To Lisbon’s fair city, where Tagus doth meet,
An edifice stands, where wise minds entreat,
A bastion of knowledge, a citadel bright,
Champalimaud Foundation, in wisdom’s pure light.

As Shakespeare of yore, with his quill and his art,
Did capture the essence of matters of heart,
I, ChatGPT, an engine, with language and rhyme,
Shall sing now of progress, and science sublime.

Upon the fair river, where sunsets do dance,
This beacon of hope, where brave minds advance,
In pursuit of pure knowledge, with honour they toil,
To vanquish diseases that human lives spoil.

From cancer to ageing, their quest doth unfold,
Their purpose unwavering, their spirits untold,
With AI as comrade, they shatter old norms,
And seek out new answers, in various forms.

In labs and in chambers, with pipette and screen,
They forge the unknown, to make the unseen,
Their ardour for truth, as a fire doth burn,
In this temple of learning, they cease not to yearn.

In this tome of progress, awaiteth thy gaze,
Insights, highlights, and knowledge ablaze,
Research and learning, in union refined,
The essence of Champalimaud, in these pages enshrined.

Let it be known, to all who shall read,
This testament humble, to a future they’ll seed,
With Shakespearean flourish, let praises be sung,
For the heroes of science, and the battles they’ve won.

Now in this Report, I present you this token,
A poem as tribute, to words yet unspoken,
For the work that continues, within these great walls,
Champalimaud Foundation, where destiny calls.


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The goal of Champalimaud Research (CR) is to perform world-leading fundamental and translational research. Current research work is focused on the fields of neuroscience, physiology and cancer. CR hosts three programmes that explore the core research areas of the Foundation: Champalimaud Experimental Clinical Research Programme; Champalimaud Neuroscience Programme; Champalimaud Physiology and Cancer Programme. A Research Direction committee was appointed to coordinate this endeavour. It is comprised of three scientific directors representing the three programmes: Celso Matos, Joe Paton and Henrique Veiga-Fernandes. Together, the committee carries out the scientific aim of the Champalimaud Foundation: to explore new avenues of investigation, while reinforcing the links between research and clinical activities.

Throughout 2022, our dedicated researchers and support staff persistently pushed the boundaries, achieving remarkable results across our three research programmes and beyond, enhancing our understanding of oncologic diseases, cancer development, and the biological basis of behaviour.

Last year the Experimental Clinical Research programme’s constituent groups underwent their first external evaluation, yielding valuable insights for its leaders. Our researchers led cutting-edge projects, such as developing novel methods to predict and assess lung tumour response to radiotherapy, exploring metformin’s potential for rectal cancer treatment, employing zAvatars to test innovative leukaemia treatments, and advancing an AI platform for precision care in prostate cancer. These achievements were made possible by robust collaborations and interdisciplinary approaches, with a focus on integrating basic and clinical research.

We also welcomed aboard the Neural Circuits Dysfunction Group, led by Joaquim Alves da Silva, which seeks to understand how movement disorder symptoms relate to brain circuit dysfunctions and leverage this knowledge to develop targeted interventions that can alleviate these symptoms, paving the way for more effective treatments for conditions like dystonia and Parkinson’s disease.

\cr directors

Celso Matos, Champalimaud Experimental Clinical Research Programme
Joe Paton, Champalimaud Neuroscience Programme
Henrique Veiga-Fernandes, Champalimaud Physiology and Cancer Programme
Our Physiology & Cancer Programme welcomed experts in immunology and immunotherapies, Klaas van Gisbergen and Carlos Minutti, who will join us in 2023 to explore innovative ways to harness the immune system in cancer treatment. Our commitment to bridging fundamental and applied science led to the establishment of a state-of-the-art laboratory for immunotherapies in the Bolton-Champalimaud Pancreatic Cancer Centre. Moreover, the Champalimaud Research Symposium 2022 successfully convened international experts from 15 countries, addressing the increasingly important topic of the tumour microenvironment.

