Appreciated the diversity of topics and numerous opportunities to network”
“My first MRF: Impressed how friendly and inclusive all members were”
The conference program consists of the following scientific sessions and topics:

**WELCOME LECTURE**

Porcine models of obesity, diabetes and diabetes complications - applications and gaps

*Berit Østergaard Christoffersen, Novo Nordisk, Denmark*

**SESSION 1: TOXICOLOGY**

Spontaneous & drug-induced arteritis in Göttingen Minipigs: comparison to other species and human relevance

*Zuhal Dincer, Covance, United Kingdom*

Transfer of drugs via placenta and milk

*Susi Søgaard, Citoxlab, Denmark*

In vitro determination of GI toxicity using a 3D organoid model

*Farzin Pourfarzad, Hubrecht Organoid Technology, The Netherlands & Joanna Harding, AstraZeneca, United Kingdom*

The Minipig for ophthalmologic applications

*Björn Jacobsen, Roche, Switzerland*

**SESSION 2: TRANSGENIC MODELS**

Genetically modified pigs as donors for xenotransplantation

*Nicolai Klymiuk, Ludwig Maximilian University of Munich, Germany*

Growth hormone receptor deficient pigs – a model for Laron Syndrome

*Arne Hinrichs, Ludwig Maximilian University of Munich, Germany*

Engineered Göttingen Minipigs displaying a highly penetrant psoriasis-like skin disease

*Nicklas Heine Staunstrup, Aarhus University Hospital, Denmark*

New opportunities for genetically engineered Göttingen Minipigs as translational models of preclinical efficacy

*John Stuart, Exemplar Genetics, USA*

**SESSION 3: ANIMAL TRAINING & WELFARE**

Creating a stimulating and cooperative environment for Göttingen Minipigs

*Kirsten Rosenmay Jacobsen, Ellegaard Göttingen Minipigs, Denmark*

Thinking out of the box – stable design considerations in Novo Nordisk and AstraZeneca pig research

*Lotte Martoft, AstraZeneca, Sweden & Stine Øvlisen, Novo Nordisk, Denmark*

Clicker training and positive reinforcement – less stress, better welfare and timely results

*Novo Nordisk and Lundbeck, Denmark (speaker names to be confirmed)*

Development of an intravesicular dosing technique in Minipigs

*Sarah De Landtsheer, Janssen, Belgium*

**SESSION 4: BETTER UNDERSTANDING OF THE GÖTTINGEN MINIPIG**

A Göttingen Minipig is a Göttingen Minipig is a Göttingen Minipig ...

*Henner Simianer, University of Göttingen, Germany*

How genetic management ensures the integrity of the breed

*Miriam Ayuso, University of Antwerp, Belgium*

Construction and activity of recombinant CYP enzymes of the Göttingen Minipig: challenges and pitfalls

*Dennis Tideman Arp, Aalborg University Hospital, Denmark*

The Göttingen Minipig imaging ATLAS

*Steven Van Cruchten, University of Antwerp, Belgium*

Drug metabolism in the Göttingen Minipig: translation to man

*Joachim Denner, Robert Koch Institute, Germany*

**SESSION 5: IMMUNE SYSTEM**

Porcine immune cells – phenotypes and functions (double slot)

*Armin Saalmüller, University of Veterinary Medicine Vienna, Austria*

Virus safety of xenotransplantation and Göttingen Minipigs

*Constanca Figueiredo, Hannover Medical School, Germany*

Minipig transplantation model – ex vivo genetic organ modifications and immunomonitoring

*Joachim Denner, Robert Koch Institute, Germany*

**WORKSHOPS**

Species selection in regulatory toxicology

Designing regulatory toxicology studies

Identifying disease model gaps

Please select one workshop of choice when registering for the MRF conference and feel free to add input for the workshop chairs to plan the best possible content for your preferred workshop. Note that your selection is not binding. You will not have to make a final selection of workshop until the first day of the MRF.

Follow MRF on LinkedIn

The Minipig Research Forum group on LinkedIn is an informative and useful platform where minipig users connect and interact, ask questions and share experiences. Apply for the MRF LinkedIn group membership at www.linkedin.com/groups/4219925
Background and objectives

The stress response is a normal part of daily life. Peripheral expression of the stress response is modulated via two systems, the sympatho-adreno-medullary (SAM) axis and the hypothalamic-pituitary-adrenal (HPA) axis.

