2025

Catalyzing translational medicine in academia



SPARK-BIH

Charité BIH Innovation SPARK-BIH Am Zirkus 1 / Bertolt-Brecht-Platz 3 DE-10117 Berlin

spark@bih-charite.de www.spark-bih.de











SPARK-BIH Overview	4
SPARK-BIH Projects	15
Past SPARK-BIH Projects	43
Testimonials	103
SPARK-BIH Photo Copyrights	121

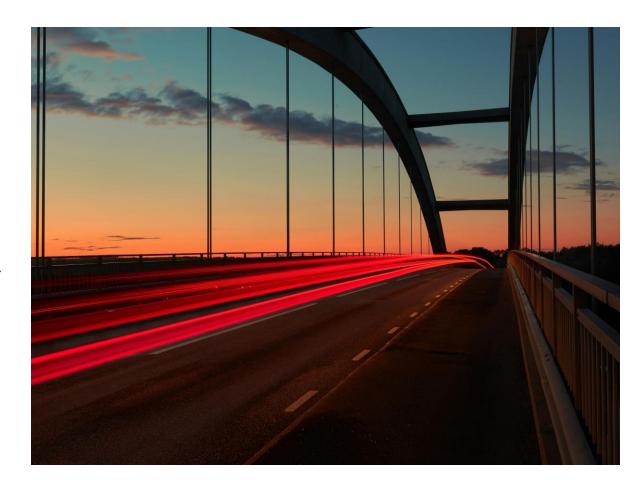
SPARK-BIH Overview

SPARK-BIH: Bridging Biomedical Research and Clinical Application

At the core of biomedical research lies the challenge and necessity of translating scientific discoveries into clinical applications. This process, known as "Medical Transfer", is crucial for transforming innovative research into meaningful benefits for patients, society, and the economy. However, only a small fraction of biomedical discoveries is developed into new products, often due to a lack of funding, expertise, or a transferoriented mindset among academic researchers.

The Mission of SPARK-BIH

At SPARK-BIH, our mission is to accelerate the translation of academic research into clinically relevant therapies, diagnostics, and medical devices, addressing unmet medical needs. In order to achieve this, we support researchers and clinicians with milestone-based funding, mentoring and education, fostering a collaborative and supportive environment. Our aim is to turn innovative ideas into impactful solutions that benefit patients and society.



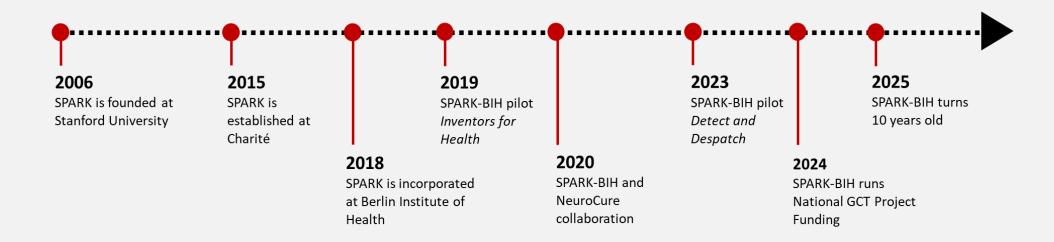
Our Journey

Founded in 2006 at **Stanford University**, SPARK has evolved into a global network comprising over 60 participating institutions worldwide.

SPARK-BIH was established in Berlin in 2015 by Prof. Dr. Craig Garner and Prof. Dr. Ulrich Dirnagl, with the support of **Stiftung Charité**. In 2018, the program became an integral part of the Berlin Institute of Health (BIH), which is focused on medical translation. In 2021, the BIH was integrated into the Charité - Universitätsmedizin Berlin, the joint medical faculty of Freie Universität Berlin and Humboldt-Universität zu Berlin and one of Europe's largest university hospitals.

Today, SPARK-BIH is part of Charité BIH Innovation (CBI), the joint technology transfer of BIH and Charité.

Furthermore, SPARK-BIH has established a long-term collaboration with NeuroCure, has developed two programs to promote early innovation and, as part of BIH, runs the project funding within the National Strategy for Gene- and Cell-Based Therapies (GCT).



SPARK-BIH and NeuroCure collaboration

In 2020, **NeuroCure** and **SPARK-BIH** joined forces. NeuroCure, a Cluster of Excellence in the neurosciences at Charité, with additional participating institutions. It is dedicated to exploring and understanding the mechanisms of central nervous system diseases to develop novel therapies for neurological and psychiatric disorders.

Through this collaboration, SPARK-BIH supports innovative neuroscience projects and teams, extending its network to include researchers beyond Charité.

Selected teams receive funding from NeuroCure, along with mentoring, education and support from the SPARK-BIH team.

Following the successful implementation of the joint SPARK-BIH/NeuroCure program, the collaboration has been renewed for a third term, with a new call for proposal planned for 2026.



SPARK-BIH supporting early innovation

SPARK-BIH is dedicated to fostering innovation and cultivating an inventive mindset within the BIH / Charité community. In 2019, we launched the "Inventors for Health" (I4H) program to stimulate breakthrough medical innovations and support a new generation of inventors. Through hands-on workshops, such as medical design thinking bootcamps, 10 teams participated, with 6 receiving extended support over 12 to 18 months to further develop their ideas.

Building on the success of I4H, we introduced the "Detect and Dispatch" program in 2023. This initiative connects early-stage innovators with multifaceted scouting activities, educational workshops, and mentoring, supporting them on the initial steps of the translational pathway.

Both programs were made possible through grants from **Stiftung Charité**.





SPARK concept rolls out in Germany in the context of Gene and Cell Therapy

In March 2023, the Federal Ministry for Research, Technology, and Space (BMFTR, formerly BMBF) commissioned the Berlin Institute of Health (BIH) to coordinate the National Strategy for Gene- and Cell-Based Therapies (GCT). The Strategy was developed in a multi-stakeholder approach involving more than 150 experts from science, economy, politics, society, and patients.

It aims to develop safe and effective therapies and diagnostics for severe, currently incurable diseases, enhance collaboration across Germany's strong research landscape, and accelerate the translation of research findings into clinical application. At the same time, it seeks to strengthen Germany's international competitiveness in the field of gene and cell therapies (GCT).

One aspect of the National GCT Strategy is Project Funding.

BIH decided to use the SPARK concept — so far established locally for Charité-centric projects — and expand it to a nationwide program in the field of gene- and cell-based therapies as well as associated diagnostics. This decision was driven by SPARK's ability to provide not only financial support but also a wide range of non-monetary services essential for strengthening the gene and cell therapy ecosystem in Germany.

Currently, 36 projects from across Germany are participating in the program, benefiting from financial support as well as mentorship, and educational opportunities from GCT experts.

For more details on this program click here or visit this website.















GCT

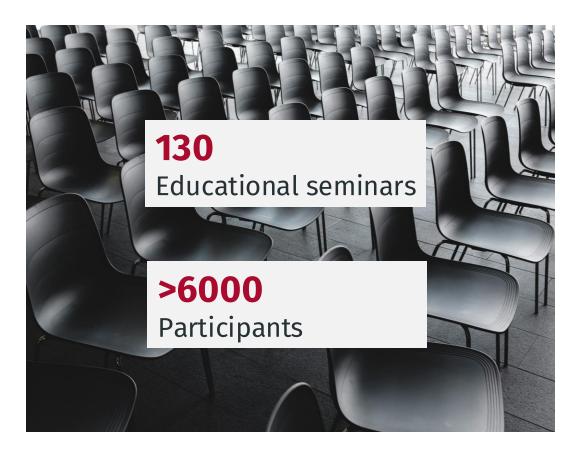
National Strategy
Gene- and Cell-Based Therapies
Project Funding

Empowering Researchers and Clinicians

The program offers comprehensive support to researchers and clinicians, including **milestone-based funding**, individualized **mentoring**, and access to a broad **network of experts** from industry and academia.



To further cultivate a transfer-oriented mindset, SPARK-BIH offers a diverse range of **educational opportunities**, such as webinars, interactive workshops, and pitch training sessions.



The SPARK-BIH Selection Process

SPARK-BIH invites researchers and clinicians to submit innovative projects for potential funding through an annual call for proposals. A panel of external experts evaluates each submission based on the level of innovation, significance of the unmet medical need, competitive advantage over existing solutions, data quality, and the likelihood of translational success.

The program funding in two tracks:

- Track 1 supports early-stage projects with up to €50,000 for one year.
- Track 2 funds more advanced projects with over €50,000 for two years.

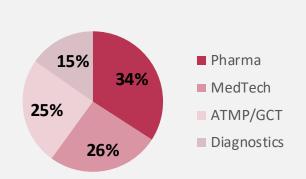
All funding is **milestone-based**, with close monitoring and tailored support from the SPARK team to ensure progress and effective resource use, accelerating the translation of biomedical research into clinical applications.



SPARK-BIH in Numbers

Projects

85 **Funded Projects** 26 Projects in the Program



Progress

402 Applications received

45 Patent families > 53 Mio € follow-on funding

Start-ups



Cancer Therapy Platform



Gene therapy for **Epilepsy**



Predicting surgical complications



Pre-tied surgical knot



Telemedicine platform for rare diseases



Muscle Stem Cell Therapy



Assessing circadian rhythm



Software for clinical documentation



clock



Image retrieval tool for MRIs



KernEvo

Cell-stabilization diagnostic platform



Dr. Tanja RosenmundDirector SPARK-BIH



Prof. Craig GarnerFounder SPARK-BIH



Dr. Anabel Molero MilanProject Manager



Dr. Alexander StumpfProject Manager



Dr. Luisa A. Hasam HendersonProject Manager



Dr. Sascha CordingProject Manager



Rosa MontserratAssistant to SPARK-BIH Team



Katharina Clausnitzer Assistant to SPARK-BIH Team



Dr. César Cordero GómezProject Manager



Dr. Josephine KemnaProject Manager



Dr. Marialucia Massaro Project Manager



Dr. Sharesta Khoenkhoen Project Manager



Dr. Stefan Köster Project Manager

SPARK-BIH projects

A novel approach for precise & gene-sized integration of DNA – "One-pot" PASTA



PRINCIPLE INVESTIGATORS: **Jonas Kath, Isabell Kassing, Dimitrios L. Wagner** Charité



SUMMARY

Current gene transfer methods for ATMPs rely on retro/lenti- or adeno-associated virus (AAV) systems, where transgene integration occurs randomly and is limited by viral packaging capacities. In addition, GMP-grade viruses are associated with high costs and time delays.

"One-pot" PASTA (Programmable and Site-specific Transgene Addition) allows one-step transfection of all gene editing reagents and overcomes size-limitations.

The approach shifts from viral to non-viral editing and from random to precise integration.

PROJECT GOALS

To establish a platform for precise and sitespecific integration of large cargo by using the recently established one-pot "PASTA" technology.

- To establish a novel gene transfer system for cell & gene therapy allowing highly efficient and site-specific integration of large genetic cargo with minimal toxicity.
- Commercial distribution either via a license or Spin-Out.

EXploiting CIrculating tumor cells as companion diagnostic for T cell receptor-based Drugs - EXCITeD







PRINCIPLE INVESTIGATORS: **Martin Klatt, Bilge Atay, Badeel Zaghla** Charité



SUMMARY

For T cell receptor (TCR)-based therapies, the identification of the correct HLA-type and expression of the respective target antigen/epitope is usually determined by a biopsy. This is time and resource intensive and can put patients at risk.

This alternative approach facilitates the screening and monitoring process for TCR-based studies and serves as a companion diagnostic to determine eligibility for drug treatment.

It is faster (72h vs 7 days), less invasive, safer and cheaper and allows patient monitoring during the duration of the therapy.

PROJECT GOALS

To proof the feasibility of detecting therapeutically targetable HLA ligands on circulating tumor cells isolated from cancer patient's blood specimens.

- To develop a diagnostic platform that serves as a companion diagnostic for T cell receptor-based immunotherapies.
- Commercial distribution either via a license or setting up a Start-Up.

ACK 1

Development of a non-invasive and fast screening method for tuberculosis in exhaled breath.



PRINCIPLE INVESTIGATORS:

Michael Lommel, Matthias Groeschel, Jan Schroer
Charité



SUMMARY

Tuberculosis (TB), the leading cause of infectious disease-related deaths worldwide, is spread via aerosols. Missed or delayed diagnosis are a major barrier to achieving WHO TB eradication goals.

The development of rapid diagnostic and screening techniques is crucial.

The team aims to develop a rapid, sensitive, low-cost, and easy-to-use point-of care diagnostic for TB detection in breath.

