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Göttingen Minipigs
MAGAZINE

ELLEGAARD
GÖTTINGEN MINIPIGS

Göttingen Minipigs Magazine | 57 | 2020

Dear reader

After having successfully celebrated 50-years with Göttingen Minipigs throughout 2019, we now look into 2020 and beyond with renewed energy – all based on the amazing support we felt from the almost 1,000 participants at our global roadshows, the many hundred attendees at our webinars and, not least, from all of you on a daily basis along with our engaged team at Ellegaard Göttingen Minipigs.

One new initiative that we will introduce this year is a total makeover of our previous Newsletters, which has been turned into the Göttingen Minipigs Magazine, that you are reading right now. The magazine has a refreshed and more modern layout and new, exciting editorial content, which I hope you will find interesting. In addition, I recommend that you follow us on LinkedIn to stay updated on scientific news, event invitations and relevant information in relation to the use of Göttingen Minipigs in biomedical research.

As usual, we are planning to attend several conferences and scientific meetings in Europe, Asia and the US throughout the year, and I would especially like to highlight the excursion to our Danish breeding facility arranged in connection with EUROTOX 2020 in Copenhagen. If you miss this unique opportunity, you are always welcome to contact us directly for a visit at our site or attend one of our in-house training courses.

Last but not least, I hope to see many of you in Lisbon for the annual 3-day Minipig Research Forum conference in May 2020, which as always offers a great opportunity to network with colleagues from around the world, share experience and gain updated knowledge on using Göttingen Minipigs.

Enjoy the new Göttingen Minipigs Magazine and I hope to see many of you in the coming year.

Lars Friis Mikkelsen, CEO
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Taking on the UN Global Goals for Sustainable Development

In 2015 the UN launched an initiative consisting of 17 Global Goals - an agreement between world leaders on how to create a better world by 2030. The goals embrace topics such as poverty, inequality and the urgency of climate change, and serves as an inspiration for both governments, corporations and private households to contribute to reaching these very ambitious goals.

Reading the global goals it becomes clear, that they aim at high-level political actions. However, there are many initiatives and adjustments both private corporations and households can adopt, by taking it to a level that you can identify with and which complies with your level of influence. “That is exactly what we intend to do”, says Lars Friis Mikkelsen, CEO at Ellegaard Göttingen Minipigs and elaborates: “Everyone needs to be aware of the footprint that they leave and take on the responsibility to make this footprint as light as possible. We all, undeniably, cause an environmental impact, so it is important to give something back to redress the balance.”

It is not an entirely new way of thinking when Ellegaard Göttingen Minipigs wishes to increase their focus on sustainable development, as they can already include geothermal heat, a straw-fired boiler and focus on welfare to the list - to name a few. It is, however, the approach on how to implement another level of sustainability that has been evaluated by turning it into a key goal in the business strategy. “The UN Global Goals have been launched as an internal workshop involving everyone in the company. We have a creative, inventive and dedicated group of employees who likes to be involved and genuinely wants to make a difference. As a company we are lucky to be able to use this at our advantage”, Lars Friis Mikkelsen explains.

Not all goals can be transferred

Out of the 17 global goals Ellegaard Göttingen Minipigs has selected 11 where they believe their efforts can have an impact. “It is vital that everyone contributes to change, but it is equally important to identify areas that are out of your area of influence. If you intend to solve everything, you most likely end up solving nothing. Therefore we have identified the goals where we believe we can contribute the most”, says Maria Bonnesen, Head of Marketing at Ellegaard Göttingen Minipigs. To simplify the process, the company has regrouped the 11 selected global goals, and turned them into 4 internal focus areas: Health and welfare; sustainable consumption and production; climate and biodiversity; action-taking partnerships. Lars Friis Mikkelsen explains: “It is important that we refine our production and cut down on consumption, and likewise keep improving the welfare of our employees and our Göttingen Minipigs. But we have made it a clear priority to not only reduce and improve the status-quo, but also give something back.”

Sustainability on more than one level

The next step is to make a comprehensive brain storming session within each focus area. “All employees have signed up to a focus area of their own choice, and we are very excited to see the outcome. No idea is too big or too small at this step, whether it concerns energy saving renovations or switching to battery-free keyboards”, says Maria Bonnesen. It is important though, that the initiatives support an environmentally, socially or financially sustainable growth strategy. Lars Friis Mikkelsen explains: “Changes for the sake of changing, makes no sense. We need to be able to deliver a statement, that our efforts and investments actually pay off either environmentally, socially or financially.”

Make your own goals

If you are interested in setting up goals for your own company or would like to know what you can do to support the UN Global Goals in your private household, we have collected a few inspirational links.

Many a little makes a mickle.

Official website
https://www.globalgoals.org/

The lazy person’s guide to saving the world
Be inspired by the 4 levels: couch, household, neighbourhood and work place: https://www.un.org/sustainabledevelopment/takeaction/

170 daily actions
https://drive.google.com/file/d/1iMdE6DLLuCqwq3K9U-DaTUWB6KyMa8QG/view

Figure 1
Internal focus areas creating the basis for Ellegaard Göttingen Minipigs’ work on sustainable development.

Health and welfare

Improve health and welfre for both animals and employees.

Sustainable consumption and production

Reduce the environmental impact through sustainable consumption and production.

Climate and biodiversity

Contribute to the environmental surroundings by giving back to the climate and supporting biodiversity.

Action-taking partnerships

Engage in action-taking partnerships to support the other 3 focus areas.

Which Examinations and Tests to Perform in Juvenile Göttingen Minipigs Within the First Weeks of Life?

By Mikkel Lykke Jensen[1]

[1]Charles River Copenhagen, Denmark

Working with and performing studies in minipigs can be challenging and sometimes even difficult, however choosing to use juvenile animals may pose additional challenges that need to be dealt with e.g. housing, feeding, administration of test item and collection of samples.

The ability to perform juvenile studies is becoming increasingly important as studies may be requested as part of regulatory packages investigating pharmaceuticals to be used in infants (1, 2), as well as in studies investigating addition of compounds to e.g. infant milk formula (3). The juvenile minipig may be a suitable model for a number of these studies.

Juvenile studies should be planned carefully to ensure that sows are mated within the same short time interval. Once the first sow begins to farrow, farrowing in the remaining sows can be induced with the use of a prostaglandin analogue to ensure that all piglets are born within 24-48 hours. This allows for cross fostering of piglets and reduce the number of siblings in groups as much as possible.

Göttingen Minipigs usually have access to solid feed from post-natal day 14 and are weaned at an age of approximately 28 days. However, it is possible to wean animals earlier, i.e. at post-natal day 3. As there is no trans-placental transfer of immunity in pigs, immunization via colostrum within the first 24-48 hours following birth is important. To support early weaning, one has to take into account that the supplied milk formula must support growth and health of the animals. Commercially available milk formulas are usually only used as a supplement in combination with sows' milk and may not be suitable as the only source of nutrition. Adult minipigs are generally fed twice daily, however, this will not be sufficient to support adequate growth and health of juvenile minipigs. Observations in a study investigating the suckling in Göttingen Minipigs suggest that piglets will drink 16 to 24 times a day for a very short duration of time, 10-15 seconds (4). Hence, feeding of piglets should preferably be similar, with feedings given at a regular interval throughout the entire day.

Housing of juvenile Göttingen Minipigs can be with either the sow, housing in suitable pens or in cages depending on study type and age of animals. Juvenile minipigs require a room temperature of 28 degree Celsius (5) and additional heat can be supplied via heating lamps. Group housing is preferred as the juvenile minipigs are very social and our experience is that weaning to milk formula is easier when animals are allowed to be group housed (picture 1).

Picture 1
Social housing of juvenile Göttingen Minipigs at Charles River Copenhagen.

Picture 2
Blood sampling of juvenile Göttingen Minipigs.

Picture 3
Eye examination of juvenile Göttingen Minipigs.

Blood samples can be obtained from the juvenile Göttingen Minipigs by puncture of the jugular vein (picture 2) or insertion of a permanent catheter for drawing blood. The amount of blood that can be sampled is limited due to smaller size of the animal. Results from blood sample analysis must be compared to data from animals of a similar age, either control group animals or historical data, as parameters can vary a lot between juvenile and adult animals (6).

As with adult minipigs the juvenile minipigs can be dosed via many different routes. Subcutaneous, oral and intravenous administration are similar to adult pigs although handling of animals is easier. Dermal application of test item is possible also while the juvenile animals are housed with the sow. If long-term dermal application is needed, housing with the sow is preferred to ensure the piglets get sufficient nutrition and to increase animal welfare.

In toxicology studies, procedures such as ophthalmologic examination and electrocardiography (ECG) are included. Ophthalmologic examination is performed using an indirect ophthalmoscope and a portable slit-lamp microscope (picture 3). ECG measurements are performed while animals placed in a sling. Both procedures can be performed within the first weeks of birth. Ophthalmology examinations require that the eyelids fully retract to allow for a thorough examination (7). Unpublished ECG data obtained in 3-week old piglets showed differences in heart rate, QRS and QT interval compared to adult animals (8).