The SAM axis mediates an initial, rapid response to an immediate stressor. The hypothalamus sends direct signals via the sympathetic nervous system to the adrenal glands, causing them to release catecholamines including epinephrine (adrenaline). Epinephrine leads to an urgent action by stimulating faster breathing and heart rate. The adrenal medulla also secretes another catecholamine, norepinephrine, which works with epinephrine to stimulate liver cells to release glucose to make more fuel available for cellular respiration. Manifestations of SAM axis activation include mydriasis, increased heart rate, increased blood pressure, cutaneous vasoconstriction, an alert state, and increased plasma glucose and free fatty acid concentrations.

A slower response to a stressor, with effects in minutes to hours or days, is mediated by activation of the HPA axis leading to the release of glucocorticoids (GCs) from the adrenal cortex. This endocrine portion of the mammalian stress response originates in the hypothalamus, with release of corticotropin releasing hormone and arginine vasopressin. These hormones in turn stimulate the release of adrenocorticotropic hormone from the pituitary gland, resulting in the production and release of GCs from the adrenal glands. Glucocorticoids influence a large number of metabolic processes, including protein, glucose, and fatty acid metabolism, and immune function, and can induce a catabolic state, while corticotropin releasing hormone suppresses gastro-intestinal motility and arginine vasopressin regulates the glomerular filtration rate (GFR), cAMP generation, and fluid balance. Acting jointly, these hormones can also influence growth, thyroid function, and reproduction.

During certain scientific procedures, it is necessary to sedate or anaesthetize animals, including minipigs. A variety of anaesthetic agents are available to researchers depending on the depth and duration of anaesthesia that may be required. In cases where one of the purposes of the experiment is to measure biomarkers of stress, then it is useful to understand the effects of the anaesthesia procedures themselves on the different markers.

We have performed an initial study where we determined the plasma levels of adrenaline in minipigs before and during, zolletil, propofol and isoflurane anaesthesia and recovery from the anaesthesia.

Procedures

Two male Göttingen Minipigs (9-10 months old) were used in the study. Central Venous Catheters (CVC) and ear vein catheters were implanted prior to the start of the experiment and were used both for intravenous injection of anaesthetics and for withdrawal of blood samples.

For the actual experiments, the animals were anaesthetised sequentially with at least 120 min between occasions.

Phase I – isoflurane anaesthesia

For the first phase, the anaesthetic agent, propofol, was given intravenously in the ear vein catheter until effect (absence of corneal reflexes and good muscle relaxation, typically 2-2.5 mg/kg, 10 mg/mL, i.e. 0.2-0.25 mL/kg supervised by a veterinarian). Immediately after effect had been obtained, the pig was intubated and maintained in anaesthesia using isoflurane anaesthesia 2%. Time 0 was identified as 20 minutes after administration of isoflurane. The anaesthesia was terminated after the last blood sampling at 150 minutes and the animal was continued on pure O₂ as appropriate before removal of tracheal tube. During anaesthesia Lactated Ringer’s Solution was administered intravenously.

Phase II – propofol anaesthesia

For the second phase, the anaesthetic agent, propofol, was given intravenously as a bolus injection in the ear vein catheter until effect (absence of corneal reflexes and good muscle relaxation, typically 2-2.5 mg/kg, 10 mg/mL, i.e. 0.2-0.25 mL/kg supervised by a veterinarian). Time 0 was defined as end of injection of propofol.
**Phase III – zoletil anaesthesia**

For the third phase the anaesthetic agent, zoletil mixture was used. An intramuscular injection in the neck (1.0 mL/15 kg body weight) of a mixture of Zoletil 50®Vet., Virbac, France (125 mg tiletamine and 125 mg zolazepam), 20 mg xylazine/mL (6.25 mL), 100 mg ketamine/mL (1.25 mL) and 10 mg butorphanol/mL (2.5 mL) was given. Time 0 was defined as 20 minutes following injection.

Periodically before, during and after the anaesthesia, blood samples at 15 time points over 150 minutes, were taken in Li-heparin vacuette sampling tubes, and centrifuged immediately (4°C, 2500g, 10 min). Within 2 minutes from centrifugation, a plasma aliquot was transferred into an L-cysteine containing tube (for stabilisation of adrenaline level), split in two and frozen on dry ice.