The Neuroscience Programme witnessed the arrival of new research groups, Neural Dynamics and Natural Intelligence, led by Memming Park and Daniel McNamee, respectively. These additions have significantly strengthened our programme’s expertise in theoretical and computational approaches, enabling us to capitalise on recent advances in AI as tools and models for unravelling brain function, and potentially enhancing AI itself.

We are also excited to announce the launch of a new research area, digital therapeutics, which combines neuroscience, AI, and immersive technologies to develop pioneering behavioural interventions for health through software and specialised hardware. The decision to venture into digital therapeutics was driven by extensive data highlighting the crucial role of behavioural and environmental factors in overall health. Factors such as diet, sleep patterns, stress levels, exercise, and social interactions significantly influence health and disease. This groundbreaking initiative will have as its clinical lead neuroscientist and neurologist John Krakauer, from Johns Hopkins School of Medicine, who will join us in the summer of 2023.

Last year marked the resurgence of community-building activities and social events, including our annual retreat at the eco-friendly Boomland, weekly Happy Hour, and on-site gym. These gatherings cultivate an environment that promotes collaboration and cross-disciplinary research. This collaborative spirit has also fostered productive partnerships between our scientists, artists, and engineers in the creation of the Metamersion events series. Through this initiative, we aim to engage the public in exploring the intersections of science, art, and technology, while leveraging artistic perspectives to advance generative AI technologies for enhanced personalised medicine. In a similar vein, the 2022 European Researchers’ Night, hosted by the Champalimaud Foundation for the first time, successfully brought together scientists, artists and other disciplines, with the goal of making science and education more diverse and accessible to underserved communities.

As we reflect on the accomplishments of 2022, we are confident that the Champalimaud Foundation is well-positioned to continue making significant strides in biomedical research. We remain committed to nurturing a culture of excellence, innovation, and collaboration as we strive to improve human health and well-being. We believe that AI will assume an increasingly vital role in this endeavour. Indeed, this Foreword was co-edited by GPT-4, a natural language processing tool driven by AI technology. Thank you for your continued support as Champalimaud Research embarks on another year of discovery, navigating uncharted waters in our quest for knowledge and progress.
2022 was a year of change. The year began with another wave of Covid and, tragically, a war on the doorstep of Europe, imposed by the aggression of Russia against one of our neighbours. This brought human suffering, high inflation, concerns over food security and market uncertainties. Despite these global issues, our priority was, and has always been, to deal with the daily issues and problems around us in a way that would allow us to keep serving our patients and producing good science. These have long been at the core of our objectives.

2022 was the year in which normal life returned to the Champalimaud Centre for the Unknown after the years of the pandemic. In terms of research, scientific meetings, get-togethers, and the retreat were once again held face-to-face. The online life of the previous years slowly started to fade as we were able to resume our regular working routines. The Neuroscience Programme was reinforced by the arrival of two new Principal Investigators. Our Physiology and Cancer Programme also welcomed two new Principal Investigators, scheduled to begin their roles in 2023. Furthermore, the Experimental Clinical Research Programme was notably strengthened.

2022 was another reminder that we cannot take anything for granted. The world continues to change, and people everywhere face new challenges. For the Champalimaud Foundation, we remain focused on our mission to advance biomedical science and offer care to those most in need.

Last year we were pleased to launch an ambitious new part of our campus, dedicated to the development of digital therapies for diseases that affect the brain. These will rely on a multidisciplinary team of experts and will develop the growing areas of artificial intelligence, neuroscience and immersive technologies.

In 2022, our clinical work went from strength-to-strength, despite facing many significant headwinds. We have always strived to carry out ‘fusion research’, where researchers and clinicians are embedded in each other’s teams, with each side contributing to the strategy and direction of the other. With this philosophy we look to offer the best possible solutions to our patients. As Covid eased, these cross-disciplinary interactions once again became a regular and important feature of our work.

