

ANNUAL REPORT

2021

Danish 3R-Center

RRR



2021

A N N U A L R E P O R T

Danish 3R-Center
RRR



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CHAIRMAN'S FOREWORD

Dear everyone

2021 started and ended under the influence of the COVID pandemic, but between these points it was also a year when we, as a centre, could return to a more normal daily life. It has been a great pleasure for us as a 3R centre to organize our scientific symposium and to hold the annual meeting of the animal welfare bodies in our capacity as a national committee. I would like to express my gratitude to the Lundbeck pharmaceutical company who provided an excellent setting for the annual meeting of the animal welfare bodies on their premises. Both events were well-attended, and the subsequent evaluation also showed great satisfaction with the meetings. We were very pleased to see that an increasing number of researchers decided to spend two days at our symposium.

Not all speakers could attend in person, and some presentations were delivered online. This form of access to a number of outstanding speakers has opened our eyes to the perspective of improving the climate footprint of our meetings in future.

We awarded the 3R Prize at the symposium, as we have done every year. In 2021, the award was given to Professor Rie Vinggaard of the Technical University of Denmark. For many years, she has studied the effect of endocrine disruptors on unborn children. In her work, she has always focused intently on developing non-animal-based research methods. She is an important role model as she has obtained a prominent position in an important research area with a scientific effort that is widely based on animal-free methods.

We have focused on a number of specialist areas in 2021. This has involved drafting recommendations that will reduce the use of animals in the production of antibodies

and for teaching purposes, and once again in 2021 we have taken a closer look at the animals exposed to the highest level of severity.

During the centre's eight years of existence, we have managed to build a strong international network which is naturally supported by the establishment of 3R centre-like organizations in our surrounding countries. We have a highly constructive dialogue with the other European national committees at regular meetings, which has actually been strengthened by an increased meeting frequency due to online opportunities. In the spring, we participated in a well-attended Nordic two-day 3Rs webinar at which various Nordic contributors presented 3R projects, and we also took part in the planning and organization of a number of European webinars with the Swedish 3Rs Center and the British NC3Rs, among others.

2021 was supposed to be the last year of the term for the current board of directors which has been getting the Danish 3R-Center off the ground since its establishment in 2013, but as one of many consequences of the pandemic, the Danish Parliament has not had the time to adopt the new veterinary agreement aimed at extending the life of the centre by a new four-year period. The existing board members have consequently been asked to stay on for another year, which everyone has accepted, with the exception of Adrian Smith. Adrian will therefore be replaced by Birgitte Kousholt of Aarhus University in the coming year.

With his large network and keen knowledge from Norway's 3R platform NORECOPA, Adrian has been of great service to the centre, for which I would like to thank him. At the same time, I would like to thank the rest of the board for their dedicated efforts in the past year.



PHOTO: KIM GRANLI

Also, we did not manage to distribute our research funding in 2021, as Birgitte's appointment had not been finalized at the board meeting in December, which is why the funding will be distributed at an extraordinary meeting in January. However, we have been pleased to see the increasing quality of applications since the first grants eight years ago. We are also pleased with the many publications resulting from the funded projects.

I wish to express my gratitude to the Danish Animal Welfare Society, DOSO, LEO Pharma, Lundbeck, Novo Nordisk and the Ministry of Food, Agriculture and Fisheries for supporting the Danish 3R-Center in 2021.

Despite some interaction having to take place online, we experience excellent dialogue with our stakeholders.

I also wish to extend my deep gratitude to our highly professional and hard-working secretariat which is the daily engine in the centre's work.

We are now looking forward to 2020 where we can hopefully get out and meet many of those who are already interested in the 3Rs and those who may become so in the future.

Best regards

Axel Kornerup Hansen

Chairman of the board of the Danish 3R-Center
Chairman of the Danish National Committee for the Protection of Laboratory Animals Used for Scientific Purposes.

1



Research

An important part of the Danish 3R-Center's work is to provide financial support to 3R research projects on behalf of the Minister for Food.

Once a year, the Danish 3R-Center thus calls for applications for research projects that in one way or another have the potential to improve the laboratory animal area.

Research funds

The Danish 3R-Center manages the allocation of DKK 1.5 million a year to support research in one or more of the 3Rs – *Replacement, Reduction and Refinement*.

Who is eligible to apply for funding?

Persons who are scientifically affiliated with an organization, institution or company in Denmark.

It is possible to apply for up to DKK 500,000.

Research funding 2023

The call for the next round of applications for research funds for 2023 is planned to open in August 2022.

Stay up to date about this on the Danish 3R-Center's website en.3rcenter.dk or sign up for the Danish 3R-Center's newsletter en.3rcenter.dk/newsletter-subscription

RESEARCH PROJECTS SUPPORTED BY THE DANISH 3R-CENTER IN 2021

The Danish 3R-Center received 16 applications for support, of which the following three received a total of DKK 1.5 million.



Human derived blood-brain-barrier spheroids to study brain infections

Yvonne Adams / University of Copenhagen

Human brain infections can be caused by a variety of pathogens including bacteria (*Borrelia* sp. Lyme neuroborreliosis), parasites (*Plasmodium falciparum*, cerebral malaria) and viruses (Varicella zoster virus – chicken pox). Animal models ranging from mice, rabbits, dogs and monkeys have all been utilised to model how the infections cause disease and interact with the blood-brain-barrier and the immune system. Sadly, none of these animal models accurately represent what happens in the human body.

To address this short coming, the project will utilise a human cell based model of the blood-brain-barrier ; by combining human endothelial cells, astrocytes and pericytes – the components of the blood-brain-barrier – they self-assemble into spheroids. These balls of cells orient themselves with an endothelial layer on the outside, underneath is the pericyte layer, and finally the astrocytes make up the central core of the spheroid. All cells are in

direct contact with each other allowing for a more natural interaction, closer to that found in the human body. Using advanced microscopy techniques, it is possible to measure the integrity of the barrier, receptor expression, and gross effects of pathogen exposure. This system also allows for the addition of immune cells, such as macrophages and T cells, to allow for investigations into the transmigration of these cells in response to infection.

This project reduces and replaces the need for animal models, allowing for the rapid investigation of multiple pathogens on human cells. Their ease of use also provides a platform to rapidly screen chemotherapeutics and antibodies for their ability to stop pathogens damaging the blood-brain-barrier, and to determine if they can alleviate the effects of exposure improving treatment and outcomes for patients suffering from these diseases.

Cellular heterogeneity as predictor for the **differentiation and regenerative potential of bone marrow stromal cells**

Ali Jamil / University of Southern Denmark

Human bone is a dynamic tissue, which undergoes continuous remodeling, that is the removal of old and damaged bone replaced by new bone matrix. The specialized cell types involved in bone formation are descendants of a pool of immature progenitor cells (BM-MSCs) residing within the bone marrow. These cells can be easily expanded in culture for which they gained a huge momentum for the treatment of degenerated bone diseases such as bone fractures and cartilage injuries.

However, the clinical outcomes of BM-MSC-based regenerative therapies have revealed varying results. This is presumably due to the injection of a heterogeneous pool of cells since isolation of BM-MSCs is based on the cells ability to attach to tissue culture plastic, a property which is not unique to BM-MSCs. Thus, BM-MSC cultures can be contaminated with cells that do not contribute to or even hamper tissue regeneration. Our aim is to investigate how patient-derived BM-MSCs differ in their BM-MSC subpopulation composition as well as how these BM-MSC subpopulations differ in their tissue regenerative potential.