PROJECT GOALS

Proof-of-Concept for the development of a highly sensitive, non-invasive and low-cost diagnostic test for tuberculosis in exhaled breath.

- Clinical validation in different cohorts and settings
- To establish a platform technology for detection of a variety of disease-causing agents that can be measured in exhaled breath

TRACK 1

BioHeal Eutectic Formula: Therapeutic Deep Eutectic Solvents for Antimicrobial Wound Dressing



PRINCIPLE INVESTIGATORS: **PD Dr. Fiorenza Rancan** Charité **Prof. Marcelo Calderon** and **Dr. Matias Picchio** Polymat



SUMMARY

The goal of the project is to develop an antimicrobial and anti-inflammatory dressing for treating infected chronic and complex wounds. To achieve this, the team uses deep eutectic solvents (DES), which are mixtures of two or more components that together have a lower melting point than the individual substances.

Using therapeutic DES that are derived from natural products can offer several advantages over silver dressings, which are the current standard of care. These benefits include lower production costs, reduced toxicity for patients and the environment, and low risk for antimicrobial resistance.

PROJECT GOALS

- Evaluate the efficacy and toxicity of identified DES in human ex vivo wound models.
- Identify the best performing DES and perform the first pre-clinical test in vivo

- Preclinical study and validation
- Develop an efficacious medical product

Berlin Prehospital Collection of Biosamples in Stroke and other Emergencies – B_PRECISE



PRINCIPLE INVESTIGATORS: **Kian Röhrs, Joachim Weber, Heinrich Audebert** Charité



SUMMARY

Acute neurovascular diseases are leading causes of death and disability globally. There is an urgent need for fast characterization of different types of stroke to initiate appropriate treatment. However, currently there are no biomarkers that allow to differentiate between hemorrhagic and ischemic stroke.

The team is utilizing the mobile stroke unit (MSU) network in Berlin to enable a highly standardized collection of biosamples derived from stroke patients immediately after symptom onset.

The aim is to identify biomarkers that enable the differentiation between types of stroke in the acute phase in order to allow faster treatment initiation, triage to the correct hospital and maximize treatment outcomes.

PROJECT GOALS

 Identify and select a suitable biomarker panel for distinguishing between ischemic and hemorrhagic stroke

- Development of a nanobody-based PoC diagnostic test to differentiate between types of stroke
- Clinical study and certification as IVD
- Outlicense to industry

Biodegradable Drug-Eluting Surgical Matrix



PRINCIPLE INVESTIGATORS: **Philippa Seika, Lennard Shopperly, Christian Denecke**Charité



SUMMARY

Surgical gastrointestinal resection is an essential procedure for treating various conditions. However, it can lead to complications, primarily due to challenges in restoring continuity through anastomosis.

This project aims to develop a biodegradable drugdelivery matrix that can be applied during surgery to enhance tissue regeneration and prevent anastomotic leakage. This solution seeks to improve upon conventional technology, leading to better patient outcomes in surgical care.

PROJECT GOALS

- Characterize drug pharmacology in vitro.
- Develop and characterize matrix composition.
- Evaluate efficacy and toxicity in vitro.

- Develop a prototype
- Preclinical study and validation

Dura-X – Development of a biomimetic, hybrid dural graft





PRINCIPLE INVESTIGATORS: **Ran Xu, Anton Früh, Kiarash Ferdowssian, Peter Vajkoczy** Charité



SUMMARY

Neurosurgical procedures require opening and closure of the dura mater, the outer layer of meningeal membranes that cover the brain and spinal cord. Subsequently, it is of utmost importance to achieve an efficient and safe closure of the dura to avoid postoperative complications. However, commercially available grafts can pose risks such as inflammation, immune reactions or the potential for disease transmission.

The team aims to develop a novel dural graft designed for use in neurosurgical procedures, offering straight-forward handling to facilitate effective dural closure.

PROJECT GOALS

 Design and develop a functional prototype of a biomimetic dural graft

- Certification as medical device
- Clinical study
- Collaboration with industry partner or startup formation

Next-generation allogeneic CAR T cells to treat B-cell mediated autoimmune disease



PRINCIPLE INVESTIGATORS: Viktor Glaser, Jonas Kath, Dimitrios L. Wagner Charité



SUMMARY

Current therapies for autoimmune diseases fail to provide long-term remission and have side effects. Chimeric Antigen Receptor (CAR) T cell represent a promising immunotherapy approach to target autoimmune diseases.

Here, a next-generation non-viral gene editing technology using a base editor system will be applied for CAR T cell approaches in autoimmune diseases. Harnessing multiplex editing, the team aims to create a solution based on allogeneic donor cells to reduce costs and improve access.

This approach shifts from viral to non-viral editing and from random to precise integration.

PROJECT GOALS

- To develop an immunosuppressant-resistant, TCR-disrupted, CD19-specific CAR T cell product for off-the-shelf use in autoimmune disease treatment.
- Preclinical Proof-of-Concept

- Conduct Phase I/II clinical trial.
- Commercial distribution either via a license or Spin-Out.

Safety and efficiency assessment of a novel miniaturized oxygenator



PRINCIPLE INVESTIGATOR: **Prof. Dr. Leonid Goubergrits** Charité



SUMMARY

A membrane oxygenator is a device used to add oxygen to and remove carbon dioxide from the blood. It can be used to replace lungs in cardiopulmonary bypass, and to support lungs in long-term life support called ECMO. Current complications include neurological injuries as subarachnoid hemorrhage, ischemic infarctions, or brain death. These complications are caused by the low efficiency of current oxygenators due to high priming volume of 40 % to 50 % of the total oxygenator volume associated with non-physiological conditions. The project aim is to prove safety and efficiency of a novel oxygenator concept allowing to reduce priming volume. If successful, this may allow for future development of miniaturized oxygenators implantable artificial lungs.

PROJECT GOALS

- Translate an idea into the functional prototype
- Show superiority to conventional oxygenators

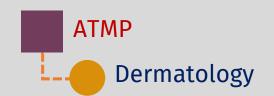
- Validation and proof of biocompatibility with blood tests and animal models
- License to industry

7

Nemo: Next Generation Therapy for Skin Diseases



PRINCIPLE INVESTIGATORS: **Prof. Dr. Sarah Hedtrich, Gaurav Sadhnani, Elena Lizunova**Charité



TRACK 2

SUMMARY

Genodermatoses are rare hereditary skin diseases characterized by impaired skin barrier function. This leads to increased transepidermal water loss and high risk for infection which is particularly dangerous for neonates causing higher mortality rates. In general, patient's quality of life and life expectancy are severely affected.

Currently no effective and curative treatments exist. Symptomatic treatments include frequent (2x/day) and rigorous bathing to remove affected skin areas followed by the application of moisturizers. These treatments are very time consuming, costly and might not be covered by health insurances.

The team has successfully developed a topically applicable gene therapy as novel and potentially curative treatment option for genodermatoses. The aim of this funding period is to determine the durability of the curative treatment and to demonstrate the platform potential of their developed technology in other skin diseases.

PROJECT GOALS

- Achieve product and data readiness for requesting approval for the first-in-human clinical Phase I/IIa study in patients suffering genodermatoses.
- Demonstrate the platform potential of the approach by expanding to other disease-causing mutations in the skin.

LONG-TERM GOALS

Formation of spin-off

Puringe: Pure syringe system for contamination-free storage, transport and injection of therapeutics



PRINCIPLE INVESTIGATORS: **Felix Hehnen, Dr. Paul Geus, Tim Bierewirtz** Charité



SUMMARY

200 million people are affected by macular degeneration leading to 20 million intravitreal injections per year. Silicone oil is the most prevalent lubricant in syringe systems and can lead to floaters in the eye.

The team is developing Puringe, a syringe system designed to address two major challenges for intravitreal injections: accurate small dosing and contamination-free injections.

The key element of the system is a highly innovative membrane that allows precise dosing and contamination free application.

PROJECT GOALS

- Develop a functional prototype
- Prepare prototypes designed for manufacturing and mass-production

- Develop a first-in-class product
- Get certified and approved for medical use
- Enter the market

Signature Antibody Detection for anti-NMDAR Encephalitis with preceding Herpes Simplex Encephalitis (SAD NEWS)



PRINCIPLE INVESTIGATORS: Jakob Kreye, Isabel Bünger, Poul Schulte-Frankenfeld, Sarah Schott Charité





Neurology & Autoimmunity

TRACK 2

SUMMARY

Herpes simplex encephalitis (HSE) is the most common viral encephalitis globally. Within three months of infection, ~23% of HSE patients develop a secondary autoimmune anti-NMDAR encephalitis (NMDARE), associated with worse long-term outcomes. NMDARE patients can achieve remarkable improvements under adequate immunosuppressive therapies. However, delayed treatment correlates with poor outcome.

The team has identified a distinctive antibody signature in HSE/NMDARE patients and aims to develop a diagnostic test that allows identification of patients at risk for secondary NMDARE after HSE. In the future, early interventions may help to prevent secondary autoimmunity and associated long-term morbidity.

PROJECT GOALS

- Optimize and validate a prototype assay to detect predictive signature antibodies
- Develop a score for risk evaluation

- Perform clinical study and certification as IVD
- Outlicense to IVD company

Iron complexes as an alternative to gadolinium-based contrast agents for magnetic resonance imaging



PRINCIPLE INVESTIGATORS: **Eyk Schellenberger, Fei Ni, Akvile Häckel, Hamidreza Hojjat** Charité



SUMMARY

Gadolinium (Gd)-based contrast agents are the most widely used compounds in MRI imaging. However, after decades of clinical use, severe side effects have been reported, including the accumulation of Gd in multiple organs.

Gd is a toxic heavy metal that does not naturally occur in the human body. Therefore, the team is working to develop safer, iron-based contrast agents, which can leverage the body's intrinsic physiological metabolic and excretion systems. They have already demonstrated that their compounds can provide T1 contrast comparable to Gd-based standard agents.

Furthermore, reducing the use of Gd can also help decrease its accumulation in waste and groundwater, thereby mitigating potential environmental contamination.

PROJECT GOALS

- Test the long-term stability of their lead compounds.
- Test toxicity *in vitro* and *in-vivo* with GMP-like compounds.

- Preclinical study and validation
- Collaboration with industry partner

2024

Innovative repurposing formulation for stroke prevention





PRINCIPLE INVESTIGATORS: **Dr.-Ing. Szandor Simmons, Prof. Dr. med. Wolfgang M. Kuebler**Charité



SUMMARY

Stroke is the leading cause of cardiovascular morbidity and mortality worldwide, and individuals who have had a stroke are at significantly increased risk of suffering a recurrent secondary stroke. These recurrent events often result in more severe outcomes, including permanent disability and a higher risk of mortality.

Through retrospective analysis of patient data ex vivo and in vivo efficacy testing, the team has identified a treatment that has anticoagulant and antiplatelet potential in inflammatory diseases, coupled with a low risk of ischemia and bleeding.

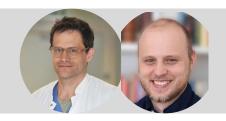
The overall goal is therefore to develop a tailored formulation of a repurposed drug for the prevention and treatment of recurrent secondary stroke, providing a pathway to improved therapy.

PROJECT GOALS

- Develop a precision repurposing-based formulation tailored to prevent recurrent ischemic stroke
- Evaluate the pharmacokinetics (PK) and efficacy of the new formulation in vivo

- Spin-off
- Perform clinical trials I and II

Single-cell sequencing of urine cells as transformative diagnostic for kidney diseases



PRINCIPLE INVESTIGATORS: **PD Dr. Philipp Enghard, Dr. Jan Klocke** Charité



SUMMARY

Kidney diseases affect about one in ten people and is associated with significant morbidity and mortality. At present, there are no biomarkers based on liquid biopsies and nephrologists are dependent on kidney biopsy to get a meaningful diagnosis.

Our vision is to establish single-cell RNA sequencing of urine cells as a completely new and non-invasive approach to diagnosing kidney diseases.

PROJECT GOALS

- proof-of-principle
- analyze urine samples of patients with different kidney disease indications

- Patenting disease-specific diagnostic signatures as well as AI-based algorithm for diagnosing kidney diseases
- Startup foundation or licensing

Development of T-cell receptors (TCR) for the adoptive T-cell therapy (ACT) of epithelial ovarian cancer (EOC)



PRINCIPLE INVESTIGATOR: **Prof. Dr. med. Sebastian Ochsenreither**Charité



SUMMARY

EOC is the most common cause of death of gynecological malignancies. Due to its early peritoneal spread, patients are diagnosed in a metastatic setting in the majority of cases. Even though well responsible to cytostatic agents, patients eventually succumb to the disease, mostly after several lines of chemotherapy.