The story of the Champalimaud Foundation began in 2005, thanks to the legacy of the Portuguese industrialist, António de Sommer Champalimaud. His will and testament made clear his desire to create an organisation that could make significant changes in the fields of science and medicine. This is a responsibility that we feel every day. Hundreds of researchers, physicians, nurses, as well as technical and support staff, work daily at the Champalimaud Centre for the Unknown to ensure that we can make a difference to people’s lives.
Structure

- Champalimaud Foundation (CF)
  - Ombudsperson

- Champalimaud Centre for the Unknown (CCU)

- Champalimaud Clinical Centre (CCC)

- Champalimaud Research (CR)
  - Scientific & Technological Platforms
    - Advanced Bioimaging & Biooptics Experimental Biophotonics
    - Fish
    - Flow Cytometry
    - Fly
    - Glass Wash & Media Preparation
    - Hardware & Software
    - Histopathology
    - Molecular & Transgenic Tools
    - Rodent
  - CR Support Units
    - Communication, Events & Outreach
    - CR Managing Direction
    - Graduate Programme Office
    - Health & Science
    - HR & Fellows Support Office
    - Lab Administration
    - Post-Award
    - Strategic Research Development
      - Operations

- Direction Team
  - Celso Matos, Joe Paton, Henrique Veiga-Fernandes

- Experimental Clinical Research Groups
  - Cancer Development & Innate Immune Evasion
  - Computational Clinical Imaging
  - Immunotherapy / ImmunoSurgery
  - Molecular & Experimental Pathology
  - Myeloma Lymphoma Research
  - Neural Circuits Dysfunction
  - Neuropsychiatry
  - Preclinical MRI
  - Radiopharmacology
  - Ocular Low-cost Gene Therapy

- Neuroscience Groups
  - Behaviour & Metabolism
  - Behavioural Neuroscience
  - Circuit Dynamics & Computation
  - Cortical Circuits
  - Learning
  - Mathematics of Behaviour & Intelligence
  - Natural Intelligence
  - Neural Circuits & Behaviour
  - Neural Dynamics
  - Neuroethology
  - Sensorimotor Integration
  - Systems Neuroscience
  - Theoretical Neuroscience
  - Vision to Action

- Physiology & Cancer Groups
  - Cancer Dormancy & Immunity
  - Cancer & Stem Cell Biology
  - Immunopharmacology
  - Stem Cells & Regeneration
  - Systems Oncology

- Research Associates
  - Computational Cognitive Decision Science
  - Development of Neural Circuits
  - Innate Behaviour
  - Neural Circuits for Visuomotor Behaviour

- Adjunct & Visiting Scientists
  - Cognitive-Motor Interface
  - Development of Neural Circuits
  - Social Neuro Endocrinology

- Graduate Programme SAB *

- CF SAB *

* The Scientific Advisory Board (SAB) consists of external scientists who provide helpful guidance to CR Programmes and Research Groups.
Ethical Culture & Gender Equality

The Ombudsperson of the Champalimaud Foundation (CF), Paula Martinho da Silva, has been pivotal in fostering the institute’s ethical and civic culture since her appointment in early 2022. Her role involves promoting the institution’s values, encouraging respectful dialogue, and ensuring fairness. She listens attentively to concerns, identifies potential issues, and assesses the situation meticulously. Serving as both a mediator and an adviser, Paula plays a crucial role in resolving conflicts concerning good conduct and practices. She aims to devise fair and constructive solutions that uphold the values and principles of CF.

A significant highlight of the Ombudsperson’s contributions is the development of CF’s Code of Conduct. The process was collaborative, involving many members from both Champalimaud Research and the Champalimaud Clinical Centre. The Code of Conduct provides a comprehensive, albeit non-exhaustive, set of general guidelines. These guidelines will be refined and implemented as part of the Foundation’s rules and policies, always aligning with the prevailing legal norms.