Unfortunately, the golden standard of identifying all progeny cell-types of a particular cell population is tracking the cell population by a method referred to as lineage tracing, which takes place in live mice. In lineage tracing, a single cell is labelled typically with a marker in such way that the marker transmits to the cell's progeny. With this, a set of labelled clones allow tracking of the single cell during its lineage differentiation pathway in a microscope to reveal all progenitor cells.

A potential alternative to lineage tracing in mice is recruiting voluntary human donors to obtain and use their cells to build a regression model through another method called single-cell RNA sequencing. Then, this model can be benchmarked by comparing the results from the sequencing experiment with experimental results that shows differentiation and bone tissue regenerative abilities of investigated BM-MSC subpopulations. Proven successful, our alternative strategy may circumvent lineage tracing in mice while increasing the confidence level of the resulting regression model that predicts cellular differentiation potential based on BM-MSC sample composition. In summary, the outcome of our project may approve of an alternative strategy to the current golden standard of lineage tracing and differentiation investigation assays in living mice.

The Danish 3R-Center's Symposium 2021

It was clear to see that many had missed seeing each other in person at conferences, as the 2020 symposium had been cancelled due to COVID-19. Here, the year's symposium is about to begin.



PHOTO: KIM GRANLI

Automated animal activity monitoring

to reduce animal use and improve animal welfare

Gabriel Pedersen / Statens Serum Institut

Vaccines are important to protect the population against viral diseases, including SARS-CoV-2, which is currently causing the COVID-19 pandemic. When developing a vaccine, it is necessary to administer virus to animals to elucidate whether vaccine candidates are protective. E.g. for testing vaccines against COVID-19, candidate vaccines are administered to animals and these are then challenged with the virus. The viral challenge is a fine tuned balance, since administering too much virus will cause unnecessary suffering and is not physiologically relevant (not reflecting the virus exposure normally encountered), whilst administering too little virus will give only few symptoms and thus requires more animals to assess if the vaccine prevents disease. Monitoring disease in itself presents some challenges. Animals are monitored by animal caretakers scoring for activity, however this is not done continuously and is based on a subjective assessment.

In this project, we will use automated monitoring to continuously assess animals following viral infection. In this way, the data quality should be improved, allowing us to use lower viral challenge doses and thus improving animal welfare. Furthermore, we expect that automated monitoring, by giving less data variation, will allow us to reduce the number of animals used to test protective efficacy of vaccines.

The Danish 3R-Center's Symposium 2021

Welcome by moderator Christine Nellemann. The moderator at this year's symposium was Christine Nellemann. Christine is a board member of the Danish 3R-Center and was chairwoman in the period 2013–2020. Professor Axel Kornerup Hansen took over as chairman after Christine.



PHOTO: KIM GRANLI



READ MORE AT
[EN.3RCENTER.DK](https://en.3rcenter.dk)

Did you know that...?

The Danish 3R-Center has supported a total of 25 projects since it was founded. You can find a list of all the projects in the appendix of the annual report, and further details about the projects are available on the 3R-Center's website: en.3rcenter.dk/research/projects

2



Dissemination of information

Dissemination of information has always been key to the Danish 3R-Center's work. Not only to individuals with a professional interest in laboratory animals and alternatives, but also to interested private individuals as well. The Danish 3R-Center believes that knowledge about the use of laboratory animals is fundamental for being able to discuss the matter on an informed basis in society.

The Danish 3R-Center's Symposium 2021

16-17 November

The largest individual event for the Danish 3R-Center is the annual, international 3R symposium. As the symposium was not held in 2020 due to the pandemic, it was particularly gratifying that this year's symposium could go ahead as planned.

The symposium is an opportunity for the Danish 3R-Center to tell about its work over the year and gives researchers financially supported by the centre a platform for disseminating their 3R project results to the laboratory animal milieu. The Danish 3R-Center also invites national and international personalities with 3R expertise to talk about their respective spheres of work.

180 people had registered for the symposium, which was fewer than in 2019. This was predominantly because most international guests chose not to travel to Denmark at a time when Covid was surging in Europe again. For the same reason, the Danish 3R-Center had offered international speakers the opportunity to give their presentations online, which worked without major technical glitches and could therefore be the norm going forward to avoid unnecessary climate impact.

It was evident that the symposium visitors had been longing to meet physically after an extensive period of online conferences, where the networking aspect in particular is under par.

The symposium visitors benefited from no less than 18 presentations, half of which were by speakers who had received support for their research from the Danish 3R-Center.

It is also at the Danish 3R-Center's symposium that the 3R-Center presents its annual award to recognize a special 3R contribution.



**READ MORE AT
EN.3RCENTER.DK**

You can find the programme, presentations and posters from this year's symposium at the 3RCenter's website.
en.3rcenter.dk/symposium/symposium-2021

The Danish 3R-Center's Symposium 2021

"Drugs and chemical safety – a scientific revolution in its making" by Thomas Hartung. Thomas Hartung is a professor at Centers for Alternatives to Animal Testing (CAAT), at the Johns Hopkins Bloomberg School of Public Health. Thomas gave an online presentation of how the technological advances in which cell cultures are combined with bioengineering are revolutionary and essential in the approach to the development of new products and their safety evaluation.



PHOTO: KIM GRANLI



The Danish 3R-Center's Symposium 2021

Status report for the Danish 3R-Center by chairman and professor Axel Kornerup Hansen. Axel gave a briefing on the work of the 3R-Center and the national committee since the last symposium (2019).

The 3R Prize

Rie Vinggaard, DTU, won the 2021 3R Prize

Rie Vinggaard was this year's highly deserving recipient of the Danish 3R-Center's 3R Prize. Rie was awarded the prize in acknowledgement of her keen focus on using non-animal models in her research. Rie Vinggaard thus became the eighth recipient of the Danish 3R-Center's 3R Prize.

Rie Vinggaard is a professor of molecular toxicology at the National Food Institute where for many years, she has been working with endocrine disruptors and their effect on unborn children. In this connection and in cooperation with mathematicians and statisticians, she has played an important role in developing computer models that can assist in predicting a large number of problematic endocrine-disruptive effects while eliminating the need for a large number of laboratory animals.

Rie was awarded the prize at the Danish 3R-Center's international symposium in Copenhagen on 16 November by Axel Kornerup Hansen, chairman of the board of the 3R-Center. On behalf of the entire board of directors, Axel expressed deep respect for Rie's work, which is characterized by a keen focus on research questions combined with an awareness of the vast potential for animal-free methods.

Axel proceeded to present flowers and a financial token of appreciation to Rie to well-deserved applause from the symposium participants.

Rie subsequently gave a talk about her work, which is largely based on research without using animals.

Winners of the 3R Prize

2014

Ellen Margrethe Vestergaard
Danish Medicines Agency

2015

Hanne Gamst-Andersen
Novo Nordisk

2016

The QSAR Team, represented by
Eva Bay Wedeby and Nikolai Georgiev Nikolov
Technical University of Denmark

2017

Grete Ostergaard
University of Copenhagen

2018

Birgitte Kousholt
Aarhus University

2019

Thomas Bertelsen
Novo Nordisk

2020

Dorte Bratbo Sørensen
University of Copenhagen

2021

Rie Vinggaard
The Technical University of Denmark



PHOTO: KIM GRANLI

The Danish 3R-Center's Symposium 2021

Presentation of the 2021 3R Prize to Rie Vinggaard. Rie is a professor of molecular toxicology at the National Food Institute where for many years, she has been working with endocrine disruptors and their effect on the unborn child. Rie Vinggaard was awarded the prize in acknowledgement of her keen focus on using animal-free models in her research.