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Göttingen Minipigs in the Era of Next-Generation Sequencing

By Henner Simianer[1,2] and Christian Reimer[1,2]

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From the beginning of the 21st century, a new class of sequencing methods started to revolutionize molecular genetics and animal breeding in an unprecedented way. Rather than conducting sequencing of single DNA fragments with classical techniques such as Sanger-sequencing, these techniques enabled generation of so-called short-reads in a massively parallelized way, representing whole-genomes of individuals. Technologies, such as Illumina's sequencing-by-synthesis or SOLiDs sequencing-by-ligation are nowadays categorized under the term „Next-Generation Sequencing" (NGS). While the initial draft sequence of the human genome (published during 2000 to 2001) took about 15 months to be finished and cost roughly $300 million, availability of newest high-throughput sequencing systems decreased that cost for a mammalian genome sequence to less than $1500.

Today, applications are multifold and range from phylogenetic studies (Reimer et al. 2018a), discovery of candidate genes (Rubin et al. 2012) and genomic selection (Bhat et al. 2016) to immunology (Mori et al. 2013). The advances in sequencing technology also hold great potential for research on Göttingen Minipigs and this article aims at giving a short introduction into basic strategies interested parties should know about.

Re-sequencing data analysis

A common strategy is the generation of short DNA-reads, e.g. few hundreds of base pairs (bp) long, from the individual of interest and to map those reads against an available reference genome. Variation in the respective individual will then be discovered by comparison to the known reference sequence. Because a reference is strictly needed, this is referred to as re-sequencing, while generation of a genome from scratch is called de-novo assembly. Re-sequencing in turn allows to massively reduce the amount of sequence data generated, leading to another reduction in cost, but its obvious limitation lies in the fact that one can only discover variation in genomic regions that are already present in the reference. As a consequence, multiple reference genomes have been generated that are potentially usable to conduct studies in Göttingen Minipigs.

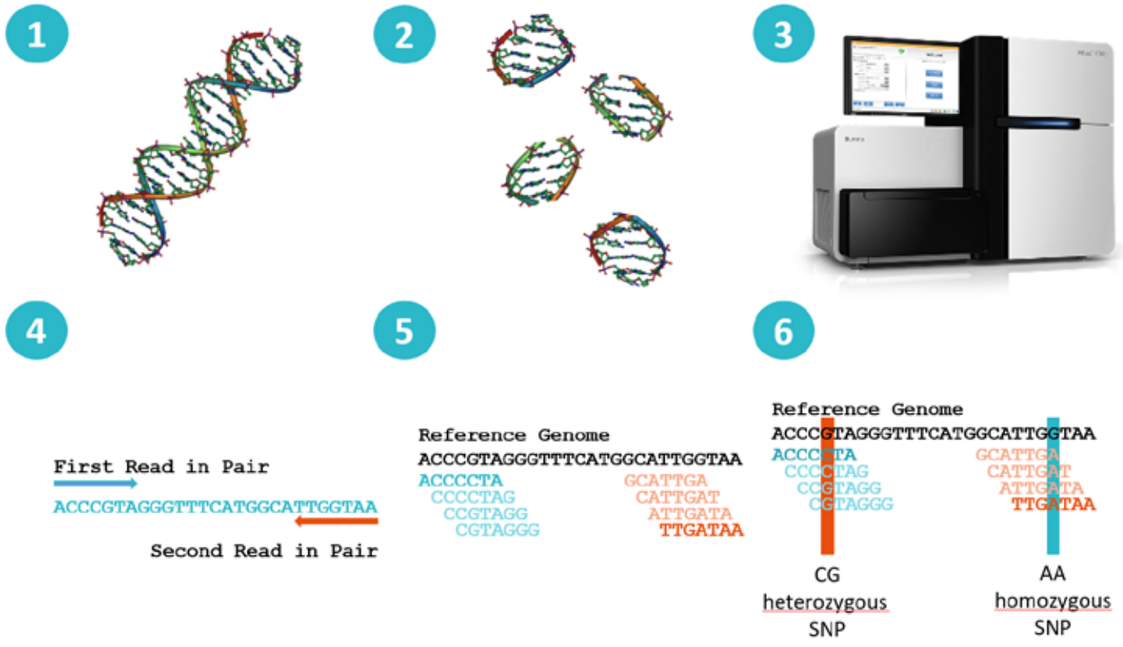

Figure 1
Exemplary re-sequencing study pipeline.
DNA: Michael Ströck (mstroeck) [CC BY-SA (http://creativecommons.org/licenses/by-sa/3.0/)]
Illumina HiSeq: https://www.illumina.com/systems/sequencing-platforms/hiseq-3000-4000.html

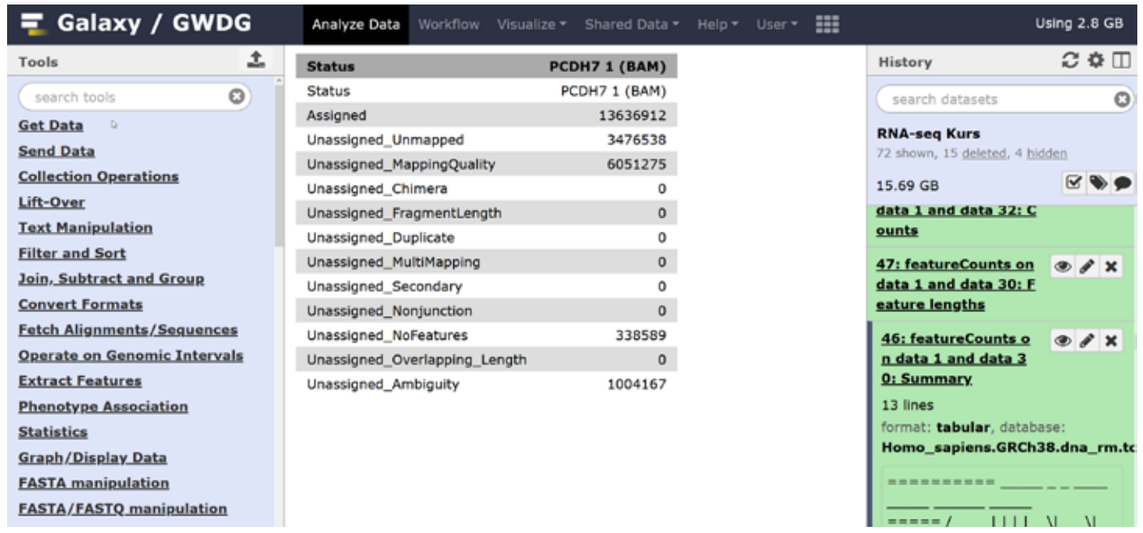

Figure 2
Screenshot from the Galaxy interface at GWDG Göttingen.

An exemplary workflow using Illuminas HiSeq technology is shown in Figure 1. (1) High quality DNA is extracted from body tissue, preferably full blood. (2) Library preparation: Raw DNA is fragmented into chunks of several hundred base-pairs, adapter sequences are ligated. (3) Libraries are put onto a flowcell where fragment clusters are generated by solid phase PCR in a so-called „bridge amplification". Sequence fragments are subsequently sequenced stepwise from both sides resulting in (4) paired-end reads. Paired-end reads are determined by a forward and a reverse read, both with fixed length and a defined insert size in between. Read length is dependent on number of sequencing cycles, usually ranging between 75 and 250 bp. (5) In the alignment step, paired-end reads are mapped against a known reference genome with pattern matching algorithms. (6) After mapping, genomic variations can be discovered by determination of sequence differences between reference and sample, as it is demonstrated for two single-nucleotide polymorphisms (SNPs).

Tools

To date, studies focussing on the analysis of farm animal genomes often used sequencing strategies that aimed at an average sequencing depth of an individual sample of up to 30X. This means that on average every nucleotide in the genome has been sequenced 30 times. Given the average length of a porcine genome of about 2.7 billion bp (2.7 Gbp), this means that up to 90 billion base calls have to be processed. To facilitate the bioinformatics processing, regularly large Linux-based server clusters are required, to run all steps in a massively parallelized fashion. Several bioinformatics tools have been developed, but one that gained outstanding popularity is the Genome Analysis Tool Kit GATK (McKenna et al. 2010; Van der Auwera et al. 2013). Application of such pipelines requires advanced programming skills to run a sequence of command line-based tools and manipulate intermediate datasets. Browser-based user interfaces are available to enable less experienced users to employ a wide range of these evaluation tools and to efficiently integrate public databases, such as Ensembl Biomart (Hunt et al. 2018). One popular representative is Galaxy, which is running on many academic clusters, but for which also public instances are available (https://galaxyproject.org/use/). Figure 2 shows the mapping statistics of an aligned data set in user interface of the Galaxy instance at GWDG Göttingen.

Reference genomes and resources

As pointed out before, the basis of re-sequencing studies using short read data is a well annotated reference genome. Genome-wise Göttingen Minipigs is a regular pig of the genus Sus scrofa. Figure 3 shows the phylogeny of Göttingen Minipigs from the Relliehausen colony in Germany and other domestic breeds. Göttingen Minipigs (red) cluster among European (green) and Asian (blue) breeds as it is expected by their breed history. As a synthetic breed established by crossing Minnesota Minipigs (mostly feral pigs with European background), Vietnamese Potbellied pigs (South Asian) and German Landrace, they still carry genome regions from all three founders (Simianer and Köhn 2010).