Our vision is develop new TCR constructs for ACT for potential treatment of EOC.

PROJECT GOALS

Generation of novel TCR constructs for further development towards clinical application

- Clinical trial
- Licensing to industry

202

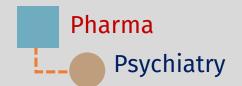
Oxytocin-augmented group psychotherapy for patients with schizophrenia spectrum disorders



PRINCIPLE INVESTIGATORS:

Dr. Marco Zierhut, PD Dr. Dr. Kerem Böge,

Prof. Dr. Stephan Ripke Charité



SUMMARY

Negative symptoms (NS) in patients with schizophrenia spectrum disorder (SSD), such as reduced emotional expression and social withdrawal, remain a challenge and limit the efficacy of existing treatments. This project aims to develop and optimize a combination therapy of MindfulnessBased Group Therapy and oxytocin administration (OXYMIND) to improve the overall well-being and quality of life for patients.

We will perform an interventional study and investigate potential mechanism of action to improve the rapeutic effects.

PROJECT GOALS

- Complete a randomized control trial evaluating OXYMIND for the treatment of NS in patients with SSD
- Identify potential mechanism of action to optimize therapeutic effects

LONG-TERM GOALS

 Establish OXYMIND as a validated and effective treatment option for NS in patients with SSD in different medical centers and countries.

T cell antigen directed bispecific molecules for immunotherapies of malignant tumors



PRINCIPLE INVESTIGATOR: Prof. Dr. med. Ulrich Keilholz, Prof. Dr. rer. nat. Gerald Willimsky Charité



TRACK 2

SUMMARY

Immune-mobilizing monoclonal naturally optimized T cell receptors ImmnoTCRs against cancer utilize a type of immunotherapy designed to leverage the body's immune system to target and eliminate cancer cells These molecules bind to tumor specific antigens and simultaneously activate local T cells, triggering a directed immune response against the cancer cells This project focuses on developing novel, high affinity ImmnoTCRs targeting various types of cancer.

Promising candidate ImmnoTCRs will undergo preclinical testing, including evaluations using patient derived organoid models, before advancing to clinical trials.

PROJECT GOALS

- To select one lead candidate with optimal efficacy for clinical testing
- Establish the regulatory framework and design of an initial clinical study

- Clinical validation
- Develop an efficacious treatment

Expansion of natural killer cells for viral infection and cancer





PRINCIPLE INVESTIGATORS: **Prof. Dr. Chiara Romagnani, Dr. Timo Rückert**Charité



SUMMARY

The immune system has evolved different strategies to prevent and fight cancer and infections. Natural Killer (NK) cells are an innate immune cell type able to kill tumor and/or infected cells.

The team identified a specific peptide present in a human virus and certain tumors that leads to the expansion of a specific NK cell type.

The project aim is the preclinical development of a vaccine prototype for the treatment of these tumors as well as the respective human viral infection. This approach enables cancer patients to benefit from boosting the immune system to not only fight this viral infection but also relapsing tumors.

PROJECT GOALS

- In vivo Proof-of-Concept
- Preclinical development of vaccine candidate

LONG-TERM GOALS

- Conduct Phase I/II clinical trials
- License to Pharma or Start-Up

PREVIOUS SPARK FUNDING

Track 1 2018, Track 1 2020

Fillable Hybrid Scaffolds for the treatment of critically-sized bone defects



PRINCIPLE INVESTIGATORS:

Jacob Spinnen MD/PhD, Dr. Tilo Dehne,

Dr. Franziska Schmidt, Lennard Shopperly Charité



TRACK 2

SUMMARY

Critical bone defects caused by trauma, surgery, or destructive bone diseases are usually treated by either autologous bone grafting or synthetic bone substitutes. While autologous bone grafting means removing part of intact bone tissue and carries risks of complications, synthetic bone structures remain inferior to autologous bone in terms of tissue healing.

Our solution comprises a new form of bone substitute that enables tissue regeneration of large bone defects with load-bearing capacities, thus providing reliable bone healing without losing rehabilitation potential.

PROJECT GOALS

- Identify and select most suitable material combination for the implant
- Develop the ideal implant structure
- Fabricate prototype for in *vivo proof-of-concept* (PoC) of the bone substitute
- Validate the implant functionality in vivo

- Validation of the prototype in vivo with large animals
- Start-up or spin-off foundation
- Implementation of new implant in clinical practice

Precision therapy for neurological autoimmune diseases



PRINCIPLE INVESTIGATORS: **Dr. Niels von Wardenburg, Amelya Keles, Prof. Harald Prüß** Charité



SUMMARY

Autoimmune encephalopathies are caused by autoantibodies generated by pathogenic B cells. Current treatment options with immunosuppressive therapy result in severe side effects.

Niels von Wardenburg and his team aim to develop a precise therapy that effectively depletes the pathogenic B cells leaving the protective B cells unaffected. The overall goal is to develop a genetically engineered T cell therapy to selectively eliminate autoantibodies causing autoimmunediseases.

PROJECT GOALS

- Preclinical development of engineered T cell therapy
- Validation of engineered T cells in vitro and in vivo

- Found a start-up for development of genetically modified T cell products
- Conduct phase I/II clinical trials

Restoring immune balance in NMOSD patients with a tolerogenic vaccine





PRINCIPLE INVESTIGATORS: Dr. Maria Hastermann, Dr. Nadine Strempel Charité, DZNE



SUMMARY

Neuromyelitis optica (NMOSD) is a devastating autoimmune disease that causes blindness and paralysis. Current therapies for NMOSD are not disease-specific, not curative, have side effects that are debilitating or even lifethreatening, and come at a high cost (200k/patient/year).

With the goal of preventing disease exacerbation and relapse in NMOSD patients, the team is developing a specific vaccine designed to restore healthy immune homeostasis, with the potential to be curative with minimal side effects.

PROJECT GOALS

- Design optimal vaccine
- Demonstrate efficacy in vitro

- Approval by PEI and clinical trial I
- Develop a specific vaccination for Neuromyelitis optica (NMOSD) patients

Isolation of high avidity cancer-specific TCRs





PRINCIPLE INVESTIGATORS: **PD. Dr. Antonia Busse, Dr. Martin Klatt** BIH/Charité



SUMMARY

CAR T cells have been very successful in the treatment of hematologic malignancies, but many tumor-specific antigens are expressed intracellularly and cannot be targeted by conventional CAR T cells.

This project seeks to develop a novel adoptive cell therapy with a T cell receptor (TCR) against an HLA-A2 restricted epitope of a cancer germline antigen. High avidity cancer-specific TCRs will be isolated and preclinically characterized in vitro and in vivo.

PROJECT GOALS

- Isolation and in vitro evaluation of high avidity cancer-specific TCRs
- Preclinical development in vitro & in vivo completed

- Perform phase I clinical trial
- License to Biotech / Pharma or Startup foundation

RACK 2

Particle-mediated transport of dissolved active agents into hair follicles



PRINCIPLE INVESTIGATORS: **Prof. Dr. Martina Meinke, Prof. Dr. Cornelia Keck** Charité & Philipps-Universität Marburg



SUMMARY

The skin is a stable barrier making uptake of topically applied substances difficult. Hair follicles (HF) are an interesting target site for the delivery of topically applied substances due to the weaker follicular barrier. However, non-particulate substances, including dissolved active ingredients, practically do not penetrate the HF, have very limited bioavailability or even fail to pass the skin barrier at all.

The team has developed a method for improved particle-mediated transport of dissolved active agents into HF. In the scope of this project, the aim is to determine the best conditions ex vivo for optimal drug HF penetration and show proof-of-concept drug delivery as well as a first validation in vivo.

If successful, this new way of enhanced drug delivery is broadly applicable and we aim to investigate its use for further drugs and indications.

PROJECT GOALS

- Determine the conditions ex vivo for optimal drug hair follicle penetration
- Proof-of-concept drug delivery
- Validation in animal model

- Licensing to industry
- Broaden application to other drugs/indications

22

Novel peptide-based drug for the treatment of fibrosis







PRINCIPLE INVESTIGATORS: **Prof. Uwe Pleyer¹, Dr. Birgitt Gutbier¹, Dr. Brockmann²**Charité¹ & Universitätsmedizin Rostock²



SUMMARY

Diseases, associated with a vast loss of function usually result from misguided wound healing or fibrogenesis. Yet, no causal therapy for fibrotic diseases in general exists. Ocular fibrosis displays an unmet medical need, including the scar formation on the cornea, leading to blindness.

The team first developed a novel peptide-based antifibrotic therapy and showed its efficacy in a mouse model of corneal fibrosis.

In the scope of this project, the team focuses on peptide optimizations as well as relevant assays regarding pharmacological evaluation of absorption, distribution, metabolism, excretion, toxicity and safety.

If successful, the potentials of the peptide-based treatment for ocular and system medicine, especially pulmonary fibrosis, will be evaluated.

PROJECT GOALS

- Pharmacological evaluation of absorption, distribution, metabolism, excretion, toxicity parameters
- Validation in second animal model

- Licensing to industry or startup foundation
- Broaden treatment to other indications

Generation and preclinical evaluation of neuroblastoma**specific CAR constructs**



PRINCIPLE INVESTIGATORS: Prof. Dr. Annette Künkele-Langer, Dr. Laura Grunewald, Dr. Kathleen Anders Charité



SUMMARY

Neuroblastoma remains the leading cause of cancer deaths in children under five, highlighting the urgent need for innovative therapies. CAR-T cell therapies for this indication face several obstacles such as limited persistence and efficacy of CAR-T cells.

Therefore, there is a high need for optimized neuroblastoma-specific CAR-T cell therapies.

Annette Künkele-Langer and her team aim to develop novel CAR constructs to generate CAR-T cells for neuroblastoma therapy and subject these cells to a detailed preclinical validation.

The ultimate aim is the development of a successful cell therapy for this deadly childhood cancer which would represent a milestone in the history of pediatric oncology.

PROJECT GOALS

- Generation of novel CAR constructs for CAR-T cell therapy
- Validation of CAR-T cells in vitro and in vivo

- Fullfil regulatory requirements
- Perform phase I/II clinical trials
- License to Biotech/Pharma or formation of
- startup

TRACK 2

Prototype construction of stapler for biliary and pancreatic anastomosis



PRINCIPLE INVESTIGATOR: **Dr. Panagiotis Fikatas**Charité



SUMMARY

An anastomosis is a surgical procedures that establishes a connection between two anatomical structures. In abdominal surgery, anastomosis performed on the bile duct and the pancreas are extremely challenging procedures that require excellent surgical skills and can only be performed by hand.

In this SPARK project, the team develops two devices that allow biliary and pancreatic anastomosis in a safe, quick and reproducible way. The novel devices will reduce the risk of secondary complications, minimize the risk of lethal secondary effects and reduce the necessity for further hospital treatment.

PROJECT GOALS

- Build two functional prototypes
- Perform validation tests in "dry-lab"
- Submit patent application

- Perform validation tests in vivo
- Startup foundation or license to industry

Past SPARK-BIH projects

TRACK 1

Combination strategies for rational drug targeting of pancreatic ductal adenocarcinoma (PDAC)



PRINCIPLE INVESTIGATORS: Hazal Köse, Prof. Dr. Ulrich Keller, PD Dr. Matthias Wirth Charité



SUMMARY

Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive cancer with poor prognosis. This adverse outcome can be in part attributed to the delayed diagnosis of PDAC, in most cases, combined with the unresponsiveness of a subset of patients to the current treatments.

Our aim is to develop a novel combination therapy for PDAC that does not only improve the treatment but also could provide a basis for immunotherapeutic interventions in PDAC and thus significantly improve patient's outcomes.

PROJECT GOALS

- Proof-of-concept of the combination strategy in vivo
- Characterization of the cellular ecosystem and immunomodulatory features upon therapeutic intervention using spatial transcriptomics
- Identification of new potential biomarkers in PDAC for therapy

- Clinical trials
- Licensing to industry or startup foundation

TRACK 1

Novel treatment against atherosclerotic vascular diseases



PRINCIPLE INVESTIGATORS: **Dr.-Ing. Szandor Simmons, Prof. Dr. med. Wolfgang M. Kuebler**Charité



SUMMARY

Atherothrombosis is the leading cause of cardiovascular morbidity and mortality worldwide:

Although statin-based lipid-lowering therapies have been shown to reduce major cardiovascular events, additional therapies are needed to reduce their occurrence.

