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PRO LOEWE NEWS

The LOEWE research initiatives report

FURTHER TOPICS, NEWS AND INFORMATION FROM THE LOEWE RESEARCH NETWORK IN THIS EDITION OF PRO LOEWE-NEWS, AVAILABLE AT WWW.PROLOEWE.DE AND ON TWITTER AT @PROLOEWE

Cover photo: LOEWE Nuclear Photonics is demonstrating practical applications for laser-driven neutron sources for the very first time. The laser coming from the left hits a thin film and generates a so-called plasma that lights up with a whitish-blue colour. Particles in the plasma are accelerated over a distance of a few micrometres to the rear side. Laser particle accelerators have the advantage over conventional particle accelerators that they can be built with a more compact design and this is opening up new opportunities for science and business. Photo: Jens Polz

LOEWE FLOW FOR LIFE: MULTIDISCIPLINARY INTERPLAY FOR A COMMON GOAL

The challenges scientists of the newly funded LOEWE research cluster FLOW FOR LIFE face are great: they want to develop controllable and measurable, artificial supply networks to provide sufficient nutrients and oxygen for organ-like three-dimensional cell cultures. It is hoped that these can be used in the future to more reliably assess the toxicity and efficacy of drugs and to reduce animal testing.

About 80% of drug candidates that have successfully passed the preclinical phase of drug development including animal tests fail in clinical trials as they turn out to be toxic or non-effective in humans. One of the major reasons for this high failure rate are animal models that do not adequately recapitulate human physiology and disease.

Three-dimensional tissue- or organ-like cell cultures produced in the laboratory are promising alternatives that allow for efficacy and toxicity tests on human cells outside the body. They could also be of interest for regenerative medicine in the future. However, the quality of organ-like cell cultures on a centimeter scale is currently not yet sufficient. In particular, there is a lack of a vascular system through which liquids can flow.

The researchers of the new LOEWE cluster are convinced that it is only possible to work toward this major, common goal by having a very, very close cooperation between different engineering and natural science disciplines. They organize their collaboration in a similar way to the way musicians play together in fusion jazz, which emerges from a combination of different musical styles.

The **FLOW FOR LIFE LOEWE cluster** combines expertise and infrastructure from various disciplines (mechanical engineering, biology, chemistry, physics, electrical engineering and information technology) and creates space for special interactions. As is typical in the jazz world, this requires hierarchies that are as flat as possible, everyone needs to listen carefully to the others, mutual inspiration is given, every single person involved is important and of course improvisation is a central element. Young scientists of the research cluster are introduced to all science fields in an introductory course. The aim is to enable them to move between fields and research groups, they will be jointly supervised by several FLOW FOR LIFE group leaders, and share ideas at regular meetings. Advice and support from outside are also important for the project, which the FLOW FOR LIFE team receives from the international scientific advisory board and three industrial companies based in the state of Hesse: Merck Healthcare KGaA, B. Braun Avitum AG and Fresenius Medical Care-Unicyte.

If all this succeeds, individual sounds can blend into harmonies and create a flow, just like the fusion jazz piece on the FLOW FOR LIFE LOEWE website: https://www.tu-darmstadt. de/flowforlife.

The *kick-off meeting* of the LOEWE research cluster took place on February 17. The first FLOW FOR LIFE mini-symposium will follow on June 15, at which two members of the cluster's advisory board will present their research. The event is open to the public and will be held in a hybrid format.