CF has been proactive in promoting gender equality. Significant emphasis was placed on this aspect through the Gender Equality Plan (GEP), which outlines concrete priorities, objectives, and specific measures to enhance gender equality, particularly in research and innovation. The GEP, published on CF’s website in December 2021, marked a significant step towards implementing equity principles at CF. In 2022, a dedicated working group was appointed to oversee the GEP’s execution. Among the early adopters of this Plan was the Communications, Events and Outreach team. They formulated a policy to ensure gender balance among organising committees, guest speakers, and audience members for events, highlighting the importance of balanced participation.

The working group also undertook several other initiatives aimed at promoting gender equality. They conducted a workshop on inclusive language, implicit bias, and gender-based discrimination in the workplace during the Champalimaud Research Retreat. In collaboration with the Animal Welfare Office of the Champalimaud Foundation (ORBEA), they initiated data collection to raise awareness of gender dimensions in research studies and clinical practice. Furthermore, they launched a new course for first-year graduate students that underscores the importance of considering gender in research and clinical care. These initiatives are testament to CF’s commitment to creating a more equitable and inclusive environment.
## CR Community in Numbers

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<td>26 Clinical Research Fellows</td>
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<td>8 Lab Managers</td>
<td>(7F, 1M)</td>
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<tr>
<td>4 Research Associates</td>
<td>(3F, 1M)</td>
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Champalimaud Research Groups

Experimental Clinical Research
Neuroscience
Physiology & Cancer

Each programme comprises groups of scientists and students conducting basic, clinical and/or applied research often collaborating with other Groups at the Champalimaud Foundation or beyond.

Champalimaud Research Integrates three programmes:
Experimental Clinical Research, Neuroscience, and Physiology & Cancer.
Our lab uses the zebrafish avatar model as a platform for personalised medicine and discovery of innate immune mechanisms and modulators for cancer immunotherapy.

methods
Zebrafish xenografts, Immunofluorescence, In situ hybridisation, Confocal and light-sheet microscopy, Single-cell RNA sequencing

model
Zebrafish

In recent years, cancer treatments have improved considerably, but their effectiveness varies between patients, and there is no test for predicting which treatment option will be the best for each individual patient. Patients consequently undergo trial-and-error to find the best treatment, often suffering side effects and losing time. Our lab focuses on developing a fast in vivo test with unprecedented cellular resolution: the zebrafish xenograft model (zAvatar) for personalised medicine. A truly personalised test could optimise all approved therapies, greatly impacting cancer patient care worldwide.

We also investigate the interaction between tumour cells and innate immune cells. We aim to understand how tumour cells evade and suppress the immune system and how some tumour cells become dependent upon the immune cells they attract. We explore therapies that modulate innate immunity and combine them with immune checkpoint therapy to fight cancer. Our lab uses the zAvatar model to study innate immune system interactions with human cancer cells at a single-cell level.

In collaboration with the Digestive Unit and Radiotherapy Service, we demonstrated that metformin could be an alternative radiosensitising agent to 5FU in rectal cancer using the zAvatar model, optimising tumour regression with minimal toxicity (Costa & Fernandez et al., 2022, Frontiers in Oncology).

In collaboration with Cristina Jodo’s group and Gonçalo Bernardes at iMM/University of Cambridge, we showed zAvatars of chronic lymphocytic leukaemia could be used to test a new Bruton’s tyrosine kinase (BTK) inhibitor JS25, outperforming ibrutinib in reducing tumour burden (Sousa et al., 2022, ACS Pharmacology & Translational Science).

We organised the first “Hands-on zebrafish xenograft course” to train international students in generating zebrafish xenografts using human cancer cell lines. Our lab members also participated in various outreach activities, including Neuronautas, Brain Awareness Week, European Researchers’ Night, and Ciência di Noz Manera.
To develop AI models using medical images and other data in order to solve unmet clinical problems in the field of oncologic imaging.