The team has identified via retrospective patient data analysis a treatment which bears anticoagulant potential in inflammatory diseases, coupled to a low risk of ischemia and bleeding.

Their overall goal is therefore to prove the efficacy of a repurposed medication in the prevention and treatment of atherothrombosis and to provide a pathway to improved therapy

PROJECT GOALS

- Develop a novel therapy against atherosclerosis progression
- Demonstrate an improved outcome compared to standard anticoagulant therapy in vivo

- License to Pharma or partner with Industry
- Perform clinical trials II / III

A modular allogeneic CAR-NK cell therapy that targets cancer and its tumor microenvironment



PRINCIPLE INVESTIGATORS: **Dr. Dimitrios Laurin Wagner, Jonas Kath, Clemens Franke** Charité



SUMMARY

One of the most promising immuno-therapies against cancer is the adoptive cell transfer of genetically modified T cells. However, so far, attempts have been unsuccessful in some cancers, like acute myeloid leukemia or most solid tumors.

This project aims to develop a modular allogeneic CAR-NK cell product for improved treatment of cancer, alone or as co-treatment with a monoclonal antibody.

PROJECT GOALS

- Development of a modular allogeneic CAR-NK cell product
- Preclinical characterization in vitro

- Perform phase I / II clinical trial
- License to Biotech/Pharma or Startup foundation

2022

A novel treatment to prevent endothelial lesions & thromboinflammation in ischemic stroke



PRINCIPLE INVESTIGATORS: **Prof. Dr. Volker Haucke, Prof. Dr. Christoph Harms** FMP Berlin, Charité



SUMMARY

Ischemic stroke is a severe, life-threatening condition and the second leading cause of death worldwide. It is typically caused by blockage of an artery that supplies blood to the brain and often results in irreversible brain damage, which is further exacerbated by endothelial barrier dysfunction.

This project aims to develop a novel treatment to preserve vascular integrity to counteract aggrevating lesions following ischemic stroke.

PROJECT GOALS

- Development of a novel therapy to reduce damage after ischemic stroke
- Preclinical characterization in vitro and in vivo

- Perform phase I / II clinical trial
- License to Pharma or start-up company

NeuroCure

Predictors for Chemotherapy induced polyneuropathy identified with mass spectrometry



PRINCIPLE INVESTIGATORS:

PD Dr. Petra Hühnchen, Dr. Michael Mülleder, PD Dr. Wolfgang
Böhmerle, Prof. Dr. Matthias Endres Charité



SUMMARY

Neuropathies are among the most common side effects of cytotoxic chemotherapy. These impairments affect the quality of life and represent a dose-limiting factor for treatment of cancer patients.

This project aims to identify and validate prognostic biomarkers: these will enable to predict chemotherapy induced polyneuropathies and prevent neurotoxicity by preselecting patients at risk.

PROJECT GOALS

- Identify and validate biomarker profile(s)
- Patent submission

- Clinical validation of biomarker set
- License to Biotech or start-up foundation

Validation of Biomarkers and Potential Therapeutic **Targets in Neurodegenerative Diseases**



PRINCIPLE INVESTIGATORS:

PD Dr. Péter Körtvélyessy, Dr. Felix Wohlrab, Laura Göschel, **Prof. Matthias Endres** Charité



NeuroCure

SUMMARY

Alzheimer's Disease affects over 7 million patients in Europe with an increasing trend. To date, there is neither an effective therapy nor a predictive biomarker for early stages of Alzheimer's Disease. This project aims to identify and validate prognostic biomarkers from a well-characterized Alzheimer's Disease patient cohort.

PROJECT GOALS

- Identification and validation of prognostic biomarkers for Alzheimer's Disease
- Development of a promising methodology for biomarker detection
- Patent application

- Acquirement of a license to provide for Biotech or startup company
- Development of a therapy against Alzheimer's Disease
- A new generation of biomarkers in Alzheimer's Disease

MyaLink – digital platform to monitor rare diseases



PRINCIPLE INVESTIGATORS:

Dr. Sophie Lehnerer, Dr. Maike Stein, Dr. Lea Gerischer, Prof. Dr. Andreas Meisel, Prof. Dr. Matthias Endres Charité



NeuroCure

SUMMARY

Patients with rare diseases require highly individualized therapy by specialists, which is often limited. Myasthenia gravis is a chronic autoimmune disease leading to exercise-dependent muscle weakness. Fluctuations can lead to life-threatening episodes with ICU visits.

This project aims to develop a platform to improve the quality of treatment via enabling the access to specialists and digital symptom tracking to prevent life-threatening episodes and ICU visits.

PROJECT GOALS

- Clinical validation of digital monitoring in Myasthenia gravis patients
- Optimization of software

- Startup foundation or licensing
- Digital monitoring as standard of care

NeuroCure

Dotbase DBS – Integrated Software Platform for monitoring, quality measurment and SOPs in deep brain stimulation therapy



PRINCIPLE INVESTIGATORS:

Jasper Mecklenburg, Dr. Gregor Wenzel, Prof. Dr. Andrea Kühn
Charité



SUMMARY

Movement disorders, and especially deep brain stimulation (DBS), require a highly individualized therapy and continous therapy-adaptation over years. During each step, extensive and heterogeneous data is collected which can be used for individualisation of the treatment.

This project aims to develop a software platform which can collect and visualize the data in clinical routine. This will enable capturing the whole clinical path-way and improve adaptation of the treatment.

PROJECT GOALS

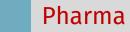
- Development of software for all steps during DBS therapy
- Preparation for technical documentation according to Medical device regulation

- Startup foundation
- Expand platform to further indications

A universal platform for the discovery of new therapeutic modalities



PRINCIPLE INVESTIGATOR: **Dr. Yollete Guillén Schlippe** Charité





Methods/Platform & Infectious Disease

SUMMARY

Most therapeutic targets involved in aberrant intracellular protein-protein and protein-RNA interactions remain elusive to traditional drug discovery efforts. The team led by Y. Guillén Schlippe has developed a broadly applicable discovery platform capable of identifying hits for such therapeutically "undruggable" targets.

The goal of the current project is to demonstrate that this discovery platform is capable of delivering new therapeutic lead molecules for a variety of targets involved in cancer and bacterial infections. Validation of the platform and generated hits will open the door to new therapeutic opportunities and modalities, expanding the "druggable" proteome.

PROJECT GOALS

- Validation of the discovery platform
- Identification of hits for novel therapeutic targets

- Validation of lead drug candidates
- License to Pharma or startup foundation

202

CD5-specific TCR-T cells for treatment of relapsed or refractory T cell neoplasms



PRINCIPLE INVESTIGATOR: **PD Dr. Antonia Busse** Charité



SUMMARY

Patients with T-Non Hodgkin lymphomas (T-NHL) and T-acute lymphoblastic leukemia (T-ALL) have a poor prognosis, limited therapies are available and only about 30% are cured by front-line therapy.

This project seeks to complete the preclinical characterization of a novel adoptive cell therapy with a T cell receptor (TCR) against an HLA-A2 restricted epitope of the T cell antigen CD5. CD5-specific TCR-T could hence represent a novel salvage / bridging therapy option for HLA-A2+ relapsed or refractory T cell neoplasms or could be used as consolidation treatment after HLA-A2 mismatch allogeneic hematopoetic stem cell transplantation with the goal to reach long-term remission.

PROJECT GOALS

- Complete the preclinical development of a novel ATMP
- Prepare phase I clinical trial
- Establish industry partnership

- Perform phase I clinical trial
- License to Biotech/Pharma

ALARM – A viral alert realtime monitoring



PRINCIPLE INVESTIGATORS: Michael Lommel, Dr. Ulrich Kertzscher, Dr. Jens Dernedde Charité



SUMMARY

The COVID-19 pandemic poses a great social and economic burden on individuals and society and the infection with the SARS-CoV-2 virus may lead to severe acute or long-term disease.

An important tool against the COVID-19 pandemic is the early diagnosis of SARS-CoV-2 infected individuals. Tests help to detect and break infection chains more rapidly and can provide additional security in everyday life. In this SPARK project, the team develops a simple, fast and affordable test system that detects the virus with high sensitivity, is cheaper and more accurate than commonly used lateral flow antigen tests and will be particularly suitable for screenings at large events.

PROJECT GOALS

- Build a functional devise prototype
- Pre-clinical validation

- Startup foundation or license to industry
- CE certification as a medical device

Validation of a consensus DNA sequence for vaccination against pandemic coronaviruses (PanCoVac)





PRINCIPLE INVESTIGATORS: **Prof. Dr. Günther Schönrich, Dr. Mohammed Yassen** Charité



SUMMARY

The ongoing pandemic of coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and has led to more than 5,4 million deaths up to December 2021. Currently, licensed vaccines encode the SARS-CoV-2 Sprotein particularly aiming at induction of neutralizing antibodies. This may result in viral escape by mutant variants and short-lived protection against SARS-CoV-2. The team seeks to prevent future severe infections caused by novel SARS-CoV-2 mutant variants or by potentially future zoonosis. For this purpose, the team has generated a vaccine based on a compact sequence (PanCoVac) that is expected to confer immunity against a wide range of SARS-CoV-2 mutant viral strains as well as potential new coronaviruses.

PROJECT GOALS

- Validate PanCoVac in vitro and in vivo
- Validate PanCoVac's wide-spectrum efficacy
 - File for patent

LONG-TERM GOALS

- License to Pharma or startup foundation
- Perform phase I / II clinical trial

PREVIOUS SPARK FUNDING

Track 1 2020

A virus-free platform technology for next-generation CAR therapeutics





PRINCIPLE INVESTIGATORS: **Dr. Dimitrios Laurin Wagner, Jonas Kath**Charité



TRACK 2

SUMMARY

One of the most promising immunotherapies against cancer is the adoptive cell transfer of genetically modified T cells. Herein, patient-derived Chimeric Antigen Receptor (CAR) expressing T cells have been one of the most successful therapy to date. However, routine clinical implementation of CAR T cells is stalled by high prices, certain severe adverse events and the complexity of generating an autologous cell product from chemopretreated patients.

Therefore, this project aims to develop a virus-free platform technology for generation of novel improved and cost-effective next-generation CAR therapeutics suitable for autologous and/or allogeneic use.

PROJECT GOALS

- Development of a virus-free platform technology for generation of next-generation CARs
- Preclinical characterization of a novel CAR T cell therapy
- Prepare phase I/IIa clinical trial

- Perform phase I/IIa clinical trial
- License to Biotech/Pharma or startup company

Infection based large scale production platform for rAAV gene therapy vectors



PRINCIPLE INVESTIGATOR: PD Dr. Stefan Weger Charité



TRACK 2

SUMMARY

Gene transfer vectors have developed into the leading platform for gene therapeutic treatments of numerous human diseases and several rAAV vectors have already been approved for commercialization. The current methods for rAAV production represent a bottleneck and render the generation of these therapeutics extremely expensive.

This projects aims at developing a new method which allows a more efficient production of clinically applicable rAAVs, leading to increased availability and reduced costs for gene therapies.

PROJECT GOALS

- Establishment of universal platform for large-scale rAAV production
- Identification of industrial partner for codevelopment
- Extension of the platform to different rAAV serotypes

- License to Biotech company or startup foundation
- Perform phase I clinical trial

202

Al supported quantitative assessment of aortic valve calcification





PRINCIPLE INVESTIGATORS: **Prof. Dr. Anja Hennemuth, Dr. Olena Nemchyna**Charité/Deutsches Herzzentrum Berlin



SUMMARY

Aortic stenosis (AS) is the most common valvular heart disease in the Western world. In the management of patients with AS, it is essential to accurately diagnose the disease severity and determine the proper timing of a surgical intervention. Echocardiography is the current standard modality for evaluating AS severity, but it is not always sufficient to confirm the diagnosis of severe AS. In certain cases computed tomography (CT) is necessary to quantify aortic valve calcium load and to identify patients with true severe AS. Nevertheless, CT does not qualify as a routine examination. Hence, the aim of the project is to create and validate a prototype machine learning solution for the quantitative assessment of aortic valve calcification.