Steffen Hardt, Regine v. Klitzing, Bastian Etzold, Ulrike Nuber, Cristina Cardoso, Andreas Blaeser, Jeanette Hussong, Markus Biesalski and Heinz Koeppl are the FLOW FOR LIFE group leaders (from left to right). Photo: Michaela Becker-Röck

LOEWE NUCLEAR PHOTONICS DEMONSTRATES HOW LASER-DRIVEN NEUTRON SOURCES CAN BE USED FOR THE VERY FIRST TIME

A team centred around Dr Marc Zimmer – a scientist at the **LOEWE Centre for Nuclear Photonics** at the Technical University of Darmstadt – has performed a promising demonstration experiment at the GSI Helmholtz Centre for Heavy Ion Research. Compact, laser-driven particle accelerators were used and applications, which previously required facilities that were up to 100 metres long, were demonstrated. This development is so significant because previous neutron sources of this kind were much more expensive and it was therefore more difficult for both research and industry to gain access to them. The research team at the Technical University of Darmstadt has now published its results in the renowned Nature Communications journal [1].

Thanks to the neutron beams from the Darmstadt experiment, objects can be examined without destroying them – in a manner similar to an X-ray machine – even if the items are surrounded by a shielding material. The special advantage of neutron beams is their high sensitivity to light elements such as hydrogen, carbon or nitrogen, which are difficult to detect with X-rays, but also for heavy elements up to and including uranium. This gives rise to a number of possible interesting applications: for example, the neutron beams could be used to examine whether there were any explosives in safety-critical cargo or the composition of radioactive waste.

In the published results, various materials were examined with neutron radiation and some applications were successfully demonstrated: on the one hand, it was possible to identify the contamination of a tungsten workpiece with tantalum without damaging the sample. On the other hand, it was possible to spatially image samples with the laser-driven neutron beams.

The support for the research work from the **LOEWE Centre for Nuclear Photonics** has been crucially important during the development work. The LOEWE junior research group leaders, Dr Christian Rodel and Dr Marc Zimmer, are working on the ongoing development of laser-driven neutron sources and tapping into new fields of use. The "Focused Energy" start-up was founded by Prof. Dr Markus Roth - also a scientist at Nuclear Photonics – as a spinoff from the Technical University of Darmstadt. This is an excellent example of how something that started as pure research can find direct applications, not "just" in science, but in business too.

[1.] Zimmer, M., Scheuren, S., Kleinschmidt, A. et al. Demonstration of non-destructive and isotope-sensitive material analysis using a short-pulsed laser-driven epi-thermal neutron source. Nature Communications 13, 1173 (2022). https://doi.org/10.1038/s41467-022-28756-0

LOEWE TBG AND DRUID CENTRES RECEIVE FUNDING COMMITMENT FROM THE FEDERAL STATE OF HESSE FOR ANOTHER THREE YEARS

There was good news shortly before the end of the year from the Hessian Ministry for Science and the Arts: the two **LOEWE centres, TBG LOEWE** and **DRUID LOEWE**, which were launched in 2018, will receive three more years of research funding from the state of Hesse from January 2022 onwards.

For the scientists involved, this undertaking provides an important basis for them to be able to continue their work, which is extremely relevant from a social point of view. "Ever since the funding started, we've sequenced about 400 different species, including trees, insects, mammals and lichens, at the **LOEWE Centre for Translational Biodiversity Genomics (TGB)** for the first time. Analysing these genomes has provided a large number of new insights, including how creatures adapt to environmental conditions, the production of natural substances and evolutionary developments. We've also set up structures through our own laboratory centre and our efficient bioinformatics to enable researchers to efficiently log and evaluate their genome data. This puts us in the best possible position during the second funding phase to particularly work out the practical implementation of the results – ranging from nature conservation and protecting species to medical applications," says the coordinator and spokesperson for TBG LOEWE, Prof. Dr Axel Janke, talking about research within the centre. TBG's genomic analyses help register and understand the enormous wealth of biodiversity for the natural world and human beings. Close research synergies have been formed with the partner institutions during the last three years and they are now being further expanded.