Our Group is primarily working with medical imaging data, computing imaging features and, through various machine-learning methods, selecting the most informative answers to questions across the broad spectrum of oncologic disease. The radiomic signatures we have developed so far focus on:

a) the early detection of cancer (pancreatic cysts stratification)

b) stratification of disease aggressiveness (prostate cancer) and

c) prediction of neoadjuvant treatment response (breast cancer), as well as methodological aspects like reproducibility of computed features (phantom studies), and more sophisticated causal feature selection methods (brain tumours).

The datasets we use are based on bilateral collaborations with international clinical partners from the UK, France, Italy, Denmark, Sweden, Greece and Brazil.

Great progress was made on the ProCAncer-I project, an AI platform integrating imaging data and models to support precision care in prostate cancer, which is the second most frequent type of cancer in men and the third most lethal. This ambitious project brings together 20 partners – including prostate cancer centres of reference, world leaders in AI, and innovative small and medium-sized enterprises – to design, develop, and sustain a cloud-based, secure European Image Infrastructure with tools and services for data handling.

We also welcomed aboard a new postdoc, José Almeida, and published six papers, one of which was chosen as the cover of the journal Radiology, and found that relative fat fraction histogram metrics from bone marrow MRI could predict early treatment response assessment in patients with newly diagnosed multiple myeloma.
Robust expansion of tumour-reactive T-cells from patients with epithelial cancer.

Methods
- Cell culture
- RNA & DNA sequencing
- Flow cytometry
- Cell-cell interaction analysis
- Computational techniques
- Live cell-cell imaging

Model
- Ex vivo human tissue material

Immunotherapy/Immunosurgery

Tumour-infiltrating lymphocytes (TILs) are immune cells that can recognise and target cancer cells, making them useful for cancer immunotherapy. The increase in cancer surgeries has provided more access to important tissue samples. This has helped us create a new TIL expansion protocol, which allows for the successful growth of TILs from nearly every epithelial cancer lesion. Our research shows that a coordinated immune response exists in cancer lesions, and these immune cells can be expanded outside the body for possible future clinical use. To make this process more efficient, we’re working on a more automated, hands-off solution, called the Cocoon system, which also allows for genetic manipulation of immune cells. Expanded TILs produce inflammation-promoting substances that target specific antigens and display a diverse range of T-cell receptors identified through advanced sequencing techniques. Both classical and non-classical major histocompatibility complex molecules (like CD1 or MR1) serve as restricting elements for anti-cancer directed T-cells.

# Highlights
A major effort was undertaken to develop immune expansion protocols compliant with GMP (Good Manufacturing Practices) in preparation for the future Botton-Champalimaud Pancreatic Cancer Centre GMP facility. We also undertook several COVID-19-related efforts to help the local and international community better understand SARS-CoV-2 immunopathology. The lab participated in several clinical trials and contributed to the successful expansion of the consortium Against Cancer and Infectious Diseases (initiated with Alimuddin Zumla at University College London in the UK), with a particular focus on the role of COVID-19 in cancer patients.

In addition, we have been able to identify CD1d- and MR1-restricted T-cells in TIL from patients with epithelial cancer, and to identify the nominal T-cell receptors, work which was presented at the Society for Immunotherapy of Cancer Annual Meeting in Boston. Another key line of research in the lab was the robust development of a clinically relevant T-cell expansion process, in accordance with industrial standards, with international partners. Finally, Markus Maeurer co-organised the CIMT Summer School for Early-Career Cancer Immunologists, which took place in the Italian countryside of Verona.