An explorative analytical method for determination of adrenaline in plasma was used for the analysis. Solid phase extraction (weak cation mixed mode) was used as sample preparation before elution by methanol with 5% formic acid. The samples were injected onto a Q-Exactive coupled with an Ultimate 3000 BIORIS UHPLC (Thermo Scientific) using a AERIS Widepore XB-C8 column (250x2.1mm, 3.6µm Phenomenex) with a mobile phase gradient of water with 0.1% Formic acid and 80% acetonitrile with 0.1% formic acid.

**Results**

As expected, there was some individual variation in the found values, and so the plasma results summarized in Table 1 show the average determined level for each anaesthesia phase and indicate differences in endogenous adrenaline levels found depending on anaesthesia procedure applied.

<table>
<thead>
<tr>
<th>Animal</th>
<th>Isoflurane</th>
<th>Propofol</th>
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<tbody>
<tr>
<td>#1</td>
<td>992</td>
<td>5632</td>
<td>1259</td>
</tr>
<tr>
<td>#2</td>
<td>608</td>
<td>1418</td>
<td>1112</td>
</tr>
<tr>
<td>average</td>
<td>821</td>
<td>3603</td>
<td>1200</td>
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</table>

Table 1: Average plasma concentrations of adrenaline (pg/mL)

**Discussion and conclusion**

Adrenaline levels were measured over time in association with 3 different methods of anaesthesia in Minipigs. Individual variations in the measured levels of adrenaline were present. The lowest levels were seen after anaesthesia with Isoflurane, the anaesthesia with the longest period of unconsciousness. Direct comparison of means during the whole blood sampling does however not define the stress level of the animals as the period of unconsciousness must be taken into consideration as this varies between the methods (few minutes for propofol, approximately 20 minutes for zoletil and 150 minutes for isoflurane) in this study.

Clearly, we cannot conclusively say on the basis of a single biomarker that one form of anaesthesia is clearly superior to others, therefore we have plans to analyze for further parameters including Cortisol, Glucose, T3, T4 and CRP. In this way we will get a better overview of the effects of the different methods. Regardless of the outcome of our investigations, we are aware that each anaesthesia method has its own advantages and disadvantages dependent on the procedure being performed, but we can already see that if certain stress biomarkers need to be followed, then the method of anaesthesia used does need to be taken into consideration when concluding on the results of a study.
Enrichment in Göttingen Minipigs: Experience at Charles River - Safety Assessment, Lyon, France

Baptiste THOREAU, Karim RIADHI, Kévin GILBERT, Laetitia HERNANDEZ and Severine BIGUEUR, Large Animal Facility, Charles River Safety Assessment, Lyon, France

Context and objectives
Our Göttingen Minipigs are housed on bedding (Litalabo S8-15, spruce sawdust; approximately 150 g per box, dispensed daily). They have, at disposal, in each box, a rest board, a basket and a metal chain to nibble. Music (from radio, ≤ à 85 dBA) is played during the day at the same time as the neon lights are on, i.e. from 6:00 am to 6:00 pm.

The food ration (SMP (E) SQC, SDS) is split in two: first distribution of 150 g early morning and second distribution at least 4 hours later. A food reward (one eighth of an apple) is also given after daily washing of the box.

These observations were compared with those made in Minipigs under the current housing conditions.

Any type of enrichment was considered to have a positive impact on Minipig behavior when the cumulative daily interaction time was 30 minutes or longer.

Tests and outcomes
1. New bedding and box cleaning process
We looked for a bedding with a high absorption capacity, in order: 1) to remove only the grossly soiled bedding every day and put back clean bedding (if deemed necessary) and 2) to replace the whole bedding and to water-wash boxes with water once a week only (with fresh bedding deposit once the box is dry). This bedding should also not prevent clinical observations such as liquid feces, diarrheic episodes.

Hypoallergenic and dusted, long strands of wheat straw, were tested. The first trials on two animals were rather conclusive in terms of absorption capacities. However, straw material passed in gutters and clogged pipes. Boxes were re-arranged (set up in the bottom of box full plate) to try and avoid these issues and straw was again tested in two groups of three females. Straw was found dirty almost every day. All the straw was changed every day.