The most widely used porcine reference genome is currently Sscrofa11.1 (Warr et al. 2019). Which is based on the Genome of a Duroc sow, named T.J. Tabasco (GenBank accession GCA_000003025.6). This genome comprises a total sequence length of 2.5 Gbp and is easily accessible through, e.g the UCSC genome browser (http://hgdownload.soe.ucsc.edu/downloads.html#pig). As it was mentioned before, roughly 70 % of the Göttingen Minipigs genome was inherited from an Asian

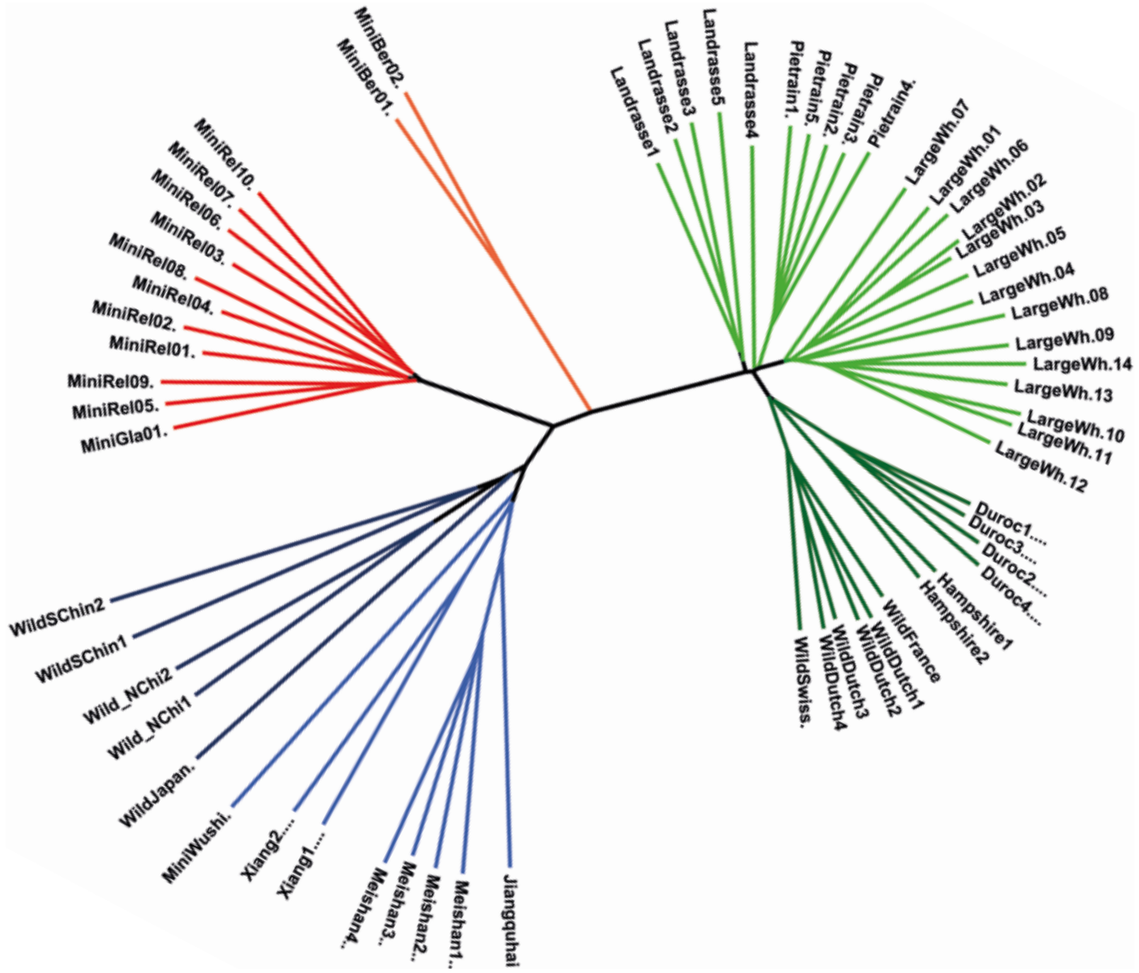

Figure 3
Phylogenetic tree neighbour-joining tree of pig breeds of various origin: Minipigs (red and orange), Asian (blue), European (green).

background (Gaerke et al. 2014), and although European and Asian breeds have mostly similar genomes compared to other geni of Sus, some features might only be represented in an Asian reference. Therefore, other reference genomes such as that of a Bama miniature pig (Asian, GenBank accession GCA_007644095.1) might be an alternative for specific analysis. There have also been efforts to build a reference sequence for Göttingen Minipigs by GSK (GeneBank accession GCA_000331475.1, (Vamathevan et al. 2013)) and F. Hoffmann - La Roche AG (GeneBank accession GCA_001292865.1 (Heckel et al. 2015)). The first assembly is only available in contigs, a sub-sub unit of chromosomes, while the second is a reference driven assembly based on the old pig reference Sscrofa10.2. Mapping a current Göttingen Minipig genome against the reference genome Sscrofa 11.1 results in 99.4 % mapping rate indicating that it is a good choice for Göttingen Minipigs studies (Reimer 2018). A list of available relevant reference genomes can be retrieved from https://www.ncbi.nlm.nih.gov/assembly/organism/9823/latest/.

Short-read sequencing costs are constantly decreasing and larger scale studies become more and more affordable. Within these studies it is often required to make all underlying data accessible in public databases. One of the databases is the European Nucleotide Archive ENA (https://www.ebi.ac.uk/ena) run by the EMBL-EBI and its partner, the sequence read archive SRA (https://www.ncbi.nlm.nih.gov/sra) with which it is synchronized. Table 1 lists all currently available samples and their accession numbers.

More sequence data is yet unpublished or currently being generated and will be available in the near future. And, although this technique is called next-generation sequencing, the following generation will be widely available soon. This third generation is using Nanopores or single molecule real time SMRT sequencing technology to generate several kilo-base pairs long reads, overcoming many of the disadvantages of the short-read technology. If you have further questions or would like to conduct your own study on Göttingen Minipigs sequencing data and are interested in a collaboration, please contact the Animal Breeding and Genetics group at University of Göttingen: tierzucht@agr.uni-goettingen.de.

Study	Publication	No. of samples	Accession numbers
PRJNA176189	Vamathevan et al. 2013	1	SAMN01731602
PRJNA291011	Heckel et al. 2015	1	SAMN03938573
PRJEB27654	Reimer et al. 2018b	10	SAMEA4828315-SAMEA4828324
PRJEB36673	Reimer et al. (2020/acepted in BMC Genomics	10 pool sequences	ERS4294318-ERS4294327

Table 1
Currently available Göttingen Minipigs samples.

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Science

Miniature Pig in Xenotransplantation

By JianFei Wang[1,2,3], RuLing Shen[3] and Gang Wang[1,2]

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Organ transplantation is the only best solution for organ failure; however, there is a worldwide organ shortage. Xenotransplantation is considered an alternative solution to this problem. Minipigs are widely used in biomedical research, compared to nonhuman primates (NHP) and the other species, therefore, minipigs are the most ideal species for xenotransplantation. However, phylogenetically, pigs are not similar to humans, therefore, immune rejection and molecular incompatibility can occur when xenotransplantation is conducted. The engineering of genetic material in pigs becomes possible due to the advancement of gene editing, somatic cell nuclear transfer and cloning technologies which has resulted in considerable progress in xenotransplantation of major organs using genetically modified pigs that are maintained in a designated pathogen-free facility (DPF).

Actually, the FDA approved a single gene Gal-knockout pigskin for clinical trials in 2018. It is predicted that xenotransplantation clinical trials for the other organs such as heart, kidney and pancreatic islets will launch soon. In particular, Göttingen Minipigs have great potential to contribute to the advancement of xenotransplantation considering its genetic and microbiological advantage.

Organ transplantation is the best solution for organ failure

Organ transplantation is the ideal treatment for organ failure in patients. It has become an essential treatment modality in saving and prolonging lives in a wide variety of clinical conditions. The most common organs routinely used for transplantation are the kidneys, heart, liver, lungs, and pancreas. However, the other vital organs, that may draw less public attention, which include the small bowel, skin, ligaments, bones, and cornea. These organ transplants may provide temporary relief or curative solutions in various clinical conditions. For patients, organ transplantation prolongs survival, increases the quality of life, and can be fully curative.

There is a worldwide organ shortage

Organ shortage is a major problem worldwide. There are more patients awaiting transplantation than there are organ donors. Improvements in medical and surgical techniques have enabled organ transplantation in cases not possible a decade ago. Unfortunately, scientific advancements have outpaced the availability of organs available for transplantation, and the issue of organ shortage has become more profound. According to the Scientific Registry of Transplant Recipients, only 36,258 out of 113,000 Americans on the organ donation waitlist received organ transplantation in 2019 (https://srtr.transplant.hrsa.gov). Every day, 20 people die waiting for transplants (Figure 1), (Sykes M et al, 2019).

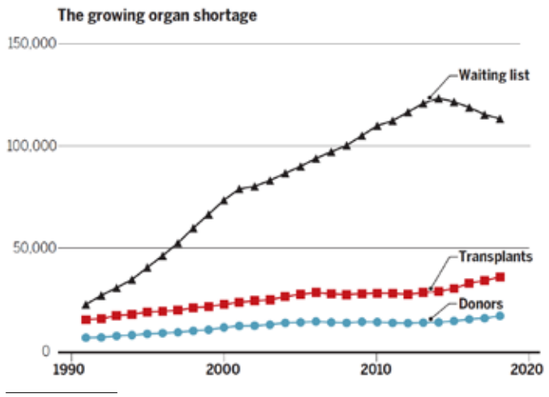

Figure 1
The growing allogenic organ supply/demand imbalance has resulted in an expanding transplant waiting list. Syke et al, 2019.