Prof. Dr Stephan Becker, the spokesperson for **DRUID (Novel Drug Targets gets against Poverty-related and Neglected Tropical Infectious Diseases)**, comments on the research at his LOEWE Centre. "Neglected Tropical Diseases (NTDs) and Poverty-Related Diseases (PRDs) are caused by infectious pathogens such as viruses, bacteria, parasites or fungi. The diseases may take highly acute, life-threatening forms, but often lead to serious chronic diseases too. Combatting them is therefore absolutely essential from a medical and humanitarian point of view in order to make a decisive contribution to breaking cycles of poverty, which not only increase the risk of infection, but also lead to life-threatening living conditions, social injustice, a readiness to use violence and migration." There are too few effective drugs for most of the diseases examined at the **DRUID LOEWE Centre**. One major focus of research at DRUID over the next three years will be on the translational aspects of research, which the centre will address by identifying new drug targets, preclinical active ingredient development and developing new diagnostics. Thanks to the LOEWE funding, the state of Hesse and the researchers at DRUID are making a significant contribution to the federal government's strategy concept on global health, the sustainable development goals of the United Nations and the World Health Organization (WHO NTD Roadmap 2021-30).

The state of Hesse is funding the **TBG LOEWE Centre** over the next three years with a total figure of approx. EUR 15.6 million. There is also support for building measures amounting to approx. EUR 2.6 million. The **DRUID LOEWE Centre** will have received a total of figure of about EUR 16.2 million by 2024.

After this first funding period, the organisational leadership at DRUID is being transferred from the Justus Liebig University in Giessen to the Philipps University in Marburg, while it remains with the Senckenberg Society for Nature Research at TBG.

Research scientists at the FCI LOEWE Centre have found a way of making it possible to treat resistant rectal tumours again. This discovery has now been published in the renowned specialist journal, Cancer Cell. The lead author is Dr Adele Nicolas, seen here examining material under a microscope. Photo: Sascha Mannel

NEW FINDINGS AT FCI LOEWE: INHIBITING AN INFLAMMATORY MESSENGER EHNANCES THE TREATMENT OPTIONS FOR BOWEL CANCER

The FCI LOEWE Centre combines research from clinics and laboratories in order to combine the challenges that doctors face in their work against cancer with the latest research methods and direct these findings back to the clinics for the benefit of patients. An interdisciplinary team led by Prof. Florian Greten from the Georg-Speyer-Haus with Dr Adele Nicolas in cooperation with Prof. Claus Rödel and Prof. Emmanouil Fokas from the Department for Radiation Therapy and Oncology in Frankfurt/Main is now demonstrating one outstanding example of how this goal can be achieved. The researchers have found a way of making resistant rectal tumours treatable again. This discovery has now been published in the renowned specialist journal, Cancer Cell; the lead author is Dr Adele Nicolas.

Huge improvements have been made in the multimodal treatment of rectal cancer in recent years; however, there are always patients who do not respond to standard radio chemotherapy or whose response is inadequate. As part of the multimodal treatment of rectal cancer in the hospital, the doctors observed that patients with what appeared to be the same diagnosis responded differently to the standard radio chemotherapy. When examining the patient samples in a laboratory, the researchers were able to determine that there are no clear genetic differences between the groups of patients who responded to the treatment well or badly. Surprisingly, the team finally found the answer to their question not in the tumours themselves, but in the cells of the connective tissue surrounding the tumour, the tumour microenvironment. If connective tissue cells are inflamed, the cancer responds less well to radiation. This resistant stage is associated with increased levels of an inflammatory messenger known as IL-1. If the scientists inhibited the inflammatory messenger, it was possible to attack the cancer again with radiation. The approach is currently being tested in an initial clinical study. The interleukin inhibitor, anakinra, which is already approved for the treatment of rheumatoid arthritis, is being used for this purpose.

Dr Adele Nicolas, a scientist at **FCI LOEWE** and the lead author of the study, is delighted by this ground-breaking discovery for radiation therapy and explains, "We've been able to help our colleagues in the hospital through our laboratory research in two ways: firstly, to indicate the point of attack, with which they can make more resistant rectal tumours sensitive to treatment again, and , secondly, to provide a method for screening affected patients for therapy resistance and finding out who is likely to benefit from concomitant anti-inflammatory therapy."