One of our suppliers proposed to test a poplar chips bedding (CP 50, ANIBED). Approximately 3 kg per box was initially de-

Materials and methods
Global design
The tests were carried out on 2 to 6 animals, aged between 5 to 9 months and weighing between 10 and 25 kg. Enrichment - except new bedding - was tested daily for at least 2 days. Housing rooms were equipped with cameras (infrared, WIFI) for offline analysis of video recordings (Europ-Camera).

Animals were checked daily for clinical signs (with special focus on occurrence of traumas/injuries) and behavior/activity quantified by rest periods, number of interactions (with enrichments), duration of interaction, etc…
posited in the box of two groups of three females each (same as that tested with straw bedding), at the beginning of the week and a weekly consumption of approximately 5 kg per box was calculated. The watering pipettes have been moved towards the gutters at the back of the box to avoid wetting the bedding. This bedding and water distribution arrangement fully met our expectations.

II. Structural enrichment:
We tested an anti-bite ball/bullet. This system is used in farm pigs, to avoid tail and ear biting, and other behavioral and aggression problems. Interactions with this system were very variable and inconsistent. Moreover, this system was difficult to firmly attach to our boxes and putting it on the floor did not trigger any special interest.

Regalaxie® (SDS) is a sturdy toy that can be filled with treats or food and is usable for several laboratory species, including Minipigs (detailed in the food enrichment section; see below). When placed on the floor, the animals played with the toy in the box, and continued to do so even when it was empty. Minipigs frequently interacted with this toy during the day. When decision was taken to remove this toy, it was always found empty.

III. Food enrichment:
Different types of dehydrated treats (Palimex) were tested by placing them on the floor to encourage natural rooting behavior in Minipigs. These were (as daily ration per animal): sunflower seeds (20 g), raisins (50 g), pineapple cubes (30 g), vegetable chips (50 g), cranberries (50 g), strawberries (30 g) and peaches (50 g); sliced fresh cucumber (100 g) was also tested.

All these food enrichments stimulated Minipigs: rooting behavior was frequently observed during the day, in contrast to poor/absent rooting activity observed with our current housing conditions.

Nibbling food blocks with red fruit taste (Plexx, 44 mm (diameter) x 22 mm (height); 1/animal) were also proposed. Due to their hard consistency, they were fixed to encourage Minipigs’ curiosity.

Ice blocks made up with about one liter of water mixed with food, hay, apple compote or fruit juice were made available by tying them to door of the box with a metal chain. Of all the varieties proposed, the most frequent interactions were observed with block made of apple compote and fruit juice. We installed a rack on the animal’s box door containing hay and dehydrated apples (30 g per animal per day) to stimulate Minipigs to forage:

This enrichment was tested on Saturday and Sunday. It was installed on Saturday morning. The next morning the rack was empty, no dehydrated apples or hay. Sunday morning, the rack was filled again with hay and dehydrated apples.

It is not possible for us to propose this rack for all our studies (not for dermal and infusion studies) because the animals could scratch against it (erythema, remove the jacket, stretch the catheter).
Conclusion
Based on our past and recent experience described in this article:
- The dog basket, metal chain and usual treat (1/8th of an apple) are kept.
- The poplar chips-based bedding (CP 50 litter, ANIBED) is now selected for bedding.
- Enrichments for which the cumulative interaction time was greater than 30 minutes are selected, namely treats (sunflower seeds, raisins, vegetable chips, pineapple cube and cranberries), either distributed on the floor (and encouraging rooting) or fit into Regalaxie®, toys as well as fresh vegetables (cucumber). We designed a program in order to ensure daily rotation of enrichments:

This program will be set up for all our Minipig studies, starting Q2-2019.

For Q4-2019 or 2020, we are planning to further develop this program.

Our experience shows that animal welfare requires careful planning and evaluation of changes in housing conditions (including enrichment) in order to ensure that our safety assessment studies are conducted in animals whose natural behaviors are respected.
The First Göttingen Minipigs Ambassadors

During our year of jubilee celebrating the first 50 Years of Göttingen Minipigs, we will have the honour and pleasure of appointing a number of Göttingen Minipigs Ambassadors! We hereby proudly announce the first two Göttingen Minipigs Ambassadors who received the Certificate of Recognition for their high-level international knowledge dissemination and promotion of Göttingen Minipigs use in biomedical research from CEO Lars Friis Mikkelsen.

