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PRO LOEWE NEWS

The LOEWE research initiatives report

FURTHER TOPICS, NEWS AND INFORMATION FROM THE LOEWE RESEARCH NETWORK IN THIS PRO LOEWE-NEWS, AVAILABLE AT PROLOEWE.DE, LINKEDIN AND BLUESKY.

Cover picture: A professional tree climber harvests oak leaves from the tree canopy in the Marburg university forest near Caldern under sterile conditions for Tree-M. Photo: Ramona Zülch

FROM THE LEAF TO THE LABORATORY: RESEARCH AND CHARACTERIZATION OF BACTERIAL ISOLATES FROM OAK TREES AS A RESEARCH FOCUS OF LOEWE-TREE-M

The scientists of the **LOEWE research cluster Tree-M** are studying the complex interactions between the environment and the bacterial leaf microbiome (i.e., the entirety of bacterial microorganisms that colonize the leaf) of oak trees. The aim is to analyze their composition and metabolic activities in order to understand what influence they have on the leaf as a habitat and food source for other organisms, such as insect caterpillars. An interdisciplinary team of researchers is investigating these questions in various sub-projects. In the long term, the findings should help to develop sustainable strategies that strengthen the resilience of Central European forests and preserve their important climate function.

One of **Tree-M**'s research approaches is to isolate cultivable bacteria from the leaf surfaces of pedunculate oak (*Quercus robur*) in order to investigate their characteristic properties and their leaf-adapted metabolic capabilities through laboratory experiments. From 2023 to 2024, professional climbers assisted the **Tree-M** scientists in harvesting oak leaves from the canopies. Care was taken to collect them as sterilely as possible to ensure accurate results. Several **Tree-M** sub-projects used the same harvested, so-called monitoring leaves for data collection. In an elaborate analysis pipeline (first in the forest - then in the laboratory), the leaves were photographed, feeding damage was documented and parameters such as weight, thickness and chlorophyll content were determined. Using a pulsifier – a device that shakes the leaves vigorously in an aqueous solution without damaging their tissue – the bacteria are then detached from the leaf surface and the resulting bacterial suspensions are plated on agar plates with nutrient medium.

For the isolation of further laboratory-cultivable bacteria, additional leaves were also collected, which were pressed onto nutrient agar plates while still in the forest in order to transfer the bacteria directly from the leaf surface. Even if not all of the bacteria on the leaves can be cultivated in this way, many develop into separate colonies after a few days of incubation at room temperature, which can be further propagated and studied in the laboratory. Around 1000 bacterial isolates were obtained in this way and stored as so-called freeze cultures at -80°C in order to spread them out again on nutrient agar plates as required and to further characterize them and carry out experiments.

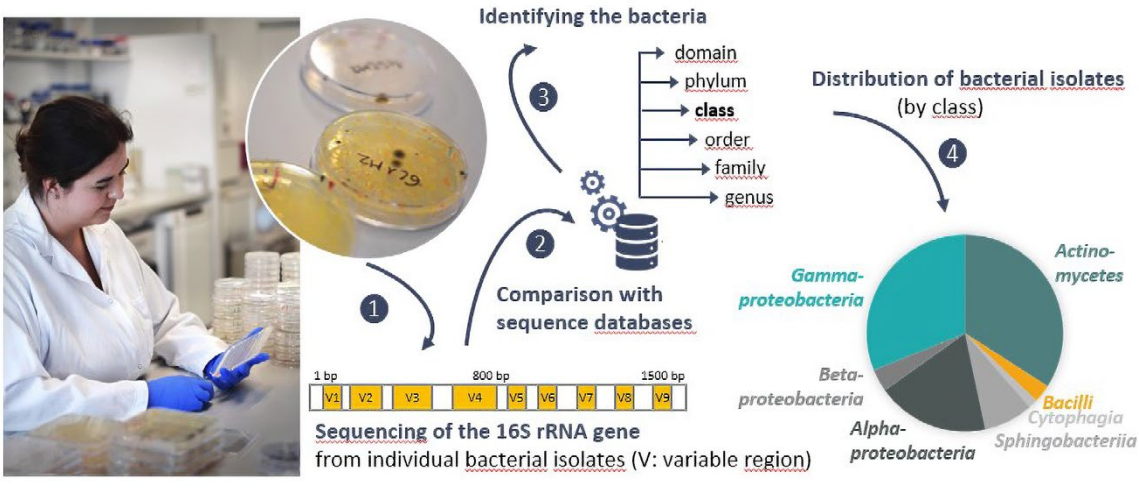
Further examinations and sequencing of specific sections or the entire genome of the isolated bacteria (see figure) allow for a more precise determination of which bacteria are present on the leaves and to which groups they belong. This identification helps to better understand their specific properties.