Xenotransplantation is a solution to solve the organ shortage

Xenotransplantation is the process of taking an organ from one species and transplanting it into another. It is one of the best solutions to solve the global organ shortage. Scientists are making great progress in xenotransplantation, hoping that animal organs can ease the human organ shortage. In the past several decades, findings from transplant experiments between humans and animals have mixed results. However, much progress has been made in certain animal species, especially pig organ transplantation in nonhuman primates. With the advancements in gene modification technologies such as CRISPR/Cas9, genetically modified pigs are less prone to immune rejection and more functionally compatible with humans. Eventually, animal organ transplants for human patients may be feasible, ultimately solving the global organ shortage (Figure 2), (Ekser B. et al, 2012).

Pig is the optimal species for xenotransplantation

While non-human primates are phylogenetically the most similar to humans, there are several drawbacks to using these animals as xenotransplant donors. The most pertinent issues include their small size, risk of infection, long gestation and growth periods, and ethical concerns. For these reasons, pigs are currently considered the most suitable xenotransplant donors. They have appropriately sized organs for life-supporting functionality in human recipients, are easy to breed in germ-free conditions, and present fewer ethical concerns than nonhuman primate research. Furthermore, pigs can be genetically manipulated to overcome immune challenges and prevent organ function incompatibility.

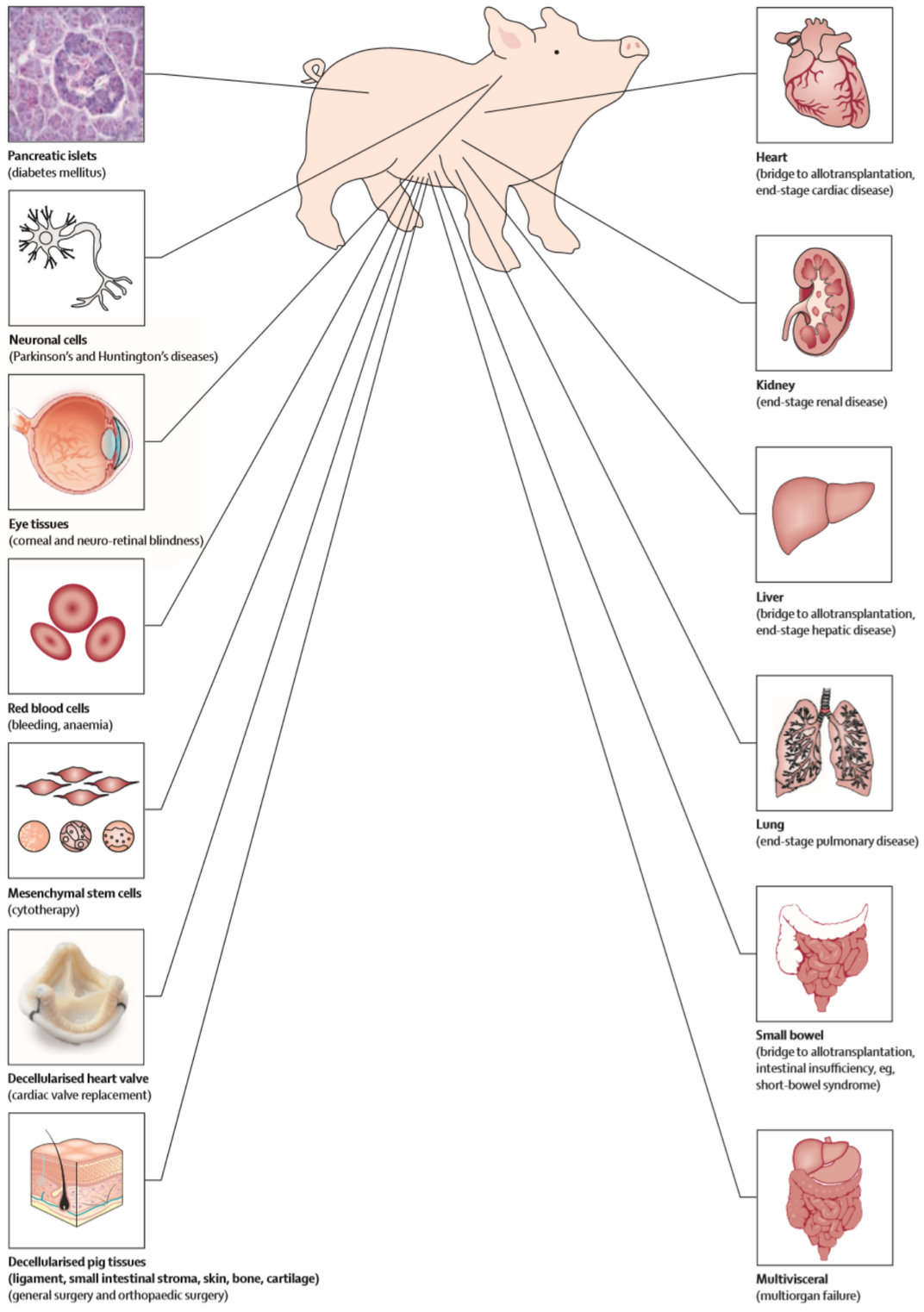

Figure 2
Xenotransplantation is the next medical revolution, Ekser B. et al, 2012

Challenges for xenotransplantation

There are still major obstacles before pigs can be successfully used as a source for organs. First, the immunological responses of the recipient against the graft need to be controlled. These include hyperacute rejection (HAR), which is characterized by binding of naturally-occurring xenoreactive antibodies that trigger the complement cascade; acute antibody-mediated rejection (AHXR), an acute humoral xenograft rejection; acute cellular rejection, and chronic rejection. Second, xenografts may have physiological limitations, such as molecular incompatibilities in the coagulation system. This may limit their use in providing functional replacement of a failing organ. Third, there is the risk of transmissible infections, such as porcine endogenous retroviruses (PERVs). To date, there have been no reported cases of humans acquiring PERV infections after being exposed to porcine tissue. However, pig cells are capable of transmitting PERVs to human cells in vitro, calling for the need for careful monitoring (Meier et al, 2018).

Solutions to overcome immune-rejection and molecular incompatibilities in the coagulation system

Genetically modified pigs have been considered favorable resources in xenotransplantation. Technologies and techniques such as microinjection of randomly integrating transgenes into zygotes, somatic cell nuclear transfer (SCNT), homologous recombination, and most recently, CRISPR/Cas9 has made transplanting of pig organs possible. Thus, multi-gene modifications in pigs can be generated via cloning using CRISPR/Cas9 editing in wildtype fetal fibroblasts. The carbohydrate xenoantigens that cause hyperacute rejection are Gal (galactose-alpha-1,3-galactose), CMAH (cytidine monophosphate-N-acetylneuraminic acid hydroxylase), and ß4GalNT2 (beta-1,4-N-acetyl galactosaminyltransferase 2). Knocking out these three-known carbohydrate xenoantigens and introducing the following genes may be beneficial in xenotransplantation. Human complement regulatory genes such as CD59, CD55, CD46 dampen immune rejection, CD47 reduces macrophage reaction, HLA-E alleviates NK cell activities, HO-1 (hemoxygenease-1) reduces chronic informatory response, EPCR (endothelial protein C receptor) reduces angiogenic injury, and THBD (thrombomodulin) reduces coagulation incompatibility. Various multiple gene-modified pig models have been generated, greatly contributing to the advancement in the xenotransplantation field (Figure 3) (Cooper et al, 2019).

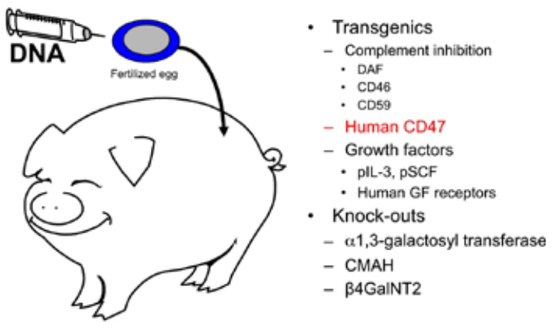

Figure 3
Genetic engineering pigs as xenograft donors. Megan Sykes, 2018.

Solutions to overcome transmissible infectious pathogens

The microbial status of pigs as a source for organs is an important factor in the safety assessment of a xenotransplantation product. Therefore, transmission infection is a major aspect of regulatory oversight. Guidelines published by regulatory authorities in the United States are widely recognized as standard documents in the field. To fulfill DPF status, specified bacteria, fungi, protozoa, and viruses should not be present in the source pig herd. These conditions are maintained using well-defined testing routines for designated pathogens, rigorous standard operating procedures (SOPs), and practices of herd husbandry and veterinary care to assure the absence of the designated pathogens. In general, pathogens that should not be present in the herd include those that affect the health of animals and those that might have the potential of cross-species transmission (i.e. zoonosis). Regular screening for DPF status is needed and the frequency depends on the status of the herd.