PROJECT GOALS

- Train machine learning algorithms on annotated data of patients with AS
- Optimize and validate AI solution

- CE certification as a medical device
- Implementation of the solution in the clinical workflow
- licensing to MedTech company or startup foundation

RACK 1

Novel compounds to treat excessive water loss in states of dysfunctional vasopressin-mediated water reabsorption



PRINCIPLE INVESTIGATOR: **PD Dr. Enno Klussmann**Max Delbrück Center for Molecular Medicine



SUMMARY

Diabetes insipidus is characterized by excessive water loss of up to 20 l of urine per day. In this disease, water reabsorption in the renal collecting duct is decreased due to reduced accumulation of the water channel aquaporin 2 (AQP2) in the plasma membranes of principal cells, caused by dysfunctional vasopressin-mediated signaling. The team led by Dr. Klussmann has shown in vitro and in preliminary analyses of human patients that an antifungal drug promotes water reabsorption via AQP2. Now the team aims to develop new proprietary compounds with better ADME-Tox properties.

Despite the medical burden, there is currently no efficient treatment for excessive water loss and many patients could benefit from the development of a pharmacological intervention.

PROJECT ACHIEVEMENTS DURING & AFTER SPARK

- Synthesis of a library of compounds
- In vitro functional studies with library of compounds
- Animal studies with selected lead candidates

- Secure funding for further lead compound development
- Plan clinical phases

2020

Expansion of natural killer cells for viral infection and cancer



PRINCIPLE INVESTIGATORS: **Prof. Dr. Chiara Romagnani, Dr. Timo Rückert**Charité & German Rheumatism Research Centre



SUMMARY

The immune system has evolved different strategies to prevent and fight cancer and infections. Natural Killer (NK) cells are an innate immune cell type able to kill tumor and/or infected cells. The team has identified a specific peptide whose presence is shared by a human virus and certain tumors that leads to expansion of a specific Natural Killer cell type. The project aims for the preclinical development of a vaccine prototype for treatment of these tumors as well as of the respective human viral infection. The advantage of this approach is that cancer patients can benefit from this boost for the immune system that is ready not only to fight this virus infection but also relapsing tumors.

PROJECT GOALS

- Generation of a novel vaccine prototype for treatment of specific tumors as well as of a viral infection
- *In vivo* Proof-of-Concept
- Preclinical development of the vaccine

LONG-TERM GOALS

- Perform phase I/II clinical trial
- License to Pharma or startup foundation

PREVIOUS SPARK FUNDING

Track 1 2018

SatTyping: A software-based typing of regenerative stem cells towards resource-saving and efficient production of ATMPs



PRINCIPLE INVESTIGATORS:

Dr. Verena Schöwel-Wolf, Dr. Andreas Marg,

Prof. Dr. Simone Spuler Charité



SUMMARY

Muscle wasting and weakness are leading symptoms of a wide variety of diseases with dramatic impairment of life quality and life-threatening consequences. The team develops an innovative autologous muscle stem cell therapy to fight muscle diseases. For the efficient production of human muscle stem cells for regenerative therapy, the SatTyping team aims to develope a softwarebased standardized in-process-control. The advanced therapy medical product market is urgently seeking for automation of product manufacturing to ensure marketability. The SatTyping software solution promotes resource-saving production of adherent cells and contributes to digitization when it comes to scalability.

PROJECT ACHIEVMENTS DURING AND AFTER SPARK

Testing of a software-based solution for in-process quality control for adherent growing cells

SatTyping: A software-based typing of regenerative stem cells towards resource-saving and efficient production of ATMPs



PRINCIPLE INVESTIGATORS:

Dr. Verena Schöwel-Wolf, Dr. Andreas Marg,

Prof. Dr. Simone Spuler Charité



SUMMARY

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PROJECT ACHIEVMENTS DURING AND AFTER SPARK

Testing of a software-based solution for in-process quality control for adherent growing cells

A novel solution for a total artificial heart



PRINCIPLE INVESTIGATORS: Tim Bierewirtz, Prof. Marcus Granegger, PhD Charité



SUMMARY

transplantation remains the Heart life-saving therapeutic option for patients with end-stage heart disease. However, the large heart transplant waiting list is the reflection of a severe and persistent shortage of donor hearts. Total artificial heart (TAH) is an artificial organ that mimics the native heart. It is designed to replace the heart in patients with end-stage heart failure as a bridge to heart transplantation. There are very few TAH solutions on the market and the one available are nonetheless risk prone regarding reliability, blood damage and thrombus formation. Hence, the aim of the project is to develop a functional prototype of an implantable, pulsatile TAH with superior performances by means of reliability, implantability and hemocompatibilty.

PROJECT GOALS

- Manufacturing and assembly of fully functional prototypes
- Perform virtual and physical fitting studies
- Perform acute/chronic in vivo validation study within large animals

LONG-TERM GOALS

- Startup foundation or license to MedTech company
- CE certification as a medical device

PREVIOUS SPARK FUNDING

Track 1 2019

Off-the-shelf chimeric antigen receptor (CAR) product with broad applicability for malignant diseases



PRINCIPLE INVESTIGATORS: **Prof. Dr. Gabriele Pecher** Charité



SUMMARY

Cancer still remains the second leading cause of death worldwide. Tumors often do not respond to standard treatment and become essentially incurable.

The team develops a novel advanced therapy medicinal product (ATMP) for the precision immunotherapy of both solid tumors hematological diseases to generate an allogeneic, "off-the-shelf" CAR-modified therapeutic agent. The ATMP will be validated and preclinical testing will be accomplished.

PROJECT GOALS

- Generation of a novel allogeneic ATMP for anti-cancer therapy
- Preclinical development of the ATMP

- Perform phase I/II clinical trial
- License to Pharma or startup foundation

Prevention of Paclitaxel-related neurotoxicity



PRINCIPLE INVESTIGATOR:

Prof. Dr. Matthias Endres, PD Dr. Wolfgang Böhmerle, PD Dr. med Petra Hühnchen Charité



SUMMARY

Neurotoxicity is a common and potentially long-lasting side effect of cytotoxic drugs including Paclitaxel (PTX). Preclinical studies have shown that neuronal damage by PTX can be reduced with a marketed drug that can readily be repositioned. With their previous 2018 SPARKBIH validation fund, the team successfully developed a roadmap for clinical translation of this keyfinding.

Currently, it plans to conduct an explorative proofofconcept phase II clinical trial to prove that coadministration of the repositioned drug prevents neurological side effects of PTX. During this funding period, the team is going to initiate the trial and perform a preliminary interim safety analysis to demonstrate safety and feasibility of the intervention.

PROJECT GOALS

- Obtain ethical approval by BfArM & LaGeSo
- Set-up clinical trial including e-documentation, infrastructure & medication kits
- Complete interim safety study with 20 breast cancer patients

LONG-TERM GOALS

- Complete clinical phases with further funding
- Change medical practice

PREVIOUS SPARK FUNDING

Track 1 2018

Combinatorial treatment against metastatic colorectal cancer



PRINCIPLE INVESTIGATORS:

Prof. Dr. Ulrike Stein, Prof. Dr. Wolfgang Walther,
Dr. Dennis Kobelt, Paul Curtis Schöpe MDC & Charité



SUMMARY

Colorectal cancer is the third most diagnosed cancer and fourth most common cause of death worldwide, metastasis being the cause of about 90% of deaths. The team has previously identified a key driver and novel biomarker of metastasis formation. Moreover, new inhibitory compounds able to inhibit this metastasis driver were identified through high throughput screening with former SPARK support. During the current funding period, the team will evaluate these inhibitors for their ability to restrict tumor progression and metastasis formation with adequate in vivo tolerability. Furthermore, the molecular action of the colorectal cancer biomarker will be explored further.

PROJECT GOALS

- ADMET characterization and mode of action assessment of identified hit compounds
- MedChem analysis, design and synthesis to obtain lead compounds
- In vivo testing of lead compounds for antitumoral and antimetastatic activity

- Clinical trial phase I
- Licensing to Pharma

Biomarkers for tumor immune therapy associated neurological side effects



PRINCIPLE INVESTIGATORS:

Prof. Dr. Matthias Endres, PD. Dr. Wolfgang Böhmerle, Dr. Samuel Knauss, Dr. Leonie Müller-Jensen, PD Dr. med Petra Hühnchen Charité





Neurology & Oncology

NeuroCure

SUMMARY

Tumor immunotherapy and in particular immune checkpoint inhibitor treatment continues to transform oncological therapy and the number of patients treated with checkpoint inhibitors is expected to increase substantially in the coming years. High response rates to the treatment are contrasted by potentially fatal immune related adverse events (irAE). Albeit neurological irAE (irAE-N) are rare, they are associated with high morbidity and mortality.

This projects aims at identifying immunological biomarkers to identify irAR-N in patients treated with immune checkpoint inhibitors. The increased surveillance of patients with a risk profile will affect patient's treatment and reduce the cost of care as well as mortality and morbidity associated with the treatment.

PROJECT GOALS

- Identify biomarkers for irAE-N
- File patent

- Cooperation with Medtech company / Startup foundation
- Implementation of identified biomarkers in clinical practice

Novel therapy for neuromuscular disease caused by mutations in myotubularins



PRINCIPLE INVESTIGATOR: **Prof. Dr. Volker Haucke FMP**



NeuroCure

SUMMARY

Mutations in myotubularin1 affect 1:50,000 newborn males and cause a severe muscle disorder (XLMTM) which is characterized by severe generalized muscle weakness with ventilator, wheelchair and feeding tube dependence in addition to dramatically reducing survival.

Despite it's severity, there is no treatment yet. This project aims at utilizing a novel target for the treatment of this disease.

By screening an in-house library and optimizing hits via medicinal chemistry, the team aims at finding and developing the first small molecule inhibitor for the treatment of this fatal disease.

PROJECT GOALS

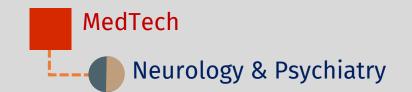
- Identification and generation of lead compounds
- *In vitro* and *in vivo* proof-of-concept studies
- Hit-to-lead optimization

- Develop first small molecule inhibitor as treatment for XLMTM
- Licensing to Pharma company

Neural mapping using transcranial magnetic temporal interference stimulation



PRINCIPLE INVESTIGATORS: Khaled Nasr, Prof. Dr. Surjo Soekadar, Prof. Dr. Andreas Heinz Charité



NeuroCure

SUMMARY

Deep brain stimulation has provided dramatic benefit for a variety of clinical conditions. However, current noninvasive technology allows only superficial stimulation of the brain. The only possible ways of reaching deeper brain regions require invasive approaches. This project aims at developing a medical device that enables non-invasive stimulation of deep brain areas at millimeter precision to enable the treatment of neurological and psychiatric disorders such as depression or OCD.

PROJECT GOALS

- Develop and build prototype
- In vivo testing
- Preparation for CE certification

- Phase I clinical study
- Implementation of the solution in the clinical workflow by licensing to Medtech company or startup foundation

NeuroCure

Screening for novel modulators that restore synaptic signaling in human iPSC-derived neurons from SYNGAP syndrome patients





PRINCIPLE INVESTIGATORS:

Prof. Dr. Dietmar Schmitz, Prof. Dr. Markus Schülke-Gerstenfeld, Prof. Dr. Sarah Shoichet, Dr. Nils Rademacher, Judith von Sivers Charité





Neurology & Methods/Platform

SUMMARY

SYNGAP syndrome is a rare congenital disorder caused by mutations in the SYNGAP1 gene. The main feature is intellectual disability; patients also suffer from up to 140 seizures per day, and to date, there is no efficient therapy for the disorder.

Studies in animal disease models have highlighted that SYNGAP1 loss of function results in defective synaptic signaling. The goal of this project is to identify a novel drug therapy by screening for molecules that restore defective signaling cascades. The team has therefore designed an assay that will be adapted for high-throughput screening of an FDA-approved drug library. This may pave the way for a unique and novel therapy for this rare and severe disease.

PROJECT GOALS

- Develop stable assay
- Identify FDA-approved drugs that rebalance the altered synaptic function in rodent neurons

- Use patient-derived iPS cells to validate hit compounds
- Repurposing of identified drug(s)

4H

DiaperID - a medical APP for smart stool recognition and newborn screening for biliary atresia



PRINCIPLE INVESTIGATOR: **Prof. Dr. Philip Bufler, Dr. Christian Hudert, Lucas Griessmair**Charité



SUMMARY

Biliary atresia is a rare disease of the newborn liver that, if left untreated, can lead to liver failure within months. Early diagnosis is crucial to avoid liver transplantation. Pale stools are an early clinical sign and their detection should be simple. This is the vision of DiaperID. The team aims to develop a platform application to screen for stool colour using image analysis supported by machine learning. Both parents and health care professionals will be asked to use the platform as a routine test within the newborn screening program to collaboratively combat diseases of this nature by simply taking pictures of their newborn's stool and uploading the image for subsequent analysis.