**Henner Simianer.** Professor of Animal Breeding and Genetics, University of Göttingen, further recognized for his extensive genetic quantification and breeding program development.

**Andy Makin.** Scientific Director and Director of Business Development & Sales at Citoxlab Denmark; further recognized for his characterization, validation and development of Göttingen Minipigs disease models.

![Dr. Henner Simianer Göttingen, Germany](image)

![Andy Makin Copenhagen, Denmark](image)

**Congratulations to both Ambassadors!**

Ellegaard Göttingen Minipigs Webinars

We invest many resources in the development and accumulation of new knowledge about Göttingen Minipigs as well as in networking with scientists all over the world working with the animal model. In support of this, we now initiate hosting scientific webinars featuring speakers with interesting research to share. We plan to broadcast two webinars each of 30-60 minutes’ duration in the spring/early summer and another two in the autumn/early winter each year. The first two webinars are:

**Wednesday 10 April at 16:00 CET**

**Background pathology in Göttingen Minipigs** by Sean McKeag from Covance, UK

**Thursday 13 June at 16:00 CET**

**Minipigs in human relevant safety assessment - learnings from Roche (Safety Pharmacology and Toxicology/Pathology)** by Susanne Mohr, Andrea Greiter-Wilke and Björn Jacobsen from Roche, Switzerland

Mark your calendar and learn more as well as sign up for the webinars via our LinkedIn company page:

https://www.linkedin.com/company/2864308/
Welcome to new faces and competences

It is with great pleasure that we present our newest team members:

<table>
<thead>
<tr>
<th>Denmark:</th>
<th>Denmark:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kamilla Flemming Hansen</td>
<td>Mette Damgaard Johansen</td>
</tr>
<tr>
<td>Kamilla joined us on 1 January 2019 as Laboratory Technician in our research barrier. She has brought with her 12 years of experience within the pharmaceutical industry working on studies involving lab animals, in particular minipigs, at Novo Nordisk and Citoxlab Denmark. Kamilla is a member of our science team and she looks forward to adding value also to our customers’ and cooperation partners’ projects involving Gottingen Minipigs. In her spare time, Kamilla enjoys horse-riding, especially show jumping competitions, with her own gelding.</td>
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<tr>
<td>Mette joined us on 1 February 2019 as Order Management and Logistics Coordinator. Her working background contains deep knowledge on handling sales orders using efficiency, structure and the ability to stay on top of all details at all times for the benefit of both customers and colleagues. Mette looks forward to handling our order management to the full satisfaction of her stakeholders. When not working, Mette is a true family person who also loves to dance, sing and listen to music.</td>
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<table>
<thead>
<tr>
<th>India:</th>
<th>China:</th>
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<tbody>
<tr>
<td>Deepu Menon</td>
<td>Jin Liu</td>
</tr>
<tr>
<td>Deepu became associated with us as of 1 January 2019 as an External Consultant in India. Deepu has a Masters in Business Management from ESERP Business School, Barcelona, Spain, and is an experienced business development executive who is also associated with the Indian CRO Palamur Biosciences and their subsidiary Isoquimen India, which is the first and only laboratory beagle dog breeding facility in India. Further, he coordinates the operations of SDS Diets in India. Deepu will assist us in marketing our Gottingen Minipigs in India to provide an alternative lab animal species to the Indian CRO and pharmaceutical industry as well as assist our Indian customers and cooperation partners locally. Feel free to contact Deepu Menon directly at <a href="mailto:dme@minipigs.dk">dme@minipigs.dk</a> or mobile +91-9177807779.</td>
<td></td>
</tr>
<tr>
<td>Jin joined us as of 1 March 2019 as our Country Manager in China. Jin’s educational background roots in research within veterinary science, and he holds a Ph.D. in Molecular Veterinary Bioscience. Jin has worked as the CEO of Shanghai Phenotek Biotechnologies since mid-2017, and his past professional career also involved working in the US for several years followed by four years with the Novo Nordisk Research Centre China, during which time he visited Denmark on more occasions. Jin will work on promoting our Gottingen Minipigs on the Chinese market as well as assist our Chinese customers and cooperation partners locally. Feel free to contact Jin Liu directly at <a href="mailto:jli@minipigs.dk">jli@minipigs.dk</a></td>
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</table>
New scientific 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. Please contact us if you have an idea for such a collaborative project. Below is a list of a few recent articles on Göttingen Minipigs.