The barrier isolating source animals from the environment is defined at multiple levels. The building itself should be at a location that is remote from any other facilities housing pigs. Animal housing should be completely closed from the environment with a barrier system, disinfected water, and irradiated food. The material must be autoclaved prior to entry. Waste disposal, particularly fluids, requires special consideration to avoid retrograde flow associated with potential contamination. Personnel entry should be limited and requires shower in/shower-out procedures and personal protective equipment. An occupational health surveillance program should be in place. In general, all activities should follow SOPs, and regulations of current Good Manufacturing Practices (cGMP) should be implemented as per regulatory guidelines. Animal husbandry is regulated according to the Guide for the Care and Use of Laboratory Animals used by AAALAC International.

Enlarging the animal population is recommended in a biosecure facility. Regulatory guidelines state that the first generation of animals in the facility should not be used as source animals. Second or higher generation animals can be used as source donor pigs. Animals may enter the facility during the population process through a number of procedures such as initial cesarean section, disinfection, artificial insemination or embryo transfer. Organ retrieval and processing should also follow SOPs and regulations of cGMP (Noordergraaf J. et al, 2018).

Progress for miniature pigs in xenotransplantation

Genetically modified pigs and the use of immune-suppressive regimens in xenotransplant has enabled pig transplants in NHPs to sustain life. Pig kidney xenografts can sustain life for up to 499 days in NHP recipients. Baboons with heterotopic cardiac xenografts from Gal-KO pig with transgenic for human complement regulatory protein CD46 and human THBD transgenic survived up to 945 days. Using the same genetically modified pig, it was recently reported that the longest survival period of orthotopic pig-to-NHP heart xenotransplantation was 195 days in a baboon recipient. A group at Massachusetts General Hospital has been able to increase liver xenograft survival to 29 days. Even wild-type pig cornea xenografts, which are immune-privileged and non-vascularized, survived up to 511 days in a pig-to-NHP model using an anti-CD40-based

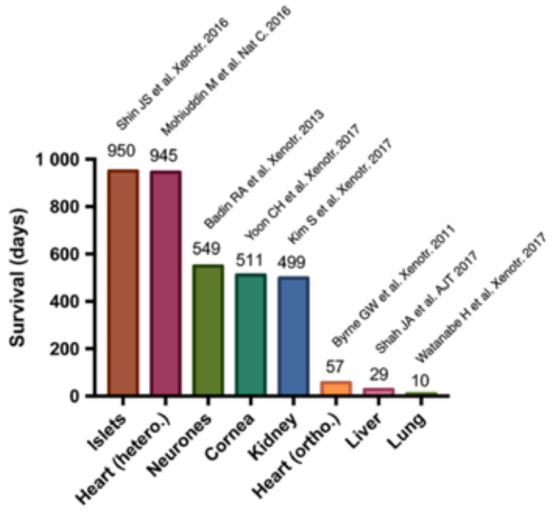

Figure 4
Survival of xenogenetic organs/tissue transplanted in non-human primates. Meier et al, 2018.

immunosuppression regimen. Currently, pancreatic islets hold the record for the longest xenograft survival time, nearing 1000 days (Figure 4) (Meier et al, 2018).

Unique advantage for Göttingen Minipigs in xenotransplantation

Göttingen Minipigs are the result of crossbreeding the Minnesota minipig, the Vietnamese potbelly pig, and the German Landrace pig. The genetic and microbiological make-up is well characterized in Göttingen Minipigs. This breed is widely used in biomedical research, it is produced in a full-barrier SPF facility, and the physiologic parameters and health status of the animals are well defined. Göttingen Minipigs are screened periodically. Nearly all microorganisms are eliminated by SPF or DPF breeding, except PERVs, because they are integrated into the genome of all pigs. However, the risk of pathogenesis from PERV is considered low (Morozov MV et al 2016). Furthermore, knocking out all copy numbers can be harmful to the pig cell, restricting the number of other genetic manipulations that can be made (Cooper et al, 2019).

As organs from conventional farm pigs may be too large, those from minipigs are better suited in some cases. Thus, Göttingen Minipigs may be considered as a donor of organs (Morozov MV et al 2016). Recently, the FDA approved the first human organ transplant for investigational use: single gene (Gal) knockout minipig skin in a human clinical trial.

Further modification of genes known to be implicated in xenotransplantation may allow other organ transplants to be successful. Such genetic modifications include deleting three known carbohydrate xenoantigens (Gal, CMAH, ß4GalNT2) and expressing three human complement-regulatory proteins (CD46, CD55, CD59), two human coagulation-regulatory proteins (THB, ECPR), the anti-apoptotic and anti-inflammatory molecule (HO-1) and human CD47. Knocking down/knocking out SLA (class I and/or class II) along with knocking in HLA-E may also contribute to the success of xenotransplantation. The genetic make-up and microbiology of Göttingen Minipigs are well characterized, and the modifications mentioned above may contribute to the success of xenotransplantation in other vital organs (Cooper et al) as the work recently done by Zou et al (https://doi.org/10.1101/2020.01.20.912105).

Conclusion

Xenotransplantation is a promising new method to treat terminal organ failure. It provides potential solutions to the worsening organ shortage facing allotransplantation today. The challenges for xenotransplantation are being gradually resolved and huge progress has been made using multiple gene-modified miniature pigs. Skin clinical trial using single gene-modified pig was approved by the FDA in 2018, and clinical trials for heart, kidney and pancreatic islets will likely take place in the near future. Genetically modified Göttingen Minipigs will be an excellent animal model for source organs which will greatly contribute to the success of xenotransplantation in humans with terminal organ failure.

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Working with Göttingen Minipigs

Describe a typical day at work
My day constists of practical tasks such as feeding, cleaning, socialising the minipigs, changing the minipigs' available toys and activity items and letting them out of the pens for excercise. Often we also have minipigs that need weighing as part of the preparation for a delivery or customer specified training to conduct.

How do you define a good day at work?
Recently we trained a group of Göttingen Minipigs to walk on a treadmill for a customer. It took time, effort and patience, so the first time we succeeded it was definitely a very good day. But to me, getting to work with animals on a daily basis, generally makes every day a good day.

What is your relationship with the Göttingen Minipigs?
In the research barrier we often house Göttingen Minipigs for a longer time than the production barriers do. Also, the research barrier does not house as many minipigs as the other barriers, so you develop a closer relationship with each animal. But it is a mutual relationship: The minipigs likewise get to know their caretakers and recognize us, when we enter the pens.

How do you unwind?
A great source for relaxation is being with my horses, either grooming or going for a ride. It gives me the opportunity to unwind and focus all of my energy and connect with the horse.

What makes you happy?
Helping other people and being around animals. There's something about animals that has a very calming effect on me, and I'm lucky to spend most of my time being with animals. My horses and dogs take up a lot of my spare time, but I also value my sports activites. Being a very social person, the time spend with my team is priceless.

What are your aspirations?
I always wanted to become a farmer, but also wanted to work around animals. After working with cows in conventional farming for a while, I realized that this was not my scene. However, at Ellegaard Göttingen Minipigs the well-being of the animals goes hand in hand with doing business. I aspire to make a difference to people and animals around me, and here, with the remarkable focus on animal welfare that we have, these apirations are met every day. Animals have always held a special place in my heart, so caring for and tending of them is something I enjoy and am good at.

How do you make a difference?
It is a huge motivation going to work knowing that what you do, ultimately makes a difference in helping other people. I'm proud to play a small role within the reseach industry, and take part in enabling the development of new knowledge and medicines. Whenever the opportunity presents itself, I also engage in charity events with my floorball team raising money for e.g. the fight against cancer.

You have also been part of the animal welfare commitee for the past 6 months. Why is that a priority to you?
Being part of the animal welfare commitee is an opportunity to use my experience from the barrier to influence the well-being of our Göttingen Minipigs. It is vital that they are offered stimulating conditions and the best living standards possible, and through the animal welfare commitee I can contribute to this and take active part in the decision making processes.

About the Research Barrier
The research barrier was build in 2016 to offer customers a state-of-the-art housing facility for Göttingen Minipigs as well as a surgical suite, enabling the development, characterization and validation of new Göttingen Minipigs disease models.

Göttingen Minipigs stabled in the research barrier are all there as part of a preparation process before delivery, for example preparation before surgery (e.g. castration or implantation of catheters), special training, selected diets etc. The only pigs being bred in the research barrier, are part of specific transgenic projects, replicating genetic alterations responsible for human disease.

In focus

Name Karoline Oldenborg
Function Animal Caretaker
Unit Research Barrier

Education
Agriculturalist, with area of specialisation in pigs.

Background
Karoline started as an Animal Caretaker of cows in conventional farming and also briefly worked in the fields as part of her education. Since 2012 Karoline has been with Ellegaard Göttingen Minipigs in one of the production barriers, and started working full-time in the research barrier in early 2019.

Interests
Passionate about animals, Karoline spends a lot of time with her two dogs og two horses, but also likes to ski and play floorball.

Pain models in Göttingen Minipigs

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

Insight provided by:
Sigal Meilin, Chief Scientific Officer at MD Biosciences

What is the project about?
The main objective of our project is to develop and validate a novel pain model in adult pigs, targeting both acute and chronic pain. Therefore, the use of Göttingen Minipigs is absolutely critical. The model development will be supplemented by the development of related biomarkers to track disease.