In this phase of the project, the bacterial isolates are characterized in the laboratory and, for example, optimal growth conditions and their resistance to UV light are investigated. It will also be investigated whether their origin from sun-exposed or shaded leaves makes a difference.

The colonization of oak leaves by representative bacterial isolates and the targeted investigation of their biological functions in the laboratory is another important part of **Tree-M**'s research. To this end, methods are being established to specifically remove genes and analyze their significance, as well as to introduce new DNA that mediates fluorescence signals, for example.

Such tools make it easier to investigate the metabolic properties of the isolates in detail and their interactions with the oak leaf in the laboratory. The latter can, for example, be carried out using a genetically defined oak clone and a specific group of bacterial strains in so-called mesocosm experiments under largely controlled conditions. In this way, further insights into the complex interplay between the leaf microbiome and tree health can be gained, helping to secure the future of Central European forests.

Doreen Meier



Fiona Ullmann, a PhD student in Prof. Dr. Anke Becker's lab, investigates bacterial isolates from oak leaves growing on nutrient agar plates. (1) She amplifies a highly conserved gene region (16S rRNA gene) present in all bacteria. However, variable sequence regions (V1-V9) enable the taxonomic identification of the bacteria. (2) The exact sequence of the 16S rRNA genes is determined by sequencing and compared with databases. (3) This allows for reliable identification of the bacteria down to the genus level. (4) The pie chart shows the distribution of the isolated oak leaf bacteria by class. Photo: Ramona Zülch, pie chart: Fiona Ullmann, total illustration: Doreen Meier