3R symposium 2022

The Danish 3R-Center's 2022 Symposium will be held in Copenhagen on 8–9 November



The Danish 3R-Center's website **en.3rcenter.dk**

One of the most essential features of the 3R-Center's website is the dissemination of news. On the website, it is possible to follow national 3R initiatives and events held by the Danish 3R-Center, the Danish National Committee for the Protection of Animals used for Scientific Purposes, and the Animal Experiments inspectorate and thus stay up to date on the latest news about laboratory animals and the 3Rs. For this purpose, the website disseminates national and international research information that can inspire the website visitor's own work.

Another important task managed by the Danish 3R-Center is the dissemination of knowledge about laboratory animals to interested individuals, including schoolchildren. Much of the website's content is intended to serve this purpose. At the website, visitors can find information about experiment targets, the number and species of laboratory animals used, and visitors can also find information on the level of severity to which laboratory animals are exposed in procedures.

The Danish 3R-Center's website

Researchers:

News from the 3R world

Information about relevant events (symposiums, mini-seminars, animal welfare bodies' annual meetings, etc.)

Newsletters

Research funds

Research projects

The 3R Prize

Resources for improving your research (e.g. PREPARE)

Articles about laboratory animals and animal testing

Presentations from 3R symposiums organized by the 3R-Center

Guidelines for implementing EU Directive 2010/63/EU

Links to teaching resources (for future users of laboratory animals)

Links to tissue-sharing services

Annual reports

Statements and recommendations

Individuals/schoolchildren:

Teaching materials on laboratory animals and the 3Rs

Factual and basic information about laboratory animals

- What are laboratory animals used for?
- How many laboratory animals are used?
- Which species are used in research?

Politicians and stakeholders:

Goals and goal-achievement forms for the Danish 3R-Center

Minutes of board meetings

Annual reports

Did you know that...?

The Danish 3R-Center has developed teaching materials about laboratory animals and the 3Rs for lower and upper secondary school classes. The class sets can be ordered free of charge on the 3R-Center's website (only available in danish).

The Danish 3R-Center's Symposium 2021

"Current JRC activities in the field of biomedical research, with a focus on indicators to monitor impact and innovation of funded biomedical research" by Francesca Pistollato. Francesca Pistollato works at the European Commission Joint Research Centre in Italy. Francesca gave a talk on the challenges of animal models and the indicators that can be used to measure the impact and innovation of biomedical research.



The Danish 3R-Center's Symposium 2021

Gabriel Kristian Pedersen, Statens Serum Institut, gave an update on his project on "Automated monitoring in animal models for studies of vaccines against viral infections", which received funding from the 3R-Center in 2021. Read about Gabriel Kristian Pedersen's project on page 14.



PHOTO: KIM GRANLI

The Danish 3R-Center's Symposium 2021

Ali Jamil, the University of Southern Denmark, gave an update on his project on "Cellular heterogeneity as predictor for the differentiation and regenerative potential of bone marrow stromal cells", which received funding from the 3R-Center in 2021. Read about Ali Jamil's project on page 12.



PHOTO: SØREN HARTMANN/DR

An inside view with Anders Agger: **Animal experimentation**

In late 2020, the Danish 3R-Center's secretariat was approached by Søren Hartmann of the Danish Broadcasting Corporation who produces the TV programme series *An inside view with Anders Agger* (*Indefra med Anders Agger*). He was doing research for a programme on animal experimentation.

As mentioned previously, the Danish 3R-Center is very interested in informing the public about laboratory animals and animal testing, which is why the 3R-Center saw the Danish Broadcasting Corporation's interest in the subject as a golden opportunity to contribute knowledge and ideas to the participants, both to ensure that the Danish 3R-Center could vouch for the technical content of programme and to use the programme to raise awareness of the field going forward.

The Danish 3R-Center is very satisfied with the programme which aired on DR2 on 16 December 2021, and the big effort made by the secretariat in assisting the programme's producer during 2021 seems well worth it.

An inside view with Anders Agger: Animal experimentation

For the first time ever, the Danish Defence gives access to a TV crew when they let Anders Agger witness how they use pigs to practice patching up gunshot wounds and other lethal lesions. At the same time, two young researchers try to justify force-feeding mice with a pesticide that induces Parkinson's and ALS. To understand the experiments he witnesses, Anders Agger contacts the Animal Experimentation Council which is tasked with ensuring compliance with all the rules.

The programme is available on
www.dr.dk/drtv/

The Danish 3R-Center's Symposium 2021

Kirsten Madsen, University of Southern Denmark, gave an update of her project on "Introduction of new human ex vivo model systems to study tumorigenesis in kidney cancer", which received funding from the 3R-Center in 2020. Read about the project on the 3R-Center's website.



PHOTO: KIM GRANLI



The Danish 3R-Center's Symposium 2021

Yvonne Adams of the University of Copenhagen gave an update on her project on "Human derived blood-brain-barrier spheroids to study brain infections", which received funding from the 3R-Center in 2021. Read about Yvonne Adams' project on page 11.

3



The Danish National Committee for the Protection of Animals used for Scientific Purposes

(the national committee)

In Denmark, we both have a 3R-Center and a national committee. As the seven members of the committee also function as the board of the Danish 3R-Center, it will probably be difficult for many to distinguish between the two initiatives, which is why this annual report will account for some of the work done under the auspices of the national committee.

The Danish National Committee for the Protection of Animals used for Scientific Purposes

Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes orders Member States to set up a national committee for the protection of these animals.

The National Committee for the Protection of Animals used for Scientific Purposes works to promote the use of the 3R principles.

The committee is set up to advise the Danish Animal Experimentation Inspectorate and animal welfare bodies in matters relating to the acquisition, breeding, accommodation, care and use of laboratory animals and to facilitate the sharing of best practices.

Note: Thus, the existence of the committee is required by law, whereas the Danish 3R-Center is a national initiative whose purpose is not only to provide advice but also initiate and disseminate information about 3R research and results.

The committee's work in 2021

In 2021, the committee has mainly focused on the following: The committee's website, Annual meeting of Animal Welfare Bodies, Drafting of three statements / recommendations on the animal welfare bodies, antibody production and the use of animals for teaching purposes.

In addition, the committee has worked on strengthening cooperation with the Animal Experimentation Council, e.g. by board chairman Axel Kornerup Hansen participating at some of the council's meetings to keep the committee abreast of the council's current debates and thus facilitate identification of potential areas of collaboration.



The Danish 3R-Center's Symposium 2021

"Investigation and analyses of internal validity in Danish preclinical research" by Birgitte Kousholt, Aarhus University. Birgitte Kousholt is a new member of the board of the Danish 3R-Center. Birgitte presented her project, which received funding by the Danish 3R-Center in 2019. Read about the project on the 3R-Center's website.

PHOTO: KIM GRANLI



The Danish 3R-Center's Symposium 2021

"Impact of shelter enrichment of metabolic cages in studies of protein metabolism" by Helle Nygaard Lærke, Aarhus University. Helle gave a presentation on her project, which received funding by the Danish 3R-Center in 2019. Read about the project on the 3R-Center's website.

The committee's website en.natud.dk

By contrast with the Danish 3R-Center's website which mainly addresses researchers and the general public, the committee's website is primarily aimed at Denmark's animal technicians. It gives them access to news within their work areas, and they can find useful knowledge about accommodation, handling and various trial procedures.

The website also provides information about the recommended structure of the animal welfare body and information about the tasks that the animal welfare body must manage.

The committee's website is also where you will find information about the Annual Meeting of the Animal Welfare Bodies.