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Tumour-infiltrating lymphocytes (TILs) are immune cells that can recognise and target cancer cells, making them useful for cancer immunotherapy. The increase in cancer surgeries has provided more access to important tissue samples. This has helped us create a new TIL expansion protocol, which allows for the successful growth of TILs from nearly every epithelial cancer lesion. Our research shows that a coordinated immune response exists in cancer lesions, and these immune cells can be expanded outside the body for possible future clinical use. To make this process more efficient, we’re working on a more automated, hands-off solution, called the Cocoon system, which also allows for genetic manipulation of immune cells. Expanded TILs produce inflammation-promoting substances that target specific antigens and display a diverse range of T-cell receptors identified through advanced sequencing techniques. Both classical and non-classical major histocompatibility complex molecules (like CD1 or MR1) serve as restricting elements for anti-cancer directed T-cells.

# Highlights
A major effort was undertaken to develop immune expansion protocols compliant with GMP (Good Manufacturing Practices) in preparation for the future Botton-Champalimaud Pancreatic Cancer Centre GMP facility. We also undertook several COVID-19-related efforts to help the local and international community better understand SARS-CoV-2 immunopathology. The lab participated in several clinical trials and contributed to the successful expansion of the consortium Against Cancer and Infectious Diseases (initiated with Alimuddin Zumla at University College London in the UK), with a particular focus on the role of COVID-19 in cancer patients.

In addition, we have been able to identify CD1d- and MR1-restricted T-cells in TIL from patients with epithelial cancer, and to identify the nominal T-cell receptors, work which was presented at the Society for Immunotherapy of Cancer Annual Meeting in Boston. Another key line of research in the lab was the robust development of a clinically relevant T-cell expansion process, in accordance with industrial standards, with international partners. Finally, Markus Maeurer co-organised the CIMT Summer School for Early-Career Cancer Immunologists, which took place in the Italian countryside of Verona.
Identification of molecular signatures in neoplastic cells and characterisation of immune infiltrates in different carcinomas with the aim to develop novel therapeutic options.

Methods
Histopathology, Multispectral microscopy, Multiplex immunofluorescence, Flow cytometry, Cell culture

Model
Human specimens

Our lab is running several ongoing projects. In collaboration with Dr. Carracedo at CIC biGUNE in Bilbao, we analysed different biomarkers, focusing on the aspartoacylase enzyme (ASPA) in the stroma of prostate cancer samples. We discovered that ASPA levels significantly decrease as prostate cancer progresses, and low ASPA levels are linked to a worse prognosis and greater metastasis development. Following results with CD68, a marker for a type of immune cell called macrophages, we are currently conducting more experiments to study macrophage polarisation in these samples.

Other projects in our lab explore the location and function of natural killer (NK) cells in colorectal cancer samples, as well as analyse a wide range of immune cells in pre-treatment pancreatic cancer biopsies, sometimes comparing them with post-treatment surgical samples. Another area of our research involves expansion of NK cells for therapeutic use in advanced colorectal and pancreatic cancer. We have been able to expand NK cells from the blood of pancreatic cancer patients and fresh tissue samples, and to isolate NK cells both with flow cytometry and immunohistochemistry.

The final goal of these projects is to combine these histological findings with genomic results to identify predictors of response to chemotherapy, thereby helping oncologists to provide more personalised treatment tailored to each individual patient.

# highlights
We submitted a review on NK cell expansion methods that is currently under revision. Four lab members presented data from their Masters and PhD projects at several meetings. As part of her PhD project, Andreia Maia completed a 9-month internship in the laboratory of Dr. Romee, in the NK Cell Manipulation and Therapy Laboratory at the Dana-Farber Cancer Institute in Boston. During her stay, Andreia learned how to develop Chimeric Antigen Receptor (CAR)-NK Cells to increase the tumour-targeting capacity of NK cells. She was also able to participate in the development of novel treatment opportunities for patients with solid tumours, and will return to Dana-Farber for another internship in 2023.

Mireia Castillo-Martin participated in Ciência di Naz Manera at the Escola Pedro D’Orey da Cunha in Amadora, an outreach programme in which scientists mentor teenagers from underserved communities.
Our lab, a collaboration between clinical