The Ellegaard Göttingen Minipigs Research Foundation
Call for project proposals 2019

We hereby invite applications for the Ellegaard Göttingen Minipigs Research Foundation with a submission deadline 10 April 2019.

The main objective of the Ellegaard Göttingen Minipigs Research Foundation is to maintain and expand the activities of Ellegaard Göttingen Minipigs A/S by providing funding for scientific research of the highest quality. The Foundation grants in total up to € 50,000 annually to support scientific research that aims to characterize the Göttingen Minipig or to promote the development of Göttingen Minipigs disease models. In addition, projects that intend to improve animal welfare and/or optimize handling or research techniques, as well as educational and communication activities related to the use of minipigs in scientific research, may receive funding. The Ellegaard Göttingen Minipigs Research Foundation’s general criteria for granting research funds are that the scientific content of the application, the qualifications of the applicant(s) and the academic environment of the host institution(s) are at a high international level. The project should generate significant background data and/or ensure knowledge dissemination and promote the use of Göttingen Minipigs in scientific research.

The Foundation has set up a Scientific Committee to ensure uniform assessment of all project applications.

Ellegaard Göttingen Minipigs Management Team will, based on recommendations from the Scientific Committee, allocate grants in accordance with statutory requirements twice a year in May and in December respectively.

Download the project application form at our webpage: https://minipigs.dk/knowledge-base/the-ellegaard-goettingen-minipigs-research-foundation/ and submit your application to Henrik Duelund Pedersen, CSO, Ellegaard Göttingen Minipigs by e-mail to hdp@minipigs.dk no later than 10 April 2019.

Meeting Calendar 2019

<table>
<thead>
<tr>
<th>Name</th>
<th>Date</th>
<th>Location</th>
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<tbody>
<tr>
<td>SOT 2019 &amp; ToxExpo</td>
<td>10-14 March</td>
<td>Baltimore, MA, USA</td>
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<tr>
<td>10th Janssen Juvenile Toxicology Symposium</td>
<td>25-26 April</td>
<td>Beerse, Belgium</td>
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<tr>
<td>50 Years with Göttingen Minipig: Scientific Symposium</td>
<td>7 May</td>
<td>Antwerp, Belgium</td>
</tr>
<tr>
<td>50 Years with Göttingen Minipig: Scientific Symposium</td>
<td>9 May</td>
<td>London, United Kingdom</td>
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<tr>
<td>13th Minipig Research Forum (MRF) 2019</td>
<td>22-24 May</td>
<td>Vienna, Austria</td>
</tr>
<tr>
<td>14th FELASA Congress 2019</td>
<td>10-13 June</td>
<td>Prague, Czech Republic</td>
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<tr>
<td>13th TALAS International Conference</td>
<td>24-28 June</td>
<td>Bangkok, Thailand</td>
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<tr>
<td>EUROTOX 2019</td>
<td>8-11 September</td>
<td>Helsinki, Finland</td>
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<tr>
<td>SPS 2019 Annual Meeting</td>
<td>23-26 September</td>
<td>Barcelona, Spain</td>
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<tr>
<td>CALAS</td>
<td>28-29 September</td>
<td>Kunming, Yunnan, China</td>
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<tr>
<td>50 Years with Göttingen Minipig: Scientific Symposium</td>
<td>Late September/early October (dates to be confirmed)</td>
<td>Shanghai &amp; Beijing, China</td>
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<td>AFSTAL</td>
<td>2-4 October</td>
<td>La Rochelle, France</td>
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<tr>
<td>50 Years with Göttingen Minipig: Scientific Symposium</td>
<td>(date to be confirmed)</td>
<td>Paris, France</td>
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<td>15 October</td>
<td>Basel, Switzerland</td>
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<td>50 Years with Göttingen Minipig: Scientific Symposium</td>
<td>29 October</td>
<td>Lahav Kibbutz, Israel</td>
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<tr>
<td>50 Years with Göttingen Minipig: Scientific Symposium</td>
<td>November (date to be confirmed)</td>
<td>New Jersey, USA</td>
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Join Ellegaard Göttingen Minipigs at LinkedIn to stay updated on our scientific events and other exciting initiatives to celebrate Fifty Years with Göttingen Minipigs

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