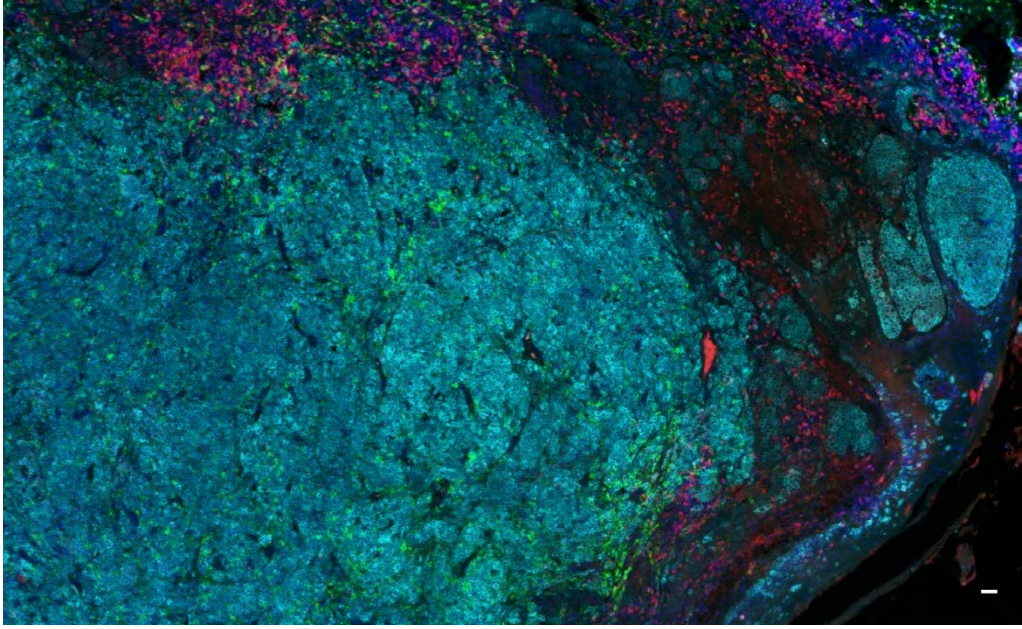


Image of an immunotherapy-resistant melanoma tumor infiltrated with immunosuppressive tumor-associated macrophages (TAMs) that protect melanoma cells from CD8 T cell attacks. TAMs (Green, CD163/CD206/ARG1), CD8 T cells (Red, CD8), melanoma cells (Cyan, MART1), DNA (Blue, DAPI); scale bar 100 µm. (Bottom right in the illustration). Photo: Mélanie Tichet

HOW MY RESEARCH GROUP AT LOEWE-FCI TRIES TO STIMULATE THE APPETITE OF PHAGOCYTES FOR CANCER CELLS – INSIGHTS INTO THE WORK OF MÉLANIE TICHET

The immune system is our body's defense method, constantly patrolling for invaders and abnormal, malignant cells. Among its most versatile players are macrophages, immune cells capable of engulfing and digesting threats – a process known as phagocytosis. However, cancer has found ways to corrupt these cells, turning them from immune defenders into allies that help tumors evade destruction.

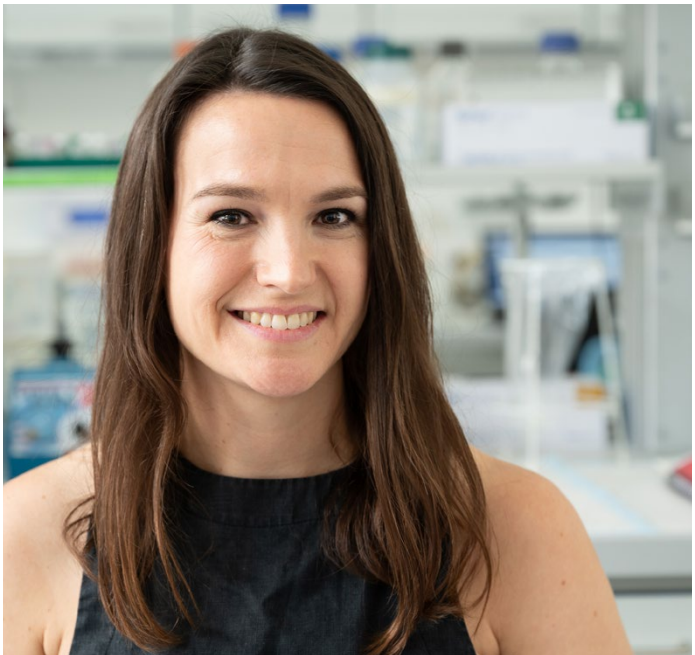
At the Georg-Speyer-Haus, my research group focuses on deciphering the complex interactions between cancer and the tumor microenvironment (TME; all cells and structures around the tumor) as tumors use the TME to create multiple barriers to evade immune destruction, leading to non-responsiveness to treatments. This interplay is important because tumors exploit the TME to create barriers to evade destruction by the immune system, causing them to be unresponsive to treatment. We – my team and I – are investigating the role and regulation of suppressive cell populations within the TME to identify vulnerabilities that can be therapeutically addressed. In this ecosystem, the aforementioned macrophages that would normally "eat" a malignant cell can be reprogrammed by cancer cells into tumor-associated macrophages (TAMs) – immunosuppressors that protect tumors from attacks and contribute to therapy resistance. Our work focuses on how these cells can be reprogrammed to fight cancer.

We take on challenges that arise from clinical observations, ensuring our research remains relevant to patients and has translational potential. This means that there is a good chance of transferring these research findings from the laboratory back to clinical application. Using preclinical models, functional assays, and single-cell technologies, we investigate how TAMs suppress immune responses and contribute to therapy resistance. By targeting key signaling pathways, we have identified combinatorial therapeutic strategies that reprogram TAMs, restoring their ability to stimulate killer T cells and directly eliminate cancer cells. Furthermore, we found that some patients resistant to immunotherapies harbor TAMs within their tumors, rendering them actionable targets for combinatorial strategies. These findings offer promising new avenues for enhancing immunotherapies, particularly for patients whose tumors are resistant to current treatments.