Prof. Greten, the Director of the Georg-Speyer-Haus and the spokesperson for the LOEWE Centre, is also very proud of the research results: "The FCI as a translational network has impressively demonstrated how the research cycle can produce solutions to relevant practical questions if the various disciplines work together in close cooperation. We've picked up one challenge from the hospital in our interdisciplinary, clinical translation programme on rectal cancer, analysed the molecular mechanism and we're now transferring the results back to the patients."

The original publication is called: Adele Nicolas et. al., Inflammatory fibroblasts mediate resistance to neoadjuvant therapy in rectal cancer, Cancer Cell (2022), https://doi.org/10.1016/j.ccell.2022.01.004

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ProLOEWE. LOEWE Research Initiatives Network
Phone: +49 561.804-2348
kontakt-proloewe@uni-kassel.de
www.proloewe.de

Postal address:
Pro LOEWE
c/o Universität Kassel
Mönchebergstrasse 19
34125 Kassel
Germany

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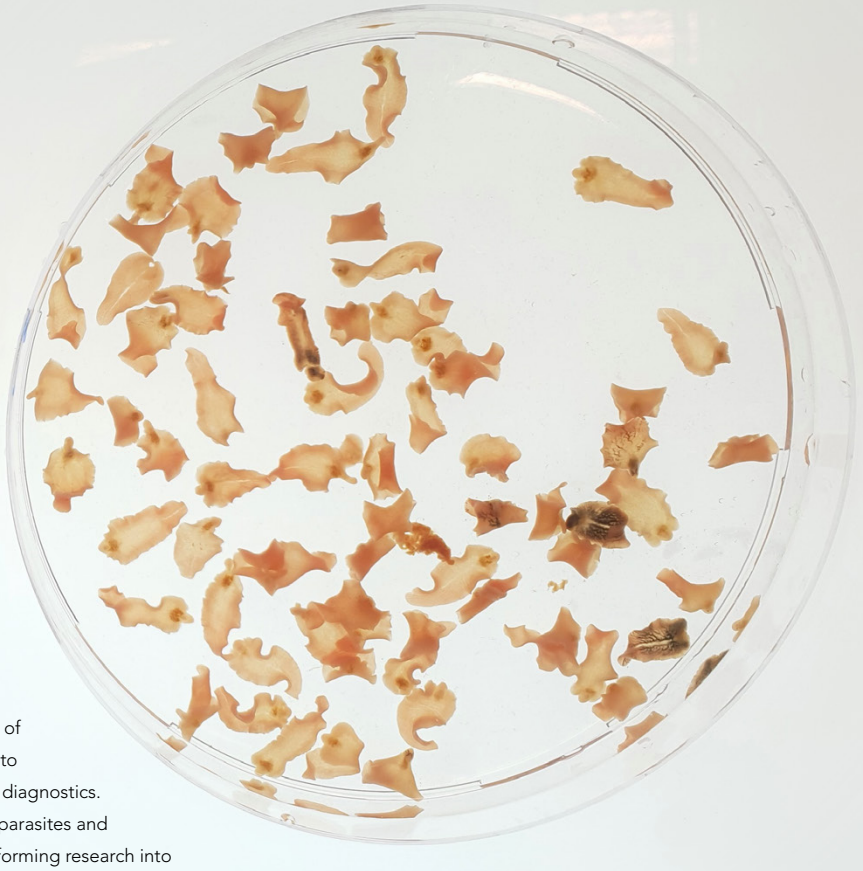

Research is being conducted into a large number of pathogens at the DRUID LOEWE Centre in order to identify new drug targets and develop drugs and diagnostics. They include viruses, bacteria, a large number of parasites and parasitic worms. Two DRUID sub-projects are performing research into the liver fluke known as Fasciola hepatica, as seen in the photo. In contrast to many other pathogens, it is possible to see them with the naked eye. Photo: Simone Häberlein