Annual Meeting of the Animal Welfare Bodies 2021

The Annual Meeting of the Animal Welfare Bodies is a forum for lectures, workshops and networking – primarily centred on laboratory animal welfare. In recent years, the annual meeting has included a market place where meeting attendants introduce one another to new solutions/3R initiatives that are usually ready for immediate application.

The 2021 Annual Meeting of the Animal Welfare Bodies was held on 16 September 2021 at Lundbeck that had made premises available to the committee.

The first part of the annual meeting (morning) is reserved for members of Denmark's animal welfare bodies, and the meeting themes were transport of laboratory animals and the organization, communication and tasks of the animal welfare bodies.

The second part of the meeting (afternoon) is every year open to everyone with a professional interest in laboratory animals. This part of the meeting also offers a number of lectures before the meeting continues at the market place where meeting attendants show one another the 3R initiatives that they have found useful in their respective laboratory animal institutions.

The 2022 Annual Meeting of the Animal Welfare Bodies will be held in Copenhagen on 1 June

The Danish 3R-Center's Symposium 2021

"A new era of 3R resources and networking: the European 3R Centres" by Adrian Smith. Adrian Smith was a member of the board of the Danish 3R-Center from 2013 to 2022. Adrian is also part of Norecopa. Adrian gave a presentation on the resources expended on initiatives relating to the 3Rs and how the first EU directive regarding the protection of animals used for experimental and other scientific purposes (86/609/EEC) and its counterpart from the Council of Europe (ETS 123) blazed the trail by including information about the 3Rs. Prior to Adrian's presentation, chairman Axel Kornerup Hansen acknowledged his great work for the Danish 3R-Center.



PHOTO: KIM GRANLI

Statements

During 2020, the National Committee for the Protection of Laboratory Animals Used for Scientific Purposes/the Danish 3R-Center published three statements on laboratory animal aspects about which the committee/board considers it essential to express an opinion. You will find the three statements below.

Danish animal welfare bodies function excellently

In 2019, the Steering Group of the Animal Welfare Bodies¹ conducted a study of Denmark's animal welfare bodies to learn about their organization, communication and tasks.²

Based on this study – compared with lessons learnt by the National Committee for the Protection of Animals Used for Scientific Purposes – the committee concludes that the animal welfare bodies in Denmark function excellently, even if their establishment was not made compulsory until 2013.

One of the reasons why the committee believes that we have well-functioning animal welfare bodies in Denmark is the close collaboration between them. The collaboration is exemplified in the above-mentioned steering group, and representatives of several animal welfare bodies also work together in the network for members of Danish animal welfare bodies.³

Both forums work with knowledge-sharing to enable animal welfare bodies to inspire each other, such as in terms of organization, communication and tasks, for the benefit of staff and laboratory animals alike.

The committee finds that Denmark's animal welfare bodies also involve themselves in the committee's work, as evidenced by the Annual Meeting of the Animal Welfare Bodies⁴ which the vast majority of Danish animal welfare bodies choose to attend, making it highly successful and presumably quite unique in an international context.

Furthermore, the above-mentioned study of the organization, communication and tasks of the animal welfare bodies does not give rise to any major concerns, also indicating that the animal welfare bodies are well-functioning.

¹ The Steering Group of the Animal Welfare Bodies comprises representatives from the National Committee for the Protection of Animals used for Scientific Purposes – including secretariat staff – and representatives of a range of Danish animal welfare bodies. One of the tasks of the steering group is to assist in the planning of the Annual Meeting of the Animal Welfare Bodies.

² natud.dk/om/rapporter/

³ natud.dk/dyrevelfaerdsorganer/det-private-netvaerk-for-dyrevelfaerdsorganerne/

⁴ natud.dk/dyrevelfaerdsorganer/dvo-aarsmoede/



The Danish 3R-Center's Symposium 2021

"Underchallenged when not at test. Boredom in laboratory mice" by Lars Lewejohann. Lars Lewejohann works at Berlin's Freie Universität.

Lars gave a presentation on boredom in laboratory mice – and on how to measure and see this, while also proposing methods to prevent boredom.

PHOTO: KIM GRANLI

Recommendation on antibodies

In 2020, the European Centre for the Validation of Alternative Methods (ECVAM) published their recommendations for production of antibodies without the use of animals (EURL ECVAM Recommendation on Non-Animal-Derived Antibodies).

Though the conclusions of the report propose the production of non-therapeutic antibodies without using animals, the National Committee for the Protection of Animals used for Scientific Purposes does not believe that it will be possible at present to implement non-animal production of all non-therapeutic polyclonal antibodies while also complying with the provisions of the Danish Act on Animal Experimentation, stipulating that non-animal methods must be equally suitable (section 6(3)).

At the same time, however, the Committee believes that based on the ECVAM report, Denmark's competent authority (the Animal Experimentation Council), should facilitate an ongoing assessment of whether a non-animal method is available for all or parts of the antibody production related to the individual application – both when reviewing new applications for permits to produce antibodies and in already approved antibody production trials.

This makes it possible to meet the requirement set out in the Act on Animal Experimentation that permission be granted for a specified type of experiments (section 3(1)) and that animals may not be used if non-animal methods must be assumed to be equally suitable (section 6(3)).

The Committee acknowledges that it can be difficult to make an advance assessment of each individual antigen and antibody and that it could entail major, difficult permit work for large companies in the event that a collective permit cannot be granted for the production of antibodies against a large group of antigens.

For the issue of permits for antibody production, the Committee therefore proposes that the permit holder:

- may still be granted a permit for the production of antibodies against a large group of antigens but must retain the services of a named expert in the production of non-animal-derived antibodies as a condition for the permit
- in connection with the annual report of activities under the permit must complete a form, stating:
 - the type of antigens against which antibodies have been produced
 - the method(s) – with or without animals – used for the purpose in each specific instance
 - the measures generally taken to ensure a continued development towards reduced use of animals for production of antibodies.

Use of animals in teaching

Since the establishment of the Danish 3R-Center and the National Committee for the Protection of Animals used for Scientific Purposes (the national committee), the board has focused on the intention of the EU directive of replacing animals with animal-free methods wherever possible. A focus area has been the use of animals in teaching.

In Denmark, animals are used in teaching at certain science study programmes. Teaching examples include 1) learning of basic skills (e.g. veterinarian training) or 2) lessons in anatomy/physiology/pharmacology, etc., where animals are used purely for educational purposes and not as training a method. It could also include teaching in connection with courses in which the above distinctions apply.

The Danish 3R-Center and the national committee in 2020 conducted a questionnaire survey on the use of laboratory animals in teaching, distributed to everyone with a permit to use animals in teaching. The point of departure was the use of animals for educational purposes and at continuing education courses at various universities, hospitals and vocational schools. For this reason, animals used in laboratory animal courses or animals used for peer-to-peer training in specific methods at companies and/or research sites were not included.

In the period 2017–2019, an average of 4,200 animals were used each year for teaching (items 1 and 2 above), including about 775 animals a year for teaching in anatomy/physiology/pharmacology, etc. (item 2 above).

In addition, the Danish 3R-Center and the national committee wanted to expand the survey to include information about animals used in teaching without requiring an animal experiment permit. This concerns animals culled without a prior permit-based procedure, for subsequent use of the body, organs or tissue in teaching. It also concerns live animals that are used for educational purposes but which are not exposed to a severity level that exceeds the needle criterion.

Everyone holding a permit to use animals for educational purposes responded to the questionnaire by the deadline, but this was unfortunately not the case for a few users at the University of Copenhagen whose use of animals for

educational purposes does not require a laboratory animal permit. The Danish 3R-Center is not a public authority per se and is thus not in a position to make demands on users of laboratory animals, but can only encourage them to participate in such a survey.