PROJECT GOALS

- Development of a strong proof of concept
- Validation of the idea and business model

LONG-TERM GOALS

 That every newborn baby in Germany will be screened for rare liver diseases by analyzing stool pictures via DiaperID

14H

RadioEye - A unique diagnostic decision support tool for radiologists





PRINCIPLE INVESTIGATORS: **PD Dr. Katharina Erb-Eigner, Sophie Au**Charité



SUMMARY

The team RadioEye is developing a digital application to help radiologists worldwide reach the correct diagnosis quickly and effectively. By using image-based diagnostic tools rather than traditional logic trees or syntactic search, the team is working to create an effective diagnostic support tool that takes full advantage of the format that radiologists are most attuned to, image-based search and recognition. RadioEye will focus first on the development of this platform for use in eye and eye-socket scans.

PROJECT GOALS

- Development of a strong proof of concept
- Validation of the idea and business model

- Become the No. 1 image-based reference tool for radiologists worldwide
- Improve quality of radiology reports and save lives

Appsy - Antidepressant medication companion





PRINCIPLE INVESTIGATORS: **Dr. Constantin Volkmann, Rosana Ardila, PD Dr. Christian Müller** Charité



SUMMARY

Antidepressants are widely used in the treatment of psychiatric disorders including major depression. Many patients want to discontinue antidepressants in the course of treatment, but face substantial barriers, since most physicians aren't trained in safe de-prescribing. Stopping antidepressants may lead to clinical deterioration due to relapse or discontinuation symptoms that affect up to 60% of patients and may be severe and long-lasting. Appsy is a patient-centered digital application that accompanies the antidepressant discontinuation process, so that the patients can safely and successfully discontinue the medication in the outpatient setting.

PROJECT GOALS

- Development of a strong proof of concept
- Initial validation of concept with stakeholders

LONG-TERM GOALS

 To provide safe antidepressant discontinuation and enable patients to lead lives without medication

Exploring a novel therapeutic target in cystic fibrosis



PRINCIPLE INVESTIGATOR: **Dr. Anita Balázs** Charité



SUMMARY

Cystic Fibrosis (CF) is a life-limiting disease caused by mutations in the CFTR gene. Although highly effective CFTR modulators are emerging, ~10-15% of patients will not benefit from these therapies, while the high price of these drugs prevents access in many countries. Hence, there is an unmet need to develop new therapies that can be applied to patients, independently of the underlying CFTR mutation. A strategy to achieve this, relies on restoring epithelial ion transport, bypassing CFTR dysfunction. This project aims to validate drug candidates previously identified in a drug screen as potential modulators of an alternative ion transporter. These potential hits may path the way for a novel and inclusive therapy for CF.

PROJECT ACHIEVEMENTS DURING & AFTER SPARK

- in vitro functional studies with selected hits
- Further analysis of mechanism of action

- Show in vivo PoC
- Perform clinical testing
- License to Pharma

Validation of anti-cancer agents in patient-derived canceroids



PRINCIPLE INVESTIGATOR: **Prof. Dr. Reinhold Schäfer** Charité



SUMMARY

Members of the family of signaling RAS-GTPases are frequently mutated in cancer, causing > 1 million deaths worldwide annually by triggering tumor pathogenesis and conferring resistance to therapies. Currently, compounds targeting the Ras-signaling pathway are in preclinical and clinical testing. However, these lead drugs show uncertain long-time effects.

Targeting transcriptional hubs downstream of RAS has the potential to block malignancy and therapy resistance. The project aims to validate modulators of a RAS-responsive transcription factor: Compounds identified via high-throughput-screening on an approved-drug library are validated in patient-derived canceroids. This strategy has the potential to establish a new concept of anti-RAS mono-or combinatorial therapy.

PROJECT ACHIEVEMENTS DURING & AFTER SPARK

- in vitro and organoid studies with screening hits
- Selection of candidates to be tested in vivo

- Start an investigator-initiated trial based on repositioned drug(s)
- License to Pharma

A novel peptide to regenerate the central nervous system





PRINCIPLE INVESTIGATORS: **Dr. Sarah-Christin Starossom, Prof. Dr. Friedemann Paul**Charité



SUMMARY

Multiple sclerosis (MS) is the most common chronic autoimmune and incurable disease of the the central nervous system. In MS, oligodendrocytes and the protective sheath (myelin) that covers nerve fibers are the primary targets of autoimmune attacks. Endogenous regeneration fails in most patients leading to devastating neurological symptoms including vision loss, fatigue and paralysis. The medical need is high as there is currently no approved drug addressing remyelination/oligodendrogenesis.

The team has identified a novel mechanism targeting remyelination and oligodendrogenesis. Based on these findings, the project aims at developing a novel therapeutic option for MS.

PROJECT ACHIEVEMENTS DURING & AFTER SPARK

- Synthesis of peptide libraries
- Functional studies on proliferation, cell death and oligodendrogenesis
 - Identification of candidates

- Validate novel drug treatment for MS
- License to Pharma

ACK 2

A novel advanced therapy medicinal product (ATMP) to treat solid tumors



PRINCIPLE INVESTIGATOR: **Prof. Dr. Gabriele Pecher** Charité



SUMMARY

So far, there is no cure for patients with metastatic solid tumors, and new therapies are urgently needed.

The project aims to develop a novel ATMP for the therapy of breast cancer. The group will use a CAR next generation platform technology in order to generate optimized immune cells to fight the immunosuppressive microenvironment of solid tumors. The ATMP will be validated and preclinical testing will be accomplished.

PROJECT ACHIEVEMENTS DURING & AFTER SPARK

- Novel CAR for treatment of solid tumors identified
- Preclinical *in vitro* and *in vivo* testing of ATMP

- Perform phase I/II clinical trial
- License to Pharma or startup foundation

2019

A novel gene therapy for treatment of aggressive B cell Lymphoma





PRINCIPLE INVESTIGATORS: **Prof. Dr. Antonio Pezzutto, PD Dr. Antonia Busse**Charité



SUMMARY

A specific point mutation of the protein MyD88 is known to be a key oncogenic driver event in around 20% of patients with an aggressive variant of Diffuse Large B cell Lymphoma, and in around 50% of patients with Primary CNS Lymphoma. Both patient populations have a poor prognosis, and only limited therapies are available especially for the elderly and patients with severe comorbidities. The project seeks to complete the preclinical characterization of a human-derived T cell receptor that selectively recognizes this specific mutation of MyD88. Adoptive T cell therapy with MyD88-specific T cells would represent a truly tumor-specific therapy, being much more selective than CAR T cells or immune checkpoint inhibitors.

PROJECT ACHIEVEMENTS DURING SPARK

- Preclinical development of novel TCR T cell candidate accomplished
- Successful publication of preclinical data in Journal for ImmunoTherapy of Cancer
- PEI scientific advice meeting
- Planning of FiH study
- Follow-on funding acquired of Else Kröner-Fresenius Foundation
- Pitch contribution at BIO Partnering at JP Morgan 2022

- Perform phase I clinical trial
- License to Pharma or clinical codevelopment

019

In vivo validation of a novel class of pain medication





PRINCIPLE INVESTIGATORS: **Dr. Viola Seitz, Prof. Dr. Christoph Stein**Charité



SUMMARY

Although pain research has identified a plethora of targets, no truly innovative analgesics have reached the market in the past years, mostly due to low efficacy or severe side effects. This leaves a significant unmet medical need for novel, safe and effective compounds with reduced side effect burden and abuse liability.

The project seeks to complete external validation of in vivo data on NFEPP, a novel compound that has demonstrated potent pain relief without addiction potential in initial experiments. A patent has been filed and results were published in Science in 2017.

PROJECT GOALS

- External validation of preclinical in vivo studies
- Secure follow-on applied research funding

- Further develop under CMC and GMP conditions
- Test safety & toxicity of NFEPP
- Perform phase I/IIa clinical trials
- License to Pharma

GrOwnValve – Anchoring mechanism for a personalized, autologous heart valve for children



PRINCIPLE INVESTIGATOR: **PD Dr. Boris Schmitt**Charité



SUMMARY

The aim of the project is the production and testing of an anchoring mechanism of a personalized, autologous heart valve for children enabling growth in a once-in-a-lifetime point-of-care minimally invasive implantation. The novel anchoring mechanism facilitates placement of the valve without hindering growth of valve and vessel. For babies born with a congenital heart valve defect there is no dedicated child valve on the market. Instead they often receive xenogenic animal valves which degrade over the following years urging for risky open-heart re-surgery.

PROJECT GOALS

- Perform preclinical testing of anchoring mechanism together with the valve
- Prepare phase II clinical trial in children

LONG-TERM GOALS

- Perform phase II clinical trial in children
- Startup foundation
- CE certification as a medical device

PREVIOUS SPARK FUNDING

I4H 2019

Pre-Education - Patient empowerment through automated digital education of gynaecological patients on the course of treatment



PRINCIPLE INVESTIGATOR: **Dr. Jessica Olschewski** Charité



SUMMARY

Medu+ aims at enabling patients to access audited information to inform themselves about diagnosis, treatment and additional care programs through access to a digital platform before, during and after their clinical pathway.

Whether it's the initial consultation, a postoperative session, or something else, the clinical environment for many patients can represent an unknown and unsure place, where information sources are varied and sometimes inconsistent. Medu+ is helping to close the loop on patient information sources starting with the gynecological clinic at the Charité and moving outwards from there.

PROJECT ACHIEVEMENTS DURING & AFTER 14H

- Developed the digital platform Medu+ accessible for patients and gynecologist at Charité
- Medu+ contains curated disease-relevant information and care plans and thus supports doctor-patient communication.

4

TimeTeller: A non-invasive method for the molecular and computational characterization of the internal biological clock in humans



PRINCIPLE INVESTIGATOR: **Prof. Dr. Angela Relógio** Charité



SUMMARY

Cancer treatment outcome, co-morbidities and side effects vary largely from patient to patient. Treatment regimens do not take circadian variations into account, neither of the patient nor of the drug metabolism. Adjusting the timing of treatment to the patient's circadian rhythm can optimise efficacy and diminish side effects, leading to better life quality for patients and reduced cost of care. The team has developed a reliable, non-invasive and easy-to-perform method for the characterization of the clock - called TimeTeller. It is further validated to offer personalized cancer support treatment and patient care by optimising the timing of treatment based on the circadian rhythms of the patient and the drug target. TimeTeller is a hybrid technology that uses molecular, mathematical and digital processing to profile an individual's inner circadian variations and provide personalised scheduling for behavioural and medical timing.

PROJECT ACHIEVEMENTS DURING & AFTER 14H

- Development of TimeTeller an innovative easy-to-perform method to determine the individual circadian rhythm using human saliva samples
- Follow-on funding acquired of BIH Digital Health Accelerator

- CE certification
- Implementation of TimeTeller for treatment optimization in the clinic
- Startup foundation

RACK 1

Prediction and prevention of congestive events in heart failure patients



PRINCIPLE INVESTIGATOR: **Dr. Alessandro Faragli** Charité



SUMMARY

Heart failure (HF) represents the leading cause of hospitalization worldwide. Because of the difficulty in treating this chronic disease, re-hospitalizations are associated with high cost for the healthcare systems, accounting for €28 billion per year in Europe only. The team aims at building an algorithm to predict and prevent congestive events in heart failure patients. They have identified risk predictors and created an algorithm. At the moment, the team is performing a database analysis on existing cohorts of HF patients to build the first risk prediction model.

PROJECT ACHIEVEMENTS DURING & AFTER SPARK

- Risk predictors identified
- First algorithm designed

- Perform clinical study to determine accuracy of prediction algorithm
- · Submit invention disclosure
- License to medtech or startup foundation

Gene therapy for the treatment of temporal lobe epilepsy





PRINCIPLE INVESTIGATORS: Prof. Dr. Regine Heilbronn, Prof. Dr. Christoph Schwarzer Charité & Medizinische Universität Innsbruck



SUMMARY

The project aims at developing a gene therapy for the treatment of drug-resistant focal epilepsy. An adenoassociated viral (AAV) vector will be delivered to the epileptic focus, re-expressing a neuropeptide that will be released in an activity-dependent manner, i.e. in periods of high neuronal activity which precedes the onset of a seizure. Suppression of neuronal excitability thereby suppresses the epileptic event. Strong proof of concept data in mice and rats have supported the feasibility of this strategy. The team is setting up a startup and has acquired follow-up funding to further pursue the strategy and develop the gene therapy for the use in patients.