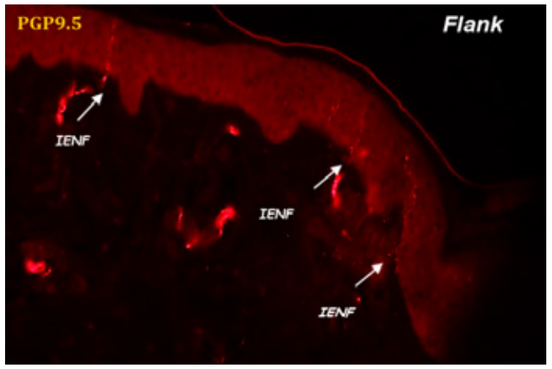
What is the purpose of the study?
There are several goals to the project mainly designed to better understand the resemblance of the minipigs to human in relation to the sensory system using novel incision or nerve injury models. This involves ground-level investigations into dorsal root ganglion (DRG) genetics, electrophysiological properties of DRG culture and in vivo electrophysiology. Furthermore, the program aims to provide reliable in vivo tools for testing drugs, devices and other methods aimed at pain relief.

Why is it important?
Traditional rodent models have contributed significantly to our understanding of pain and pain mechanism. However, translation of the scientific rodent data collected over the past few decades into truly new, effective and safe clinical analgesics has been frustrated by lack of success. This has led to lower reliance on rodent pain studies in favor of more extensive and expensive testing of humans. The failures of rodent-driven programs in human studies are related to adverse effects and lack of efficacy in human studies for drugs that seemed to be both safe and effective in rodent models. Although pain is by no means alone in having an uninspiring translation record, improvement of the animal models has become critical for developing pain therapies.

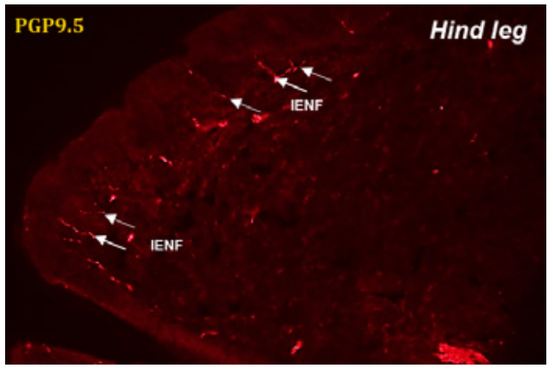
The peripheral nerve system and the skin of pigs resembles that of the human in many ways, making pigs the best-chosen animal for developing of topical treatments. One of the many examples is the development of HTX-011 local Bupivacaine/ Meloxicam formulation for the treatment of post-operative pain (POP) published in 2019 (Ottoboni T, et al. Reg Anesth Pain Med 2019;0:1–7). Not only was the correlation between the activity in domestic pigs and human shown but also the mode of action of the HTX-011 formulation was shown in MD Biosciences' porcine model of acute POP. These results could not be obtained using rodent models. However, since this work was done in domestic pigs, it could only be done in very young animals. There is a great relevance is transferring the model to Göttingen Minipigs. Unlike models in domestic pigs, the minipigs enables to develop these models in adult pigs which are more relevant to the studies of pain and pain management.

A second model in Göttingen Minipigs, the peripheral neuritis trauma (PNT) model for peripheral nerve injury induced neuropathic pain, which we run in our lab, is one of the few animal models that show true chronic pain (>3months) (Castel et al., NeuPsig London 2019 Abstract number NEUPS-0036).

Evaluation of spontaneous behavior in animals experiencing painful procedure or conditions is an additional issue facing the performance of animal models. The two models mentioned above offer refined behavior scores, as well as methods for assessment of approach time and specific analysis of the animals' behavior in the open field.



Picture 1
Nerve ending staining from flank.



Picture 2
Nerve ending staining from hind leg.

Lastly, electrophysiology may be applied in these models to assess the direct activity of drugs on nerve properties. As an example, transient receptor potential cation channel subfamily V member 1 (TRPV1) is similar between pigs and humans, but different than that of rats (McIntyre et al., British Journal of Pharmacology 2001; 132; Ohta et al., Biochemical Pharmacology 2005; 173-187). This point contributes to a dissonance between the expected effect of a compound studied in rodents and translating into humans, while the homology with the minipig provides translatable results. Direct recording from the nerves provides an objective and quantitative observation of the direct effect of any drug candidate the nerve (such as local anesthetics or ion channel blockers).

What makes this study particularly interesting?
This study is interesting because of its relevance and its potential to accelerate the success of novel, non-opioid analgesic compounds. Anyone working in the pain field would like to have a system that would be as close as possible to and predictable as possible of the human response.

Which challenges have you met during the study?
We faced two inter-related, main challenges; scientific and acceptance. On the scientific part, since there were very few models in pigs and none in Göttingen Minipigs for pain, there was very limited literature on the behavior of pigs in pain state. The pain states mentioned in publications were very acute (not lasting more that 24 hours) and did not provide a robust tool to assess new therapies. We needed to develop objective measurement methods to evaluate the behavior of Göttingen Minipigs in the state of pain.

Acceptance proved to be a challenge as well. Since rodent are standard and easily accessible in both the academic and industry, the acceptance of the pig model (whether domestic or minipigs) as the best tool in the development of drugs in the field of pain took a long while. Thanks to pioneering work, including much work performed at MD Biosciences, the pig model is accepted as the best alternative for certain purposes, providing an excellent tool for drug development and for de-risking human clinical trials. Translating these results to Göttingen Minipigs is the next step since they are well accepted animals for the development of drug and device industry.

How do you recommend going about species selection?
Understanding target engagement is perhaps the most important point in species selection. It is imperative that the species express the same target and that the target modulation or as in the case of pain, stimulation, is similar between the selected species and the human. Another important point relative to species selection is that the desired method of application in humans is also relevant to the selected animal species. For examples topical treatments or nerve blocks are assessed better using pig models than in rodent models. For that reason, we recently have developed a new model of modified post-operative pain, to allow the assessment of new nerve block therapies in minipigs.

Lastly, it is important to select the correct model with respect to the time of application (whether therapeutic or preventative) and with applicable, correct readouts. Designing the right protocol with the right parameters, including the correct choice of species, increases the chance of success and translation to humans.

Any learnings you would like to share?
Our experiences with working with pigs have shown great success in the rapidly developing field. Many challenges remain, however, but careful planning and understanding of the science will lead us to creating increasingly relevant and reliable platforms for testing drug candidates and de-risking clinical trials.

Spotlights

Whitepaper

Rapid one-step generation of genetically modified Göttingen Minipigs for human disease modelling

Göttingen Minipigs have become an increasingly attractive animal model to be genetically modified for human disease modelling. Using advanced genetic techniques has significantly reduced the development time of tailored modifications, still making it possible to replicate genetic alterations responsible for human disease.

A study performed by a collaboration between Genome Biologics, Charles River Laboratories and Ellegaard Göttingen Minipigs confirmed how the time challenges can be significantly reduced.

Interested in receiving the whitepaper? Please contact Ellegaard Göttingen Minipigs at ellegaard@minipigs.dk.

Treadmill training

Recently, a training session was conducted at Ellegaard Göttingen Minipigs, teaching a group of Göttingen Minipigs to walk on a treadmill, with a target speed of 4 kilometres per hour.

"Göttingen Minipigs are curious by nature and are usually easy to train when the preliminary work, such as socialisation and target training, has been performed properly - and when using the right rewards. Therefore, most of the minipigs were quick to adapt and step onto the belt. Only a few were a bit more sceptical and it took patience and repetition to get them used to the process, as it is important that they have a positive experience during the training", explains Kamilla Flemming Hansen, Laboratory Technician at Ellegard Göttingen Minipigs.

The entire training process took 4-5 weeks, from launching the target training until the minipigs were able to run on the treadmill. Kamilla Flemming Hansen elaborates: "Once they got used to standing on the non-moving treadmill, they very quickly got the idea and after only a few practices, they were able to walk at a slow pace. The speed was increased gradually as was the time spent on the moving belt. When it was time for them to leave, they had all learned to use the treadmill."

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Ensuring a safe and comfortable journey

In December 2019 all drivers at Ellegaard Göttingen Minipigs attended a driving course at the local road safety center, to brush up their driving skills under challenged conditions. "It's important that our drivers' skills behind the wheels are maintained and certified regularly, so both they and the Göttingen Minipigs they transport across Europe are ensured a safe and comfortable journey", says Søren Vangsgaard, Production Manager at Ellegaard Göttingen Minipigs.

Likewise, the drivers appreciate the prioritisation of the practical courses. After the course Jørn Frydenberg, Driver at Ellegaard Göttingen Minipigs, said: "Driving about 100.000 km around Europe every year might give you quite a lot of driving experience. Still, it's nice to attend a course, where you can be updated on the latest security features in the cars and try to drive them to the "limit" under secure conditions and get to know how the cars will react in an emergency situation. Also, it is great to spend a day with your colleagues and share experiences, as we spend a lot of time alone on the roads."

Whitepaper

Göttingen Minipigs in ADME Studies

Recently, the specific advantages of using Göttingen Minipigs in ADME studies was summarized in a whitepaper, briefly reviewing the literature on especially the use in pharmacokinetic studies and studies focused on drug metabolism. "Göttingen Minipigs are generally accepted as a good model for human drug absorption and metabolism, which is why we are focussing on this species for translational research in our lab", says Professor Steven Van Cruchten of the University of Antwerp.

Interested in receiving the whitepaper? Please contact Ellegaard Göttingen Minipigs at ellegaard@minipigs.dk.