An example of animals used for purposes that do not require a laboratory animal permit is the use of frogs in physiology/pharmacology courses. In this instance, it may be relevant to ask whether the necessary learning could be obtained without using animals. In addition to the frogs used in the course itself, many frogs die, both in transit to Denmark and during subsequent accommodation.

Based on the survey on the use of animals for educational purposes, the Danish 3R-Center and the national committee wish to draw attention to the following:

- The majority of laboratory animals used for educational purposes in Denmark are used for learning basic skills (e.g. teaching of medical doctors, veterinarians or the like). The Danish 3R-Center/the committee generally finds this use acceptable. However, it should always be considered, also for this type of teaching, whether the learning targets could be achieved without using laboratory animals and if the use of non-animal methods (dummies, simulators, video recordings, etc.) could replace laboratory animals in part or in full.
- For educational activities whose purpose is not to learn a technique and the animals are only used for learning purposes (e.g. within anatomy/physiology/pharmacology, etc.), the Danish 3R-Center/the committee generally believe that laboratory animals should not be used. This also applies to the use of animals in situations that do not require a laboratory animal permit.
- The use of animals for purposes which do not require a laboratory animal permit is a special problem, as these animals are not included in the Danish statistics because the animals do not have to be reported to the Animal Experiments Directorate, which makes it difficult to estimate the exact number.

4

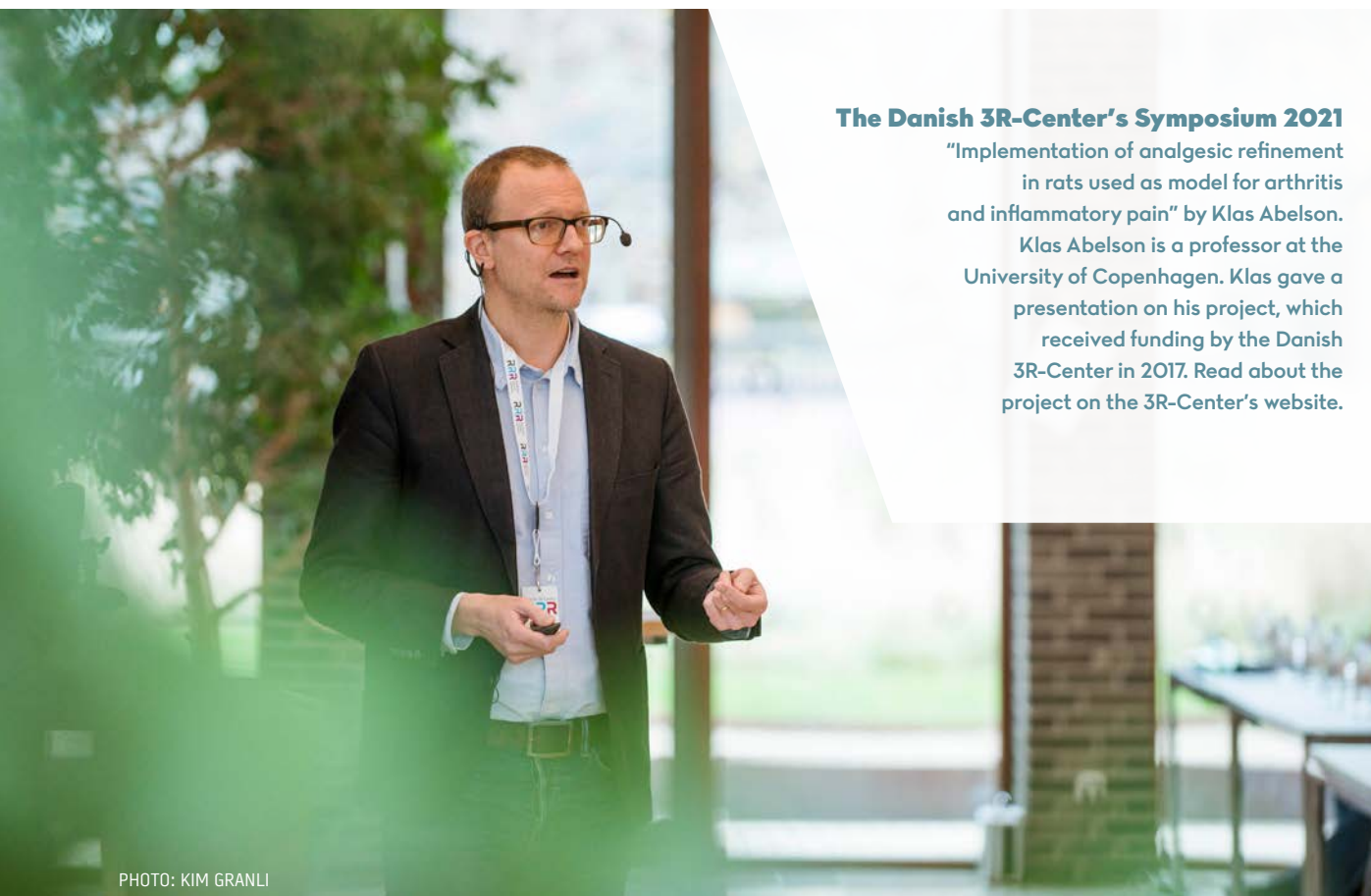


3R activities at external research institutions

In recent years, the Danish 3R-Center has given researchers from a number of external research institutions the opportunity to describe their 3R-related activities in our annual report to give an impression of the widespread efforts in Denmark to improve the area of laboratory animals.

In recent years, the University of Aarhus, Novo Nordisk, the Technical University of Denmark, the University of Copenhagen, LEO Pharma and Lundbeck have thus assisted in this.

This year, the University of Southern Denmark has provided a valuable contribution to our annual report.



The Danish 3R-Center's Symposium 2021

"Implementation of analgesic refinement in rats used as model for arthritis and inflammatory pain" by Klas Abelson.

Klas Abelson is a professor at the University of Copenhagen. Klas gave a presentation on his project, which received funding by the Danish 3R-Center in 2017. Read about the project on the 3R-Center's website.

PHOTO: KIM GRANLI

3R initiatives at the University of Southern Denmark (SDU)

Louise Langhorn, veterinarian / **Diana Hansen**, animal keeper responsible for training / **Stefanie Kolstrup**, veterinarian

At the University of Southern Denmark, laboratory animals are used for basic research, translational research and education; mainly in the field of health sciences with particular focus on cardiorenal, neurobiological, cancer and inflammation research. In addition, laboratory animals are also used in scientific and technical research.