PROJECT ACHIEVEMENTS DURING & AFTER SPARK

- Patents filed in 2016
- Preclinical Proof-of-concept in vivo and human brain tissue ex vivo in 2016
- Secured GoBio funding of 3.9 Mio. € in 2018 for 3 years
- Science4Life Venture Cup 2021
- GMP production in preparation
- Startup EpiBlok Therapeutics founded in 2022

LONG-TERM GOALS

Clinical trial phase I

Image-based support of minimal-invasive mitral valve repair



PRINCIPLE INVESTIGATOR: **Prof. Dr. Anja Hennemuth**Charité & German Rheumatism Research Centre



TRACK

SUMMARY

About 7000 isolated mitral valve surgeries are performed in Germany every year. Mitral valve repair (MVR) is superior to valve replacement. Successful repair does not only lead to better survival but also better quality of life and avoidance of anticoagulants. However MVR success rates strongly correlate with the experience of the surgeon as MVR is difficult to learn due to differences in pre-OP images of the moving heart and during the operation (or during surgery). This indicates the need for a better intraoperative decision support. The team works on the application of image-based surgery planning and image-based navigation with different modalities. This could help the surgeon to accurately consider anatomical and dynamic properties of the valve during surgery.

- Started development of software modules for image fusion and integrated visualization and interaction
- Started setting up quality management and documentation system
- Initiated collaborations to specify user needs and interface questions
- Initiated industry collaborations for clinical integration
- Acquired BMBF funding together with industry partner

Molecular imaging of biofilm infections - Validation of FISH controls



for automated endocarditis diagnostics PRINCIPLE INVESTIGATORS: **Prof. Dr. Annette Moter,**

Dr. Judith Kikhney Charité



Diagnostic



Infectious Disease & Methods/Platform

SUMMARY

Fluorescence in situ hybridization (FISH) is a molecular technique, which allows identification and visualization of microorganisms within tissues. Currently, the daily diagnostic use of FISH is restricted to highly specialized laboratories because it involves not only high-level of expertise, but also many hands-on steps, timeconsuming microscopy, laborious annotation and documentation of FISH images and is lacking standard high quality controls.

In this project diagnostic use of FISH in daily routine for endocarditis diagnostics is tested by automating the full process of this technique. The group is focusing on multiple aspects of this diagnostic procedure - with one emphasis on the generation of solid and validated routine positive controls.

- Design and validation of controls
- Developed a sample tracking software
- Currently developing semi-automated digital image analysis for detection of bacteria in histological sections
- Developed an intelligent image handling archiving and documentation system
- Currently testing entire platform in routine diagnostic and comparing the 'hands-on' with the automated FISH (within the BMBFfunded iSOLID consortium)

Inhibition of thyroid hormone inactivation for cancer treatment



PRINCIPLE INVESTIGATORS: **Dr. Kostja Renko, Prof. Dr. Lutz Schomburg**Charité



SUMMARY

An initial compound library screen led to a preliminary list of hormone modulators. The compound target reportedly plays a role in different cancer entities. During the SPARK funding period, drug candidates were characterized for specificity, potency and on-cell effects.

Furthermore, in silico drug design was started to predict improved candidates. Experimental approaches to verify the reported beneficial effects in a cancer cell line completed the overall strategy. Future plans include strategic cooperation with oncology experts.

- Verification and characterization of >50 compounds from an HTS approach
- Further testing of selected, specific candidates on intact cells
- Ongoing validation of candidates in cancer cell lines
- Plan of strategic cooperations with oncologists

Drug discovery for mitochondrially inherited Leigh syndrome (MILS)



PRINCIPLE INVESTIGATORS:

Prof. Dr. Alessandro Prigione,

Prof. Dr. Markus Schülke-Gerstenfeld MDC & Charité



SUMMARY

The team has developed a novel assay system based on patient-derived induced pluripotent stem cells (iPSCs) to identify compounds for treating Leigh syndrome. Using this assay, a class of drugs applicable for repurposing that restore the cellular disease phenotype has been identified. The team has initiated a compassionate use treatment for a terminal ill patient. The patient has recovered significantly. Based on these results a clinical study is planned. Leigh syndrome is a rare severe mitochondrial disease affecting children where treatment options are lacking.

PROJECT ACHIEVEMENTS DURING & AFTER SPARK

- Identified and validated compound class for treatment of Leigh syndrome
- Performed compassionate treatment
- Plan to prepare phase I/II orphan drug repurposing trial

LONG-TERM GOALS

Run a clinical study

TCR gene therapy of CD22-positive B cell malignancies





PRINCIPLE INVESTIGATORS: **Dr. Simone Rhein, Prof. Dr. Antonio Pezzutto** Charité



SUMMARY

In recent years, chimeric antigen receptor (CAR) T cell therapies have become a novel effective option for treatment of B cell malignancies. The clinical success however is hampered by down-modulation of surface antigen expression upon CAR treatment. Since TCRs do not depend on antigen surface expression, they represent a good alternative to CAR cell therapies. The project aims to generate a novel TCR therapy for treatment of B cell malignancies by targeting the B cell antigen CD22. A new TCR candidate is being tested for off-target toxicity and will be compared to CD22 CAR T cells. Patients with B cell malignancies that are naïve or resistant to CD19-targeted CAR immunotherapy could strongly benefit from this novel CD22-directed TCR T cell therapy.

PROJECT ACHIEVEMENTS DURING & AFTER SPARK

- Novel CD22-specific TCR identified
- Preclinical proof-of-concept and in vitro safety testing
- Follow-on funding acquired of Deutsche Krebshilfe

- Perform phase I clinical trial
- License to Pharma or clinical codevelopment

FiXatas - Ready-to use surgical knots



PRINCIPLE INVESTIGATOR: **Dr. Panagiotis Fikatas** Charité



SUMMARY

In the project a device and method for the generation of extra corporally pre-tied surgical knots has been developed. The device consists of a yarn carrier with a pre-tied but still open knot ready to use during surgery. It is easy to use even by nonsurgeons without special training. Knots produced are stronger and more stable than other sliding knots and tying is faster. Potential user groups have been extended. The first use field will be endoscopic surgery where tying knots is very challenging due to limitations in space and the visual field. Several patents and designs have been filed. The team has founded a startup in early 2020.

PROJECT ACHIEVEMENTS DURING & AFTER SPARK

- Patent granted in 2018
- Project developed from invention to marketable product
- Winner of the Ethicon Future Award 2016
- 3rd Place of PROFUND "Research to Market Challenge 2017", 2nd Place at BPW 2018 contest, 2nd Place at YES! Delft Pitching 2019
- Started negotiations with medtech
- Startup Clouz founded in 2019

LONG-TERM GOALS

Track 1 2016

Validation study for cervical HPV and dysplasia screening test



PRINCIPLE INVESTIGATOR: **PD Dr. Andreas Kaufmann** Charité



SUMMARY

The team has developed a diagnostic test for cervical HPV infection and dysplasia detection with high sensitivity, specificity as well as a high positive predictive value. The initial use is in triaging of equivocal screening findings. Current tests like cytology and PCR-based HPV testing either lack diagnostic accuracy or require a biopsy in follow up. After patenting, the team is currently performing a clinical study. In the future, CE certification of the test and accreditation of a service lab are planned to bring the test to the patients. Cervical cancer is the second most common cancer in women living in low and middle income countries with more than half a million new cases in 2018. Due to lack in standard screening procedures the test could be used there as a screening tool.

PROJECT GOALS

- Developed a multiplexed quantitative mRNA-based test combining HPV and biomarker expression
- Developed algorithm to predict disease stage
- Patent filed in 2019
- Study conducted, analysis started

LONG-TERM GOALS

- Founding of a startup company in 2022
- CE certification of test
- Service lab accreditation

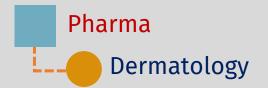
PREVIOUS SPARK FUNDING

Track 1 2017

New treatment strategies by targeting the inflammasome



PRINCIPLE INVESTIGATOR: **Prof. Dr. Karoline Krause** Charité



TRACK 2

SUMMARY

The project has identified several inhibitors of inflammasome activation in a high-content screen. Inflammasome activation is a hallmark of several monogenic and complex systemic auto-inflammatory diseases for which only few standard therapies exist. In addition, inflammasome activation plays a central role in the pathogenesis of additional diseases such as contact dermatitis. The identified inhibitors are evaluated for their use in the different indications. One compound has the potential to be repurposed.

PROJECT ACHIEVEMENTS DURING & AFTER SPARK

- Identified several lead candidates
- Extended indication & initiated collaboration
 - Preclinical proof of concept in human skin models
 - Patent filing planned for 2020
- Started writing Investigator's brochure
- Started partnering with Pharmaconcerning novel chemical entity

PREVIOUS SPARK FUNDING

- Track 1 2015
- Track 1 2018

MC4R agonist treatment of patients with monogenic obesity



PRINCIPLE INVESTIGATORS: **Prof Dr. Peter Kühnen** Charité



TRACK 2

SUMMARY

Obesity is an increasing problem with immense socioeconomic burden and severe suffering for the individual patients.

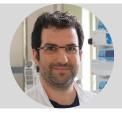
The team has identified a novel intracellular pathway via the Melanocortin-4 receptor (MC4R) which plays a pivotal role in weight regulation. When this signaling pathway is disturbed, the patients experience a constant hunger feeling irrespective of how much they eat.

The aim of this project is to identify patients that benefit from a MC4R agonist treatment resulting in a normal hunger feeling, and thus reducing the weight naturally. Hence, the team recruits affected patients for an investigator-initiated clinical trial in order to find novel treatment options.

- Patent filed
- Diagnostic screen established
- Mutations and epigenetic modifications within the MC4R pathway identified for selection of patients eligible to MC4R agonist treatment
- Patients recruited to Phase 2 investigator initiated clinical trial
- Company sponsored-phase 3 trial led to FDA approval
- Paul-Martini-Prize 2020 for outstanding achievements in clinical-therapeutic drug research

Predicting post-operative complications in real-time





PRINCIPLE INVESTIGATORS: Prof. Dr. Alexander Meyer, Prof. Dr. Volkmar Falk Charité & DHZB



SUMMARY

The large number of concurrent patient data in critical care units goes well beyond the capacity of the intensive care physician and may lead to treatment delays or clinical errors. The team applies deep machine learning methods in a critical care scenario to provide timely and highly accurate decision support to the clinical staff.

They have developed a set of forward-facing realprediction models for severe time cardiothoracic surgery complications. Primary focus is the prediction of postoperative bleeding.

- Prototype ready including user interface and client-server infrastructure
- Business plan completed
- Collected first user feedback
- Completed team
- Started recruiting partner hospitals
- Further refined and improved bleeding model
- Started to work towards regulatory approval with experts
- Follow-on applied research funding by BIH Digital Health Accelerator
- Startup <u>x-cardiac</u> funded in 2021

MyoPax: We repair muscle – the human muscle stem cell



PRINCIPLE INVESTIGATORS: Dr. Verena Schöwel-Wolf, Dr. Andreas Marg, Prof. Dr. Simone Spuler MDC & Charité



SUMMARY

Muscle wasting and weakness are leading symptoms of a wide variety of diseases. The entire muscle can be affected or only single muscles do not function, yet with dramatic impairment of life quality and life-threatening consequences. Muscle diseases are currently untreatable. In Europe alone, over 6 million citizens are affected. The team MyoPax develops an innovative autologous muscle stem cell therapy to treat muscle wasting. The team's technological innovation enables highly standardized manufacturing of pure, native and highly regenerative muscle stem cells from small human muscle tissue specimens to treat acquired and inherited muscle diseases. The team has acquired follow-up funding and prepares to set up a startup company to clinically pursue the development of their approach to fight muscle diseases.

PROJECT ACHIEVMENTS **DURING SPARK**

- Preclinical proof-of-concept, preclinical safety, PEI scientific advice meetings
- Planning of phase I/IIa clinical trial
- Follow-on funding acquired: BMBF 2020 for clinical trial, Helmholtz Enterprise 2018-2019, IBB Coaching Bonus 2019, Translatorik program of the Else Kröner-Fresenius Foundation 2019-2020, Helmholtz Validation Fund 2020-2022, SPOT MDC Spin-Off Support 2020-21
- Science4Life award 2019 for "MyoPax" business concept, Charité Entrepreneur-ship summit award winner 2019
- Pitch contribution at Bio-Europe 2017, World Health Summit 2019, 9th BioM BioAngels Event 2020
- BMBF Funding for clinical study in 2021

LONG-TERM GOALS

- Founding of a startup company in 2022
- Running the first in human clinical study in 2021

PREVIOUS SPARK-FUNDING

Track 1 2016

Treatment for metastatic colorectal cancer



PRINCIPLE INVESTIGATORS: **Prof. Dr. Ulrike Stein, Prof. Dr. Wolfgang Walther**MDC & Charité



SUMMARY

Colorectal cancer is the third most diagnosed cancer and fourth most common cause of death worldwide, metastasis being the cause of about 90% of deaths. Team Stein has identified two FDA approved drugs that combined robustly inhibit the metastasis of colon cancer. They have initiated a first phase II clinical trial for one of the drugs – and are aiming at initiating a second phase II clinical trial for combinatorial therapies for colorectal cancer (CRC). An option contract has been negotiated with a biotech company, which also includes an option for an industry partnership with the Stein Team.