Göttingen Minipigs Symposium 2020

The date for the next Göttingen Minipigs Symposium in the USA, conducted by Marshall BioResources, has been set. This year the symposium takes place at:

University of Maryland School of Medicine
Baltimore, Maryland
21-22 May 2020

The focus for this year's symposium will be on the use of Göttingen Minipigs in biodefense research, offering the opportunity to take part in many interesting presentations and discussions. For scientific program and registration, follow updates at marshallbio.com/gottingen-minipigs-symposium-2020.

We enable the development of safer and more effective medicines

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

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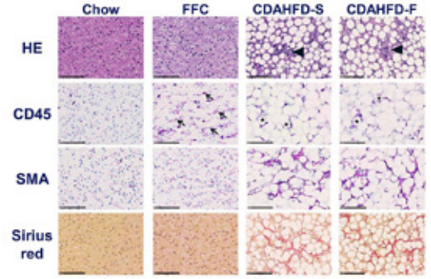


Publications and reseach results
Articles, whitepapers, posters etc. involving Göttingen Minipigs.

Ellegaard Göttingen Minipigs Research Foundation
Call-out for projects happens twice a year.

New publications!
Be notified about new publications.

Liver stiffness assessed with Shear Wave Elastography correlates with biopsy data in Göttingen Minipigs with non-alcoholic steatohepatitis

Henning Hvid[1], Sara T Hjuler[1], James W Perfield[2] and Henrik D Pedersen[3]
[1]Novo Nordisk, Måløv, Denmark; [2]Eli Lilly & Co, Indianapolis, USA; [3]Ellegaard Göttingen Minipigs, Dalmose, Denmark

Background and Aims: Non-alcoholic steatohepatitis (NASH) can be induced in Göttingen Minipigs by using a choline-deficient, amino acid-defined high fat diet (CDAHFD). The disease progression can be monitored by taking needle biopsies, and shear wave elastography (SWE) is being evaluated as a non-invasive way of monitoring the disease progression. This study aimed to evaluate the correlation between SWE data and the collagen proportionate area found in needle biopsies in Göttingen Minipigs fed CDAHFD.

Methods: 3-month-old, castrated male Göttingen Minipigs were fed either chow (n = 8) or CDAHFD (n = 16) containing 20% fructose, 30% saturated fat (w/w), 1% cholesterol, 0.35% cholic acid and 0.1 % methionine for 3 months. SWE was performed on anesthetized minipigs in dorsal recumbency using the Aixplorer ULTIMATE ultrasound system and a SL 10-2 transducer (SuperSonic Imagine). In each animal, an average of three measurements was used.

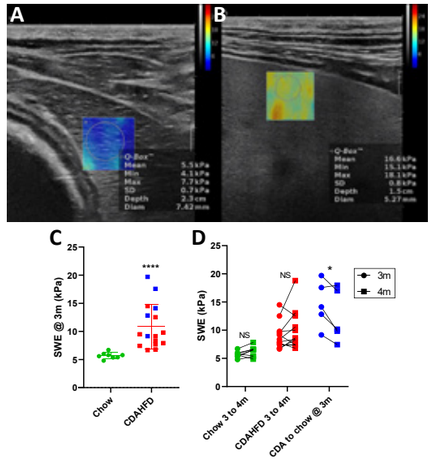


Figure 1. A: Liver with normal stiffness (5.5 kPa) from a chow-fed Göttingen Minipig. **B:** Liver with increased stiffness (16.6 kPa) from a Göttingen Minipig fed CDAHFD for 3 months. The increased size and echogenicity of the liver to the right reflects the marked steatosis found in these animals. **C:** After 3 months, SWE was significantly increased in minipigs fed CDAHFD. Blue squares: Animals switched to chow at 3 months. **D:** In the five minipigs, which were transferred to chow at 3 months, liver stiffness had decreased at 4 months.

Scanning results: After 3 months, the minipigs on CDAHFD weighed more than the controls (14.3±2.0 versus 11.7±1.6 kg; P=0.004) and showed no clinical signs of disease. Results from SWE indicated increased liver stiffness in pigs on CDAHFD (5.7±0.6 versus 10.9±3.9 kPa; P<0.0001; Figure 1C). For a subset of the pigs, the diet was changed from CDAHFD to chow at 3 months, and one month later, the liver stiffness for these pigs interestingly had decreased (Figure 1D).

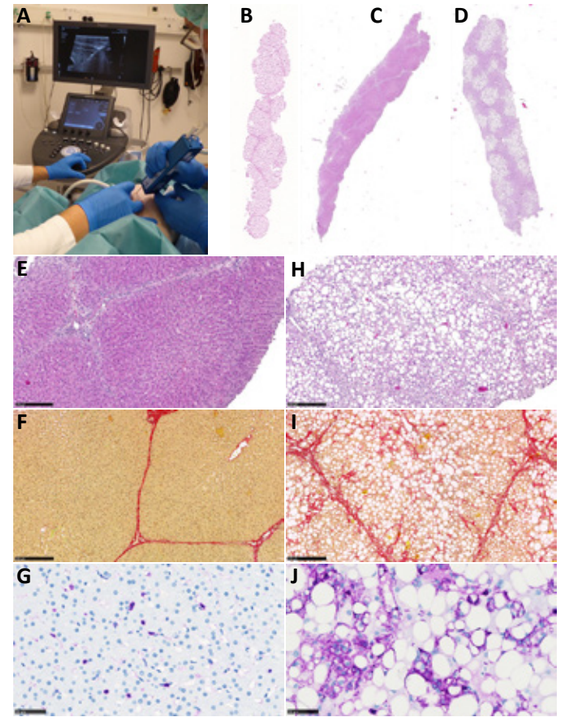


Figure 2. 14G Liver biopsies were taken ultrasound guided. The vacuum-assisted Vacora® Biopsy System **(A)** allows biopsies to be taken even in very fragile steatotic livers early in the course of disease **(B)**. Biopsies from an animal on Chow **(C)** and one that has been on CDAHFD for longer time and therefore has developed more fibrosis **(D)** are shown for comparison. The biopsies were subsequently analyzed histologically, and panels **E, F** and **G** show HE-, PSR- and anti-CD45-stained sections, respectively, from a Chow-fed minipig; and panels **H**, **I** and **J** show the corresponding sections from a minipig on CDAHFD.

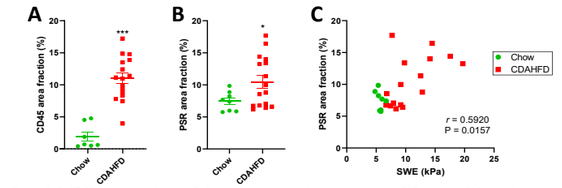


Figure 3. A: CD45 proportionate area. **B:** Collagen proportionate area assessed by PSR staining. **C:** Association between collagen proportionate area and SWE at 3 months. A significant correlation was found in pigs on CDAHFD.

Histology results: Liver biopsies were successfully taken from all animals and histologically, macrovescicular steatosis was found, progressing from zone 3 to the whole lobule. Compared to the controls, the minipigs on CDAHFD had more inflammation (CD45 proportionate area 1.9±0.7 versus 11±0.8 %; P<0.0001) and larger collagen proportionate area (7.4±0.5 versus 10.5±1.0 %; P=0.0499) morphometrically. The SWE data correlated with the collagen proportionate area in the animals on CDAHFD (r = 0.59 (Pearson); P=0.016).

Conclusion: In Göttingen Minipigs with CDAHFD-induced NASH, liver stiffness assessed with SWE correlated with the collagen proportionate area in liver biopsies. Further studies are needed to evaluate these correlations more extensively across the NAFLD/NASH continuum.

The 14th Minipig Research Forum

Join the 14th Minipig Research Forum - a unique opportunity for minipig users to meet, discuss and share knowledge and experiences within all areas of minipig use related to biomedical research. Take part in this 3-day conference packed with scientific lectures, poster presentations and the opportunity of networking with minipig users from all over the world.

SCIENTIFIC SESSIONS

- Nutrition and Metabolism
- Juvenile and Reproductive Toxicology
- Pain - Models and Management
- Pharmacological Models
- Immune System

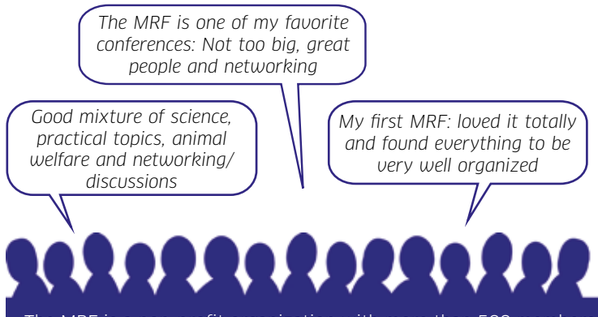
BREAKOUT SESSIONS

- Dosing and Sampling (continuing education)
- Training and Monitoring Welfare (continuing education)
- The Ethical Landscape (open forum discussion)

POSTER SUBMISSION

Every year the best MRF poster is elected and awarded.

Posters with technical content (e.g. tips and tricks) or scientific content (including data) are accepted. Poster intructions incl. deadline for submission are available on www.minipigresearchforum.org



PRACTICALITIES

Starts at **13 May 2020** (Wednesday)
14:00 hrs CEST
(Registration desk opens at 13:00 hrs CEST)

Ends at **15 May 2020** (Friday)
12:00 hrs CEST

Registration fee **Early Bird: €350** (register before 1 April 2020)
Late registration: €400

The registration fee covers welcome lecture, five scientific sessions, one breakout session of choice, catering (lunch, coffee and snacks), get-together dinner Wednesday evening incl. dinner, drinks and network, event Thursday evening followed by buffet dinner at venue hotel, and conference material.