A common feature of the use of laboratory animals at SDU is that as a central laboratory animal facility, the Biomedical Laboratory is responsible for procurement and care of the animals and for providing assistance for experiments and veterinary advice. The Biomedical Laboratory staff

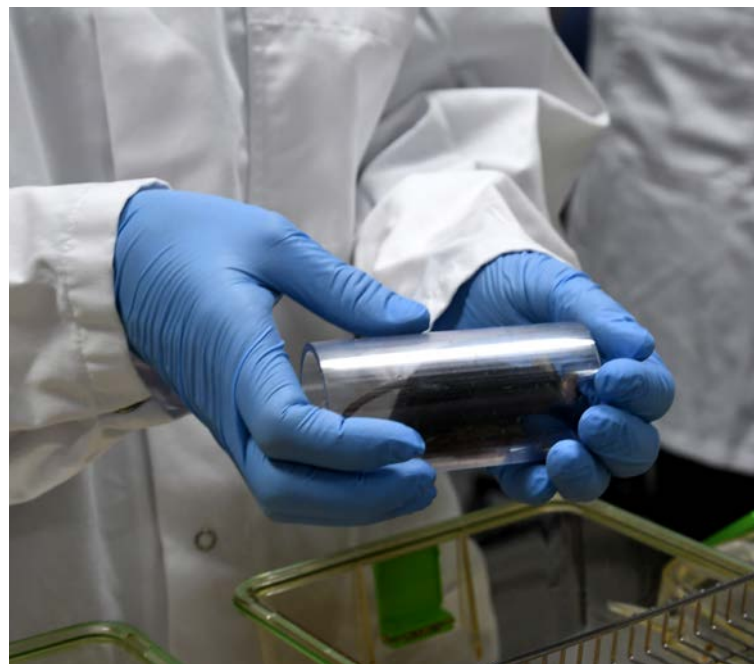
give high priority to animal welfare and the 3Rs, which they consider to be fundamental for the university's ambition to make laboratory experimentation accessible to researchers.

Two of the 3R activities launched by the Biomedical Laboratory are the introduction of tunnel handling of mice and the training of sheep and pigs. Both initiatives aim to help reduce handling-related stress in laboratory animals. In addition, the use of simulation training is introduced in post-graduate programmes in surgical specialties as an initiative to reduce the number of pigs required for training surgical skills.



PHOTO: BIOMEDICINSK LABORATORIUM

Tunnel handling for mice



Introduction to tunnel handling for mice

In November 2019, we introduced tunnel handling for mice as the preferred method for lifting mice out of their cages at the Biomedical Laboratory. Several animal keepers tested tunnel handling on a small scale before, but believed it to be too time-consuming for routine cage changes.

At the Annual Meeting of the Animal Welfare Bodies in May 2019, members of the animal welfare body had a discussion with the authors of a poster about introducing tunnel handling for mice at another institution. It was emphasized that you strong management backing is required in order to introduce a brand-new working method such as tunnel handling, and that it is important to have scheduled adjustment plans in place for staff and researchers. Based on this discussion, the poster authors were invited to Odense to present the lessons they have learnt from introducing tunnel handling. They also held a hands-on workshop for all animal keepers to test tunnel handling and cupping.

This was followed by an introduction programme with two "ambassadors" who served as mentors for colleagues and researchers. Now, some two years later, tunnel handling has become routine and most researchers have now introduced this method for handling animals.

We introduced tunnel handling as we believed it would improve animal welfare and reduce anxiety and stress in mice and, importantly, increase job satisfaction. It soon turned out not to take longer, but that it was important to allocate sufficient time to learn the method and get used to it. We therefore chose to set aside slightly more time for cage changes during a transitional period.

Our experiences are generally positive, and the animal keepers who originally were more reluctant to use the method have grown to like using it. To ensure that future researchers become comfortable with the method as well, we teach tunnel handling at our laboratory animal science courses.

Training of pigs and sheep

The Biomedical Laboratory aims to give priority to the training of pigs and sheep so that the animals participate voluntarily in experiments wherever possible. The advantage of this is that both animals and experiments are less impacted by stress, while reducing the occupational risks of handling large laboratory animals. Focused, targeted training of laboratory animals requires adequate time and attention to each animal, which can be challenging in a packed daily work routine. The Biomedical Laboratory has appointed an animal keeper to be responsible for training and for developing training programmes for specific trials. The responsible person regularly attends seminars and courses in the subject to manage the task and keep our knowledge on new techniques and training methods up-to-date. Knowledge sharing with colleagues is essential for staying motivated and succeeding with the project.

The training starts as soon as we receive the animals so that they feel safe and comfortable about our presence as soon as possible. Pigs and sheep are obtained from local farms and are usually unaccustomed to close human contact. Training ensures that the animals are calm and easier to work with, for instance when inducing anaesthetics.

Pigs are curious by nature; they like to explore things and do not share the escape instincts and herd mentality of sheep. For this reason, we take different approaches to training these animals.

In the acclimation phase, we habituate the animals to the proximity of humans during mucking out and feeding and by our presence in the pen, offering varied treats in the form of apples, raisins, bananas, apple juice and sour milk. We make an effort to activate the pigs every day, both those used for surgical training and for research projects. Activation involves activities such as roaming the pig house, paper bags packed with treats or feed, wrapped hay (for eating and nesting), various enrichment items suspended in the housing unit, rummaging materials (wood chips as bedding), baths in the corridor and touching. When performed for about a week, this activation will often be adequate for the animals to accept being injected without being fixated.

If a project requires pigs to participate voluntarily in special procedures, we use clicker training. This will often focus on teaching the animals to stand still while administering an injection or checking on a permanent urine catheter.

The Danish 3R-Center's Symposium 2021

"Use of primary isolates from human kidney to study the molecular aspects of blood pressure regulation" by Henrik Dimke. Henrik Dimke is an associate professor at the University of Southern Denmark. Henrik gave a presentation on his project, which received funding by the Danish 3R-Center in 2017. Read about the project on the 3R-Center's website.



PHOTO: KIM GRANLI



PHOTO: BIOMEDICAL LABORATORY

We aim for all training to be as positive as possible, and we often use positive reinforcement in the form of treats.

For clicker training, we use a target which the animals are trained to stand near and/or follow. We aim for all training to be as positive as possible, and we often use positive reinforcement in the form of treats. It is important that we make the task as easy as possible for the animals to perform. This means that we make sure to eliminate any interference during training and to make the training set-up as simple as possible: it is our job to give the animals a successful experience at each training.

We divide the training into sub-targets and raise the criterion slowly (based on achievements), requiring more and more from the animals until they achieve a target. By way of example, we start by rewarding mere attention to the target, though we ultimately want the animal to be touching the target. Pigs in particular are quick learners due to their curiosity and intelligence, which enables us to rapidly raise the criteria and learn them new behaviour. The next step for the pigs is to introduce a whistle instead of a clicker, as this enables the trainer to perform a procedure using both hands.

It takes more patience to train sheep than pigs. If, on top of things, they are also stressed or frightened, the task is even more difficult. We have successfully trained a sheep to follow a target and get in position to be strapped down for blood sampling. This sheep has now become so sociable and safe that she will follow us around and offer this behaviour also outside training situations. The sheep in question became so comfortable with us that it was impossible to move her from the flock to train by herself. If sheep can be removed from the flock without being stressed, training becomes significantly easier.

We use clicker training for sheep in the same way as we train the pigs, i.e. using treats. Suitable treats for sheep can consist of concentrated feed, apples, dry pasta and raisins. Previously, training of sheep at the University of Southern Denmark mainly involved using feed and habituation to enable handling, and clicker training as a method has only been put into use for sheep in recent years.

We introduced yet another form of training in the autumn of 2021: CAT (Constructional Approach Treatment). The method is ideal for larger groups of animals and is based on the animals' safety threshold in relation to how close we can approach them. This form of training is conducted without treats or physical contact. The reward for remaining calm when we approach is that we stop and give the sheep space by walking away again. CAT is negative reinforcement where we show the sheep that with another response, they can achieve the same as they would by running away, i.e. that they increase our distance to us. This means that when the sheep stay calm, we will move away. We will slowly diminish the threshold distance for their escape response so that we can eventually go right up to them and continue training with positive reinforcement. So far, this new type of training shows promising results in the form of a safer flock of sheep that seeks contact proactively. We found the inspiration for this from a course on clicker training for animals held by Annette Pedersen, training coordinator at Copenhagen Zoo, and Dorte Bratbo, veterinarian and training enthusiast at the University of Copenhagen.