The genomic analyses at the TBG LOEWE Centre are helping record and understand the enormous value of biological diversity for nature and human beings. This is also the aim of the public ballot to select the "Mollusc of the Year", an international initiative launched by the TBG LOEWE Centre, the Senckenberg Society for Nature Research and Unitas Malacologica in 2020. The sea butterfly pictured here was one of the five finalists in 2022. Photo: Linda Ianniello

Stefanie Dehnen is Professor of Inorganic Chemistry at the Philipps University in Marburg and is a research scientist at the MOSLA LOEWE cluster. Photo: Jochen Mogk

Professor Stefanie Dehnen
Printed long-term data storage media

Professor Dehnen, you're a scientist at the MOSLA LOEWE cluster, which is focusing on molecular storage for long-term archiving. Can you tell us something about the project and your work there? *With pleasure! The project involves developing new methods for securely and permanently storing data. We want to use this to counteract a „Digital Dark Age". To this end, we're testing various molecular-based approaches in the MOSLA consortium. While most other projects are dealing with storage on the basis of DNA molecules, we're working on inks as the long-term data storage medium. To this end, we're trying to use cluster compounds, which have extremely non-linear optical properties, to create inks that differ in terms of their optical response after they have been stimulated by simple CW infrared laser diodes. As a result, we can create two- or multi-colour printing based on these very robust and durable molecules. We've now come very close to fulfilling this goal, but the pathway was full of obstacles because we had to deal with issues that we'd not been focusing on in the past. As a result, we spent many months testing the composition and tolerance of inks, especially the solvents used in the printer cartridges - and learnt a great deal in the process. We now know which components are crucial to determine the printability of a certain type of molecule and we've therefore taken a huge leap forward.*

You studied chemistry, a subject that tends to be unpopular with most people at school. Do you have an idea what could be done to make chemistry and STEM subjects more attractive in general and for girls in particular? *In general, chemistry unfortunately has a poor reputation with many people and often has to contend with negative reporting in the press too – but almost everything that surrounds us is chemistry – the natural substances such as air, water or all kinds of biochemical substances or the many consumer goods that have become an integral part of our daily lives. It starts with the material for toothbrushes, sanitary towels and (currently) masks and includes high-tech materials for mobile phones or outdoor active clothing. In my opinion, we need to work to create an awareness of this fact and also remove the fear of chemistry both as a „dirty science" and as „incomprehensible school material". In fact, thanks to the knowledge and skills of chemists, it's possible to make most of what the chemical industry produces (at least in this country) cleanly and safely. The constraints from public authorities are enormous and rapid progress is being made, especially in the area of sustainability. As far as education is concerned, schools need to start teaching natural sciences seriously as early as possible. Small children have an incredible ability to absorb these interrelationships – and just as it's advisable for foreign language lessons not to start at an intermediate level (and therefore during puberty!), it would be helpful for physics and chemistry lessons to begin earlier and therefore in a more natural way too. This would also simplify the gender balance, since school interests are even more similar at an earlier age. We're experiencing week after week the enthusiasm and impartiality with which young children in particular deal with the topic of chemistry, perform experiments and are being inspired by this wonderful subject at the Chemikum Marburg laboratories.*

Even before you became involved in MOSLA, you were participating in other LOEWE projects as a scientist. What do you think makes the LOEWE programme so special and important for (pure) research? *The inter-university format is a special feature and this at least sets the LOEWE clusters apart from special research departments that are mostly locally based. As a result, those involved inevitably broaden their horizons and opportunities for cooperation open up, which would certainly not have been feasible before the start of the project. The programme is therefore making a crucial contribution to network building in Hesse – both interdisciplinary and intradisciplinary. Because so much importance is being attached to these aspects, the LOEWE clusters can open up a new dimension of joint "pure research with a vision".*

The entire interview is available online at proloewe.de