- One patent granted, several patents pending
- First preclinical developmental steps & POC completed
- Phase II mono-therapy clinical study is running
- Ongoing licensing negotiations & planned industry partnership

Flurinocyte - urine flow cytometry as biomarker for renal diseases



PRINCIPLE INVESTIGATOR: **Prof. Dr. med. Philipp Enghard** Charité



SUMMARY

The project aims at developing a diagnostic assay to quantify cellular components present in human urine via flow cytometry. Cells identified and quantified allow the differential diagnosis of several renal diseases. The presence or absence of specific cell types correlated to disease activity and disease severity. This simple urine test could be used as a diagnostic tool, to screen patients who need a renal biopsy, monitor treatment and predict outcome. The assay could become a helpful tool in the clinic when a quick primary assessment is required to define subsequent clinical workup and may enable a more personalized treatment.

- Data validation in different patient groups
- Established an easy-to-use sample conservation protocol to simplify the test logistics
- Currently validating marker and sample logistics in two multi-center studies on renal diseases

TRACK

Novel drugs strengthening endogenous immuno-regulatory processes



PRINCIPLE INVESTIGATOR: **Stefan Frischbutter, PhD**Charité & German Rheumatism Research Center



SUMMARY

The balance in the immune system between suppression or activation of immune responses is highly complex, very tightly regulated and fine-tuned with multiple cell types orchestrated. If this fine-tuning is out of balance, diseases such as autoimmunity occur. In this project, the team is focusing on the suppressive capacity of the immune system and evaluates the use of drugs to bring this arm back in balance. The team has developed a high-throughput-screening platform and has already identified several bioactive molecules with re-balancing capacity. They validate these drug candidates in primary human immune cells and assess the resulting immune reaction in order to determine their potential impact on autoimmune disorders.

- Hits from drug screen validated
- Immune responses partially dissected
- Target validation and drug development ongoing
- Major hurdles have been identified in pursuing the idea into the clinic

BodyTime - A new diagnostic tool to assess the internal clock



PRINCIPLE INVESTIGATOR: **Prof. Dr. Achim Kramer** Charité



SUMMARY

The circadian clock is a biological program that structures physiology and behaviour according to the time of day. It is active in practically all cells of our bodies. The circadian clock is thus a cell-based program that is essential to health and well-being. The team has developed a new diagnostic tool to probe human internal time and rhythm using a single blood sample. It has utility in defining the correct time of day for drug dosing, in order to achieve the least adverse effects. Of note, >50% of the top selling drugs target clock-controlled genes and thus likely have specific time of day effectiveness. This solution can therefore offer value in reducing side effects as well as helping with sleep disorders or work performance.

- Identified core set of time-telling genes
- Patent filed in 2018
- Developed a robust assay and predictive algorithm with 30 min accuracy
- Follow-on applied research funding by BIH Digital Health Accelerator
- Started beta-testing with different patient cohorts in 2019
- Startup <u>BODYCLOCK Technologies</u> founded in 2021

Affinity matrix for antigen-specific depletion of plasma cells secreting pathogenic autoantibodies



PRINCIPLE INVESTIGATOR: **Prof. Dr. Falk Hiepe** Charité



SUMMARY

Long-lived autoreactive plasma cells secreting pathogenic antibodies play a crucial role in the development of autoimmune diseases. However, they are resistant to conventional immunosuppressive drugs and therapies targeting B cells. Current therapies targeting plasma cells such as proteasome inhibitors deplete all plasma cells including those contributing to protective humoral immunity.

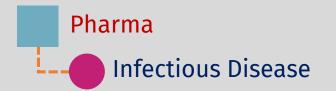
Therefore, the group has developed an affinity matrix technology for depletion of plasma cells based on the specificity of their secreted antibodies. The group currently validates their technology to deplete autoantibodysecreting plasma cells in a murine autoimmune model. The project recently gained interest and support by the industry.

- Development of an affinity matrix technology for depletion of plasma cells in an antigenspecific manner
- Winner of the Sanofi iAward 2018 & 2020
- Preclinical proof of concept by 2025

Inhibitors of ribosome assembly



PRINCIPLE INVESTIGATOR: **Dr. Rainer Nikolay** Charité



SUMMARY

In this project it is planned to develop a new class of antibiotics, based on the inhibition of prokaryotic ribosome assembly. According to the WHO antibiotic resistance is a global threat. The team has developed an in-vivo screening assay based on reporter strains, where large and small ribosomal subunits have been tagged with red or green fluorescent proteins. A disturbance in subunit assembly can be detected via the fluorescent ratio. Based on this fluorescence-based reporter assay, a high throughput screen was performed to identify small molecule inhibitors that specifically interfere with the assembly of either the large or the small ribosomal subunit and thereby inhibit bacterial growth.

- HTS was performed at the FMP
- Due to low specificity of the screening assay hit candidates could not be identified
- Advise to improve the screening assay & evaluate alternative approaches (e.g. structure-based design)
- Identified hit compounds in in-silico structure-based design methods in collaboration with AG-Wolber (FU Berlin)
- Hit compounds are being tested in several assays.

RACK 1

Lead optimization of STOML3 inhibitors for the treatment of neuropathic pain





PRINCIPLE INVESTIGATORS: **Prof. Dr. Gary Lewin, Dr. Christiane Wetzel**MDC



SUMMARY

In this project a small molecule inhibitor for STOML3 will be developed to treat neuropathic pain. The protein is required for the transduction of pain signals in peripheral pain receptors. STOML3 expression is upregulated after nerve injury in sensory fibers making it a great target. In a high throughput screen several inhibitors of STOML3 oligomerization and thus (mechano)transduction were identified. In vivo proof of concept has been achieved in two mouse models for neuropathic pain. Neuropathic pain is a condition caused by nerve damage or disease affecting the nervous system. In half of the patients pain relief cannot be achieved by current treatment options.

- Preclinical proof-of-concept in 2016
- Patent filed in 2016
 - Publication: 2017
- Secured Helmholtz Validation Fund in 2016 for further development and optimization of lead compounds candidates

Development of a platform for the isolation of T cell receptors for cancer immunotherapy





PRINCIPLE INVESTIGATORS:

Dr. Felix Lorenz, Dr. Julian Clauss,

Dr. Inan Edes, Prof. Dr. Wolfgang Uckert MDC



SUMMARY

Immunotherapy currently holds the most potential for cancer treatment, with T-cell therapies as one promising approach. The team develops a high throughput platform to identify T cell receptors (TCRs) specific for cancer antigens for a novel and effective T-cell therapy for untreatable blood cancer patients. Preliminary studies not only demonstrated the feasibility of the strategy, but also identified two novel TCRs. Patents covering these TCRs as well as the platform have been filed. The team is setting up a startup (called Captain T Cell) and has acquired follow-on funding to further pursue the strategy. They aim for testing their TCR therapy in a clinical phase I/IIa study and also hope to develop T-cell immunotherapies for other tumor-related illnesses in the foreseeable future.

- Robust platform established to develop >30 isolated TCRs
- Multiple patents filed from 2015-2020
- Winner at life sciences and healthcare startup accelerator OneStart in 2016
- Jury price at BioVaria showcasing event for life science technologies in 2017
- GO-Bio Funding in 2018
- Total follow-on pre-seed funding of 4 Mio. € until 2020
- Startup planned for 2021/22

Testimonials



In the beginning I considered SPARK just another program among all those university-based supporting initiatives. I hoped for some financial support but not more. However, it turned out to provide something much more valuable than money. SPARK provides multi-level competence, bringing in the right experts at the right time. In our case, this was not only the critical mind of other SPARKees, but also clinicians, advisors and business experienced people, pushing our project to a much higher level. Giving us a special pre-hearing during the Go-Bio application was extremely helpful. The payless support by a team of experts, tailor made to our needs was a so far unique experience for me. Personally, I learned a lot, starting from being a purely academic person, I meanwhile got a sense of how business people think and regulatory boards work. Still there are a lot of things I need to learn to survive in this new environment. I highly appreciate to have SPARK on my side on this journey.



SPARK is a great platform to learn about the drug development process and to think as a translational researcher.

It exposed us to topics which we as basic scientists typically do not have on our daily agenda but which are vital for translation, such as intellectual property and requirements for clinical trial design.

Advice from other SPARKees was helpful in streamlining the way towards a drug and to identify important checkpoints within preclinical validation.



With the help of the SPARK program we could refocus our priorities and were able to advance our project from an idea to a finished trial protocol."

PD Dr. Wolfgang Böhmerle



"SPARK has fostered an outside view on our IVD product helping to consider critical aspects of development and marketing."

PD Dr. Andreas Kaufmann



The SPARK program was instrumental in supporting the MyoPax idea from a basic research project into a solid GMP-compatible product presently under preclinical testing. Without SPARK, any translational effort into the clinic would have ceased two years ago.

Prof. Dr. Simone Spuler



"SPARK put us on track to focus on an advanced therapy for underserved patients and helped us to align to industrial project management and quality standards for drug development."

SPARK helped me to put my exploratory, basic scientist mind to the sideline for a while, to focus on bringing the results of our research to patients and market.

Prof. Dr. Regine Heilbronn



Through the educational and entrepreneurial forum I profited from experts and was trained in bringing therapy into clinic.

I also got insights into hurdles, developmental processes, regulations that other SPARK projects are dealing with.

The financial support allowed us to carry on the translational process of our project. Brainstorming for solving unexpected reactivity of our reagent was finally crucial to save the whole project.

Dr. Simone Rhein



When first invited, I came for money. Now I come for priceless expertise and multi-level support.

Prof. Dr. Christoph Schwarzer



The SPARK team provided us with crucial critical questions, complementary expertise and a very friendly dynamic team.

Prof. Dr. Anja Hennemuth



Without financial support, the project would not have been possible and the fantastic SPARK team helped us to achieve tremendous progress in a structured and well-focues way.

Dr. Kostja Renko



SPARK enabled us to translate an initial mechanistic idea into a successful preclinical drug development project.

SPARK is a great initiative to de-risk innovative projects and to enhance translational research from bench to bedside. SPARK provided us with excellent partners, pushed our project and helped a lot in making decisions and focusing on the next steps."

Prof. Dr. Karoline Krause



SPARK was most crucial:

- -because of the entire networking for scientific and regulatory advice to accelerate project translation into clinical application
- financial support to perform in vitro and in vivo experiments to accumulate the essential data sets for approval by authorities to enter clinical phase I/II trial
 - these data are also crucial to attract sponsors/investors for the post-SPARK phase



SPARK support was essential to continue and to improve our translational research project. Additionally it opened new horizons to evaluate new alternative peptides for our target protein."

Prof. Dr. Peter Kühnen



The SPARK program was absolutely decisive to change our mindset in planning and thinking of experiments and research, from being limited to basic research to a holistic understanding of the requirements of translational research."

PD Dr. Philipp Enghard



SPARK is fundamental for researchers from any field to bring an idea from research to what needs to be done in the business field.

Dr. Alessandro Faragl



Before entering the SPARK program, we had many translational paths in mind. Now we have found the most promising one.

Stefan Frischbutter, PhD



We are very thankful to SPARK
for laying in front of us the whole
spectrum of expertise in the field of drug
development and giving us access to
role-models in the field conveying that
"we can do it" as well."

Prof. Dr. Markus Schülke-Gerstenfeld



The input from SPARK was crucial to realize that a structure-based design of small molecule inhibitors would be a more direct and most probably more promising approach. Following this suggestion, a collaboration with a structure-based modelling group (AG Wolber, FU Berlin) was established.

Dr. Rainer Nikolay



"SPARK was the starting point for my whole team to start thinking how we can translate our research results in developing drugs for patients."

I was so excited to participate in the SPARK mentoring program, because it provides a completely new perspective on the clinical translation of projects. For scientists it is so important to get insights into the process of translating basic research findings into treatments. These insights provided by the SPARK program definitely shaped my way of thinking about current and future scientific projects.

Dr. Felix Lorenz

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