At the Biomedical Laboratory, we consider training to be a good, necessary investment for the benefit of both animals and keepers.

Surgical skills courses

Surgical training courses generally use pigs for surgical and laparoscopy training. Minimally invasive surgery such as laparoscopy is used in several surgical specialities, such as general surgery, gynaecological and urological surgery. The Danish Health Authority defines the framework for mandatory general courses required for medical specialties. The courses include operative and laparoscopic surgery on pigs, held at the Biomedical Laboratory, for instance. The courses are aimed at doctors in course positions within surgical specialties.



PHOTO: BIOMEDICAL LABORATORY

Before the course participants work on sedated pigs, they must complete a theoretical course and simulation training. The theoretical course both involves theory and hands-on exercises using bead plates and other dummies. After the first compulsory exercises, the participant moves on to the simulation component to train surgical procedures in a computer simulator.

Only after completing the simulation component are the participants allowed to attend a day course to train on a sedated pig. The use of computer simulations significantly reduces the need for sedated pigs to give the participants sufficient skills. In addition, the prior theoretical and practical training ensures that the participants will have obtained some experience in handling instruments and tissue, for instance, as well as knowledge of how to minimize and manage the risk of perioperative complications before the procedures can be carried out in sedated pigs. These skills can advantageously be obtained without the use of animals, and the condition for participation in the pig course is a passed simulator test.

The Biomedical Laboratory works with the simulation centre at Odense University Hospital to ensure an optimal, modern framework for surgical skills training with minimal use of animals. Despite an increase in activities in this area, the number of pigs used for surgical training has not increased in recent years.

Simulation training

Refinement

Within the 3Rs, the Biomedical Laboratory primarily works with *Refinement*, as illustrated by the examples of tunnel handling and clicker training. To a lesser extent, we work with *Reduction*, as shown by the use of simulation training. However, the effect of *Reduction* is not conspicuous due to a general increase in course activity. Of course, this does not mean that the University of Southern Denmark does not work with *in vitro* or non-animal research.

This is typically performed by the individual research groups in their own labs and not at the Biomedical Laboratory as the central laboratory animal facility.

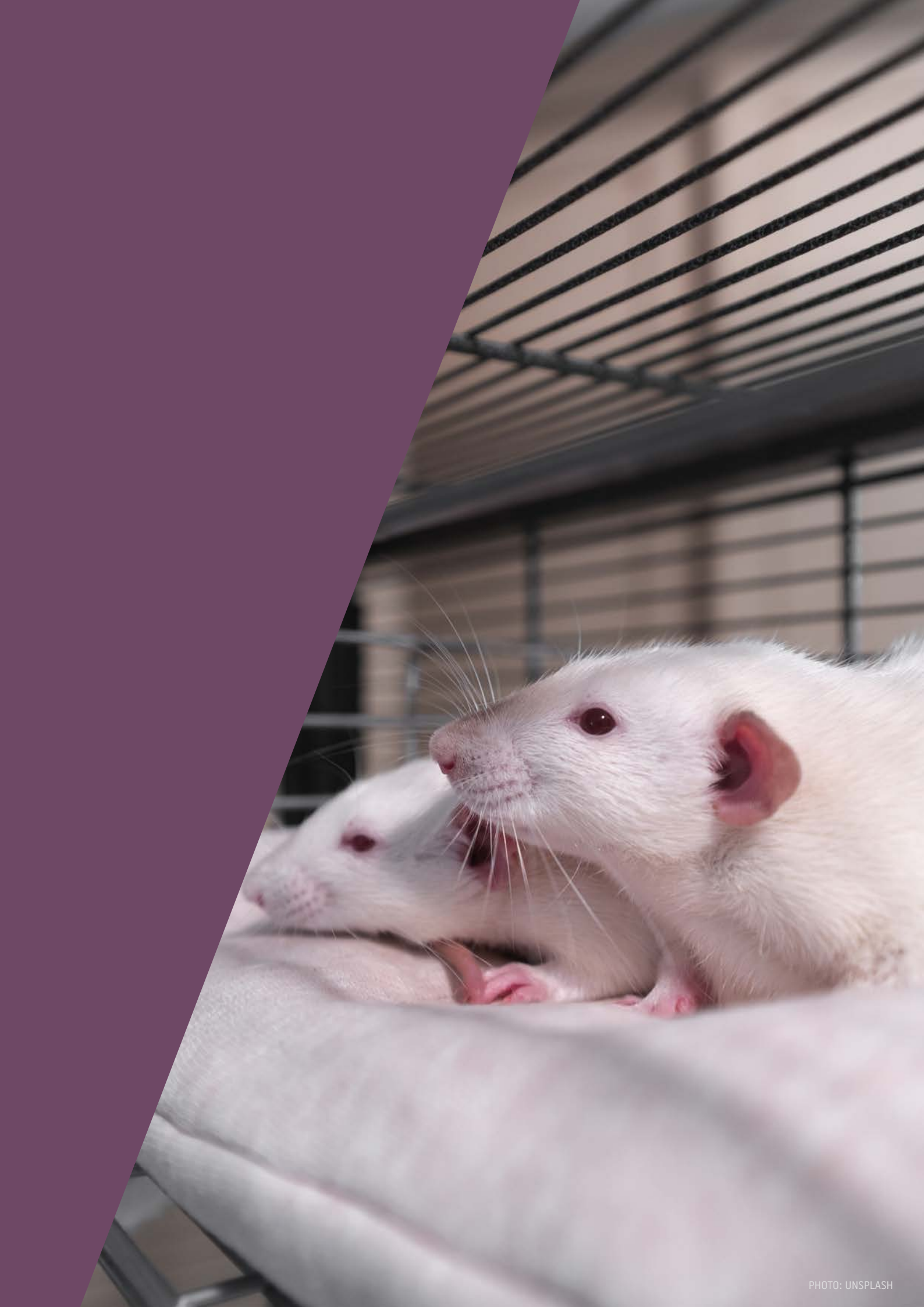
At the Biomedical Laboratory, we therefore consider *Refinement* our primary task and we will always ensure that the individual animal welfare takes priority.



The Danish 3R-Center's Symposium 2021

"Transport and metabolism of azol antifungal drugs in the human term placenta" by Bjarne Styrisshave. Bjarne Styrisshave is an associate professor at the University of Copenhagen. Bjarne gave a presentation on his project, which received funding by the Danish 3R-Center in 2018. Read about the project on the 3R-Center's website.

PHOTO: KIM GRANLI



Appendix

The following is an overview of all the projects that have received support since the Danish 3R-Center was founded in 2013.