Venue **Hotel Iberostar Selection Lisboa**
Rua Castilho 64, Lisbon

The venue is located in the heart of the city and only 15 minutes from the airport.

Accommodation Rooms can be booked at a special MRF conference rate of €175/night incl. breakfast. Download the booking form from our website and email it to the hotel ASAP.
Alternative accommodation may also be found in the area.

IMPORTANT NOTICE: Book your accommodation now!
Lisbon is a very popular destination during May. Therefore the hotel will gradually release the MRF room allotment to accommodate the demand.

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

Minipig Research Forum Program 2020

The conference program consists of the following scientific sessions and topics:

WELCOME LECTURE

Developing clinically relevant models of self-poisoning in Göttingen Minipigs at the Edinburgh Large Animal Facility

SESSION: NUTRITION AND METABOLISM

Feeding of the trial animal – bear in mind possible effects of the ration

Early life glycemic nutrition and later life metabolic health in female Göttingen Minipigs

Characterization of a small DIO Göttingen Minipigs model

Microbiome alterations in response to dietary fiber and protein in obese Göttingen Minipigs

SESSION: JUVENILE AND REPRODUCTIVE TOXICOLOGY

Regulatory toxicity studies in juvenile animals – an industry perspective with a focus on minipigs

Embryo-fetal development studies in Göttingen Minipigs - technical feasibility and special considerations

What's good to know when considering the minipig for juvenile toxicology studies

Non-standard use of Göttingen Minipigs in juvenile/repro tox studies, thinking 'outside the box'

Case Study: Safety assessment of food additives in juvenile Göttingen Minipigs

SESSION: PAIN - MODELS AND MANAGEMENT

Overview of anesthesia and analgesia in Göttingen Minipigs

Side effects of pain and analgesia in animal experimentation

Machine vision for facial recognition in pigs: animal welfare applications

SESSION: PHARMACOLOGICAL MODELS

Diet-induced model of non-alcoholic steatohepatitis in Göttingen Minipigs

Going beyond occlusion-reperfusion models for myocardial infarction in Göttingen Minipigs

Assessing cardiovascular control mechanisms in pharmacodynamic studies – species considerations and experiences using telemetry in Göttingen Minipigs

Lessons on immunosuppression in Göttingen Minipigs

SESSION: IMMUNE SYSTEM

Postnatal development of leukocyte populations in Göttingen Minipigs

Göttingen Minipigs in translational immunosafety sciences: an example

Göttingen Minipigs as a model for skin immunology

BREAKOUT SESSIONS

Introductory talk: Medicated gelatine cubes used in refinement of oral dosing in Göttingen Minipigs

Dosing and Sampling

Training and Monitoring Welfare

The Ethical Landscape

Please select one breakout session of choice when registering for the MRF conference and prepare your own concrete cases, if any, for discussion. Note that your selection of breakout session is not binding and can be changed until the first day at 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

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New publications on Göttingen Minipigs

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

Landau AM, Noer O, Alstrup AKO, et al.
Type of Anaesthetic Influences [11C]MDL100,907 Binding to 5HT2A Receptors in Porcine Brain.
Mol Imaging Biol. 2020; Jan 28. [Epub ahead of print]
https://www.ncbi.nlm.nih.gov/pubmed/31993926

Juhásová J, Klíma J, Martínek J, et al.
Two types of autologous cells in stricture development prevention after complete circular endoscopic dissection in minipig.
Rozhl Chir. 2019;98(12):497-508
https://www.ncbi.nlm.nih.gov/pubmed/31958964

Imwinkelried T, Beck S, Schaller B.
Pre-clinical testing of human size magnesium implants in miniature pigs: Implant degradation and bone fracture healing at multiple implantation sites.
Mater Sci Eng C Mater Biol Appl. 2020;108:110389. doi: 10.1016/j.msec.2019.110389
https://www.ncbi.nlm.nih.gov/pubmed/31923970

Krüger L, Kristiansen Y, Reuber E, et al.
A Comprehensive Strategy for Screening for Xenotransplantation-Relevant Viruses in a Second Isolated Population of Göttingen Minipigs.
Viruses. 2019;12(1). doi: 10.3390/v12010038
https://www.ncbi.nlm.nih.gov/pubmed/31905731

Schwarz ML, Reisig G, Schütte A, et al.
Report on a large animal study with Göttingen Minipigs where regenerates and controls for articular cartilage were created in a large number. Focus on the conditions of the operated stifle joints and suggestions for standardized procedures.
PLoS One. 2019; Dec 26;14(12):e0224996
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Keller EE, Patras I, Hutu I, et al.
Early sacral neuromodulation ameliorates urinary bladder function and structure in complete spinal cord injury minipigs.
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Telinius N, Spinozzi D, Rasic D, et al.
Göttingen Minipig is not a Suitable Animal Model for in Vivo Testing of Tissue-Engineered Corneal Endothelial Cell-Carrier Sheets and for Endothelial Keratoplasty.
Curr Eye Res. 2020;Jan 6. [Epub ahead of print]
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Towards a Göttingen minipig model of adult onset growth hormone deficiency: evaluation of stereotactic electrocoagulation method.
Heliyon. 2019;Nov 28;5(11). doi: 10.1016/j.heliyon.2019.e02892
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Siefert J, Hillebrandt KH, Moosburner S, et al.
Hepatocyte Transplantation to the Liver via the Splenic Artery in a Juvenile Large Animal Model.
Cell Transplant. 2019;28(1_suppl):14S-24S.
https://www.ncbi.nlm.nih.gov/pubmed/31842585

Ludvigsen TP, Olsen LH, Pedersen HD, Christoffersen BØ, Jensen LJ.
Hyperglycemia-induced transcriptional regulation of ROCK1 and TGM2 expression is involved in small artery remodeling in obese diabetic Göttingen Minipigs.
Clin Sci (Lond). 2019;133:2499-2516
https://www.ncbi.nlm.nih.gov/pubmed/31830262

Mármol-Sánchez E, Cirera S, Quintanilla R, Pla A, Amills M.
Discovery and annotation of novel microRNAs in the porcine genome by using a semi-supervised transductive learning approach.
Genomics. 2019;Dec 6. [Epub ahead of print]
https://www.ncbi.nlm.nih.gov/pubmed/31816430

Nies A, Proft L, Nehring ME, et al.
Growth-related micromorphological characteristics of the porcine common carotid artery.
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https://www.ncbi.nlm.nih.gov/pubmed/31797410

Soebadi MA, Bakula M, Hakim L, Puers R, De Ridder D.
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Sucrose intake lowers μ-opioid and dopamine D2/3 receptor availability in porcine brain.
Sci Rep. 2019;Nov 15;9(1):16918. doi: 10.1038/s41598-019-53430-9
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Safety evaluation of silver-ion dressings in a porcine model of deep dermal wounds: A GLP study.
Toxicol Lett. 2020;319:111-118
https://www.ncbi.nlm.nih.gov/pubmed/31715245

Olesen ML, Christensen BB, Foldager CB, Hede KC, Bergholt NL, Lind M.
No effect of platelet-rich plasma as adjuvant to bone marrow stimulation for the treatment of chondral defects in a large animal model.
Arch Orthop Trauma Surg. 2020;140:77-84
https://www.ncbi.nlm.nih.gov/pubmed/31664573

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J Clin Exp Hepatol. 2019. Doi.org/10.1016/j.jceh.2019.09.004
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Rasmussen MK, Scavenius C, Gerbal-Chaloin S, Enghild J.
Sex dictates the constitutive expression of hepatic cytochrome P450 isoforms in Göttingen minipigs.
Toxicol Lett. 2019;314:181-186
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Transdermal Delivery of Sumatriptan Succinate Using Iontophoresis and Dissolving Microneedles.
J Pharm Sci. 2019;108:3649-3656
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Olesen ML, Christensen BB, Foldager CB, Hede KC, Jørgensen NL, Lind M.
No Effect of Platelet-Rich Plasma Injections as an Adjuvant to Autologous Cartilage Chips Implantation for the Treatment of Chondral Defects.
Cartilage. 2019;Jul 22 [Epub ahead of print]
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Where to meet us in 2020

CONGRESS / SYMPOSIUM	DATE	LOCATION
SOT and ToxExpo	15-19 March	Anaheim, California, USA
AST Congress	24-26 March	Edinburgh, Scotland
Minipig Research Forum (MRF)	13-15 May	Lisbon, Portugal
Göttingen Minipigs Symposium	21-22 May	Baltimore, Maryland, USA
AFSTAL	27-29 May	Marseille, France
AFLAS	22-26 June	Chiang-Mai, Thailand
World Congress (WC11)	23-27 August	Maastricht, Holland
EUROTOX	6-9 September	Copenhagen, Denmark
SPS	13-16 September	Montréal, Canada
GV-SOLAS	16-18 September	Würzburg, Germany
Janssen Juvenile Toxicology Symposium	15-16 October	Beerse, Belgium
3R's Research and Progress	19-20 November	Hyderabad, India
LASACON	21-22 November	Hyderabad, India
CALAS	TBA	China

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