The **LOEWE-FCI program** has been instrumental in supporting this research, providing cutting-edge technology and a dynamic environment to tackle these pressing challenges. Importantly, **LOEWE** fosters interdisciplinary collaboration, which is particularly valuable in a competitive field like cancer research, as integrating data from various areas yields comprehensive insights. Understanding how to redirect the appetite of phagocytes for cancer cells could open new therapeutic possibilities, helping to tip the balance in favor of the immune system in the fight against cancer.

Mélanie Tichet and Sandra Schmitz

***Dr. Mélanie Tichet** has been a group leader in the LOEWE-FCI at the Georg-Speyer-Haus since January 1, 2024. She has extensive expertise in immuno-oncology, which she acquired in Lausanne in the laboratory of Douglas Hanahan. Photo: www.federmann-kampczyk.de*



Participants at the annual meeting of LOEWE-DYNAMIC at Rauischholzhausen Castle. Photo: Alexander Henß

LOEWE-DYNAMIC: INNOVATIVE APPLICATIONS OF ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING IN THE TREATMENT OF MENTAL ILLNESSES

Using an innovative approach, researchers at the **LOEWE research centre DYNAMIC** want to develop a fundamentally improved understanding of mental illnesses and their treatment. To this end, the research project, which was launched in 2024, organized a large-scale, two-day retreat in January 2025 to bring together researchers from the fields of psychotherapy, psychiatry and computer science in particular. The declared aim of **DYNAMIC** is to bridge the professional gap between the disciplines and make joint progress in the network analysis of mental illnesses.

The main topics of the presentations and discussions at the retreat were the potential uses of artificial intelligence (AI), the potential of machine learning in predicting the course of mental illness and the innovative research of the participating scientists at TU Darmstadt, whose focus is on research into machine learning and, in particular, natural language processing (NLP), i.e. the AI-supported analysis and evaluation of human language.

A central role at the conference was played by AI researcher Dr. Hiba Arnaout from **LOEWE-DYNAMIC**, who emphasized the importance of AI in her presentation, as it is fundamentally changing the world – and thus also science and its "rules of the game". Numerous Nobel Prizes in 2024 went to AI researchers from a wide range of disciplines such as physics, chemistry and others. But corresponding publications have also become significantly more frequent in the field of psychiatry and clinical psychology. Around 55% of all publications in 2023 and 2024 in these two disciplines were published with contributions from AI researchers. According to Dr. Arnaout, the quality of contributions in the field of mental health with the participation of AI scientists has unfortunately often varied so far, as they are dependent on close interdisciplinary cooperation in order to produce practice-relevant results, which is not always given or possible.

Dr. Arnaout also described specific areas of application for the use of AI methods in clinical psychology and psychiatry. They can already be used today, for example, to summarize the most important findings of a therapy session and significantly reduce the time required by patients and therapists. In addition, specialized models are used for emotion recognition during therapy or a hospital stay and thus help to assess the further course of a therapy session and an illness.

Such information is invaluable for therapists. Finally, AI-analyzed speech data can also help to predict relapses in certain mental illnesses. Dr. Arnaout cited schizophrenia as an example, where the first studies on predictability based on patients' statements on social media have already been carried out – provided, of course, that they have given their prior informed consent.

In her presentation, Dr. Arnaout outlined the enormous potential of AI-supported speech and text analysis for all areas of clinical psychology and psychiatry: from relapse prediction and progression diagnostics to increased efficiency in the documentation of therapy sessions, and concluded her presentation with a concrete example of interdisciplinary collaboration between AI researchers and experts from the field of mental health, which could also serve as a model for the **LOEWE research centre DYNAMIC.** The follow-up discussion already revealed points of contact and great mutual interest in concrete cooperation in the research projects.

As a result, the retreat and the exchanges that took place there have once again immensely increased the hope for innovative research results and the anticipation of joint research work in the coming years.

Alexander Henß and Max Berg

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MANY WOMEN, ONE MISSION: LOEWE TOP RESEARCH FROM HESSE.

FEBRUARY 11: WOMEN AND GIRLS IN SCIENCE DAY.

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LOEWE
Excellent Research for Hessen's Future

"Many women, one mission: LOEWE top research from Hessen." This was the motto of the joint campaign of the ProLOEWE network on February 11, the International Day of Women and Girls in Science. The response was impressive, and the result is something to be proud of 41 female scientists from top LOEWE research were featured on the poster. They illustrate how diverse and committed women are in different areas and positions of basic research in Hessen.

Prof. Dr. Franziska Matthäus was the spokesperson for the LOEWE research cluster CMMS, which was funded from 2020 to 2024. The project, which was based at the Frankfurt Institute for Advanced Studies (FIAS), was dedicated to the multi-scale modeling of biological processes. Photo: Uwe Dettmar

Prof. Dr. Franziska Matthäus
Development of digital twins of biological systems

Prof. Matthäus, you were the spokesperson for the LOEWE research cluster "CMMS – Multiscale Modeling in the Life Sciences", which was funded from 2020 to 2024, can you describe the research carried out as part of this project? *Some areas of the life sciences can already be investigated much better with the help of computers than with experimental approaches. By developing new mathematical and computer-aided models, LOEWE-CMMS aimed to expand these possibilities even further to make complex processes that are difficult to capture in the laboratory accessible to research. In doing so, we considered different spatial and temporal scales – from individual proteins and their interactions, to cells, tissue and entire organisms. Our aim is to better understand systems, their behavior and the underlying mechanisms, and to make predictions. One example of a practical application are simulations that show how drugs interact with cell receptors, and thus exert their effect. During the corona pandemic, members of CMMS were actively involved in modeling the epidemic, and in the prediction of the course of the pandemic. However, the core of our work is basic research. We are constantly trying to improve our models to make them faster and more precise so that we can investigate larger and more complex biological systems. For example, we are gaining detailed insights into the interaction of proteins with structures inside cells, and a better understanding of the movement and deformation of tissues during the development of an organism.*

You are a biophysicist – a subject that inspires respect in many people, and we often hear that women are in the minority in the natural sciences. What motivated you to study this subject? *At school, I was equally fascinated by all the natural sciences, so I wanted to study as many of them as possible. The subject of biophysics at Humboldt University was the perfect solution: biosciences, physics, chemistry, mathematics and computer science were strongly represented. In retrospect, this was exactly the right decision for me – especially because a new "Institute for Theoretical Biology" was set up right next door with new professorships and interesting research topics during the period of my studies. Incidentally, women were not in the minority on the biophysics course. In fact, the ratio was almost exactly 50 percent, which is perfect. The small size of the course was also particularly advantageous; even in the first semester there were only just over twenty first-year students. This resulted in a student-to-staff ratio that many other students can only dream of.*

Now that the funding for LOEWE-CMMS has expired at the end of 2024, can you tell us what you think is special about the Hessian research funding program? *The LOEWE program is very flexible and promotes interdisciplinary collaboration. This allows ambitious research alliances to be set up, with which new paths can be taken thematically and structurally – as we have succeeded in doing in the case of LOEWE-CMMS. Thanks to the LOEWE funding from Hesse, we were able to bring together a consortium of scientists from many departments in the Max Planck Institutes in Frankfurt who were interested in the modeling and simulation of biological systems. We also integrated experimental groups who supported the model development with their data. And lastly, were able to establish four additional junior research groups with additional third-party funding, and to integrate them into CMMS at the start of the funding period. As a result, modeling in the life sciences has become a focal point at FIAS (Frankfurt Institute for Advanced Studies). Last but not least, LOEWE-CMMS also acted as a catalyst for the new SCALE excellence initiative, which has been very successful to date. Its core project involves the development of a digital twin of the cell, and several CMMS researchers are involved in this project. Digital twins – multiscale models with a strong quantitative focus, and the integration of different modeling approaches and artificial intelligence – are already an important new core topic at FIAS. In the recent years, we have successfully organized FIAS conferences in this area with the participation of international speakers.*

The interview was conducted by Tanja Desch, you can find it in full length on proloewe.de.