Overview of supported projects, 2014–2021

Project	R	Project Manager	Status	Publication
2014				
'Artificial blood vessels' – a model for investigating diabetic atherosclerosis	Replacement	Mette Bjerre University of Aarhus	Completed	To be published once additional studies have been done and more results achieved
Standardizing gut microbiota in mice as a tool for reducing the number of animals in the individual experiments	Reduction	Axel Kornerup Hansen University of Copenhagen	Completed	Published in Scientific Reports in March 2017 (link at the Danish 3R-Center's website)
Refinement of animal models of pain: Development of methods to limit pain in laboratory rats used in pain research	Refinement	Klas Abelson University of Copenhagen	Completed	Published in the Scandinavian Journal of Laboratory Animal Science, March 2020 (link at the Danish 3R-Center's website) Plos One in January 2020 (link at the Danish 3R-Center's website)
Pathological and immunological consequences of murine blood sampling	Refinement	Dorte Bratbo Sørensen University of Copenhagen	Completed	Published in the Journal of the American Association for Laboratory Animal Science in May 2019 (link at the Danish 3R-Center's website)
2015				
Developing an in vitro method to predict acute pulmonary toxicity from aerosol proofing products	Replacement	Jorid Birkelund Sørli (tidl. Søren Thor Larsen) National Research Centre for the Working Environment	Completed	Published in ALTEX Online First in August 2017 (link at the Danish 3R-Center's website)
Can chickens be immunized with an aerosol combined with vaccination? Investigating a non-invasive method for producing antibodies	Refinement	Otto Kalliokoski University of Copenhagen	Completed	Not published (negative results) (Link to the report on the Danish 3R-Center's website)
Artificial skin in a Petri dish as an alternative to laboratory animals	Replacement	Mette Elena Skindersø (June Lissa Hansen) Statens Serum Institut	Completed	Publication expected in the near future (link on the Danish 3R-Center's website)

Project	R	Project Manager	Status	Publication
2016				
Development of computer models for predicting chemicals' impact on thyroid hormones	Replacement	Marianne Dybdahl DTU FOOD	Completed	Published in Computational Toxicology in January 2017 and Computational Toxicology in 2017 (link at the Danish 3R-Center's website)
Using cell cultures to minimize the need for laboratory animals in developing and manufacturing vaccines for farmed fish	Reduction/ Refinement	Niels Lorenzen University of Aarhus	Completed	Supplementary experiments must be conducted to enable publication
Towards better treatment of brain cancer with new cell-based models and less animal testing	Replacement	Bjarne Winther Kristensen University of Southern Denmark	Completed	Published in the Journal of Neurooncology in August 2016 and PLOS ONE in May 2016 (link at the 3R-Center's website)
2017				
The use of primary kidney isolates from humans for studying the molecular aspects of blood-pressure regulation	Replacement	Henrik Dimke University of Southern Denmark	Completed	No plans for publication
Implementation of pain-treatment methods for rats used as a model for inflammatory arthritic pain	Refinement	Klas Abelson University of Copenhagen	Completed	Publication expected in the near future (link on the Danish 3R-Center's website)
Development of cell-based assays for measuring antibody-mediated protection against the chlamydia bacterium	Replacement	Jes Dietrich Statens Serum Institut	Completed	Published in the Journal of Quantitative Cell Sciences in March 2018 (link at the Danish 3R-Center's website)
2018				
Murine Passport	Reduction	Axel Kornerup Hansen University of Copenhagen	Completed	Publication expected in the near future (link on the Danish 3R-Center's website)
New advanced blood-infection model	Replacement	Thomas Emil Andersen University of Southern Denmark	Completed	Published in Scientific Reports in March 2021 (link at the Danish 3R-Center's website)
Transport and metabolism of fungicides in the human placenta	Replacement	Bjarne Styrishave University of Copenhagen	Completed	Publication expected in the near future (link on the Danish 3R-Center's website)

Project	R	Project Manager	Status	Publication
2019				
The significance of cage enrichment for protein metabolic experiments	Refinement	Helle Nygaard Lærke Aarhus University	Completed	Publication expected
Genetic murine modification without a need for extensive breeding	Reduction	Per Svenningsen University of Southern Denmark	Completed	
Study and analysis of internal validity with Danish preclinical research	Reduction	Birgitte S. Kousholt Aarhus University	Completed	
2020				
New methods for exploring the interplay of cells, surrounding tissue and mechanical forces in vascular disorders	Replacement	Julián Albarrán-Juárez Aarhus University	Completed	Published in Cells in August 2021 (link at the Danish 3R-Center's website).
Meta-analyses to identify the shortcomings of behavioural testing in preclinical medicine	Replacement	Otto Kalliokoski University of Copenhagen	Expected to be completed in May 2023	
Introduction of new human ex vivo model systems to study tumorigenesis in kidney cancer	Replacement	Kirsten Madsen University of Southern Denmark	Expected to be completed in November 2022	
2021				
Human derived blood-brain-barrier spheroids to study brain infections	Replacement	Yvonne Adams University of Copenhagen	Expected to be completed by the end of July 2022	
Automated monitoring in animal models for studies of vaccines against viral infections	Reduction Refinement	Gabriel Pedersen Statens Serum Institut	Expected to be completed by the end of July 2022	
Cellular heterogeneity as predictor for the differentiation and regenerative potential of bone marrow stromal cells	Replacement	Ali Jasim Mohammad Jamil University of Southern Denmark	Expected to be completed by the end of March 2024	



PHOTO: KIM GRANLI

The Danish 3R-Center's Symposium 2021

After two successful days at the symposium with interesting presentations, networking and socializing, it was time for a brief roundup. Tom Bengtsen (left), head of the secretariat, talking with secretariat employees Birgitte Ibenforth and Sofie Reumert Biering-Sørensen as well as board member Christine Nellemann. Rasmus Normann Nielsen (right), communications officer for the Danish 3R-Centre, talking with Lisa Andersson, his Swedish colleague from the Swedish 3Rs Center.

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THE DANISH 3R-CENTER IN BRIEF



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The Danish 3R-Center is a collaboration involving the Ministry of Food, Agriculture and Fishery, the Danish Animal Welfare Society, DOSO, LEO Pharma, Lundbeck and Novo Nordisk. The Danish 3R-Center works to promote the 3Rs in Denmark to bring focus to bear on alternatives to animal experimentation and create even better conditions for laboratory animals.

The Danish Animal Welfare Society

"In the view of the Danish Animal Welfare Society, the use of laboratory animals must be restricted wherever possible. This is why the Danish Animal Welfare Society actively supports the Danish 3R-Center's efforts to replace, reduce and refine the use of laboratory animals. In particular, we have great confidence that efforts to promote the development and knowledge of alternatives to laboratory animals will contribute to realizing DAWS' ambition to phase out the use of laboratory animals."

DOSO (Cooperation Organisation of Animal Welfare Bodies)

"The overarching aim of DOSO is to abolish animal experimentation. Towards this end, DOSO is actively engaged in promoting the development, validation and implementation of alternatives to animal testing based on the 3R principles. Making an active effort and supporting the Danish 3R-Center provides a good opportunity to achieve this goal."

LEO Pharma

"Many of our tests and testing models in the development of pharmaceuticals for treating skin disorders have been replaced in part by laboratory testing.

However, we still need to use laboratory animals in the development of medicine to reliably assess the efficacy of medicines and comply with regulatory requirements. LEO Pharma's animal welfare policy is focused on the 3Rs and we have initiated measures to reduce, replace and refine the use of laboratory animals in so far as possible. It is consequently a natural element of this policy to support the national 3R-Center to increase resources within the 3Rs."

Lundbeck

"To facilitate the development of safe and effective medicinal products, we have to use laboratory animals at Lundbeck. We continuously seek to optimize the conditions for these animals, and we use alternative methods wherever possible. For this reason, it was a natural choice for us to support the Danish 3R-Center so that we can stay abreast of 3R developments. With this collaboration, we support the continued development of all 3Rs while staying up-to-date on new ideas and initiatives that can benefit our laboratory animals."

Novo Nordisk

"It is still not possible to develop medicine that is efficacious and safe for patients without using laboratory animals. Novo Nordisk and the Danish 3R-Center share the same wish to promote the development of alternatives to animal testing, reduce the use of laboratory animals, improve conditions for laboratory animals and disseminate knowledge about alternatives to animal testing. Novo Nordisk actively works to achieve these goals, which is why we also actively support the Danish 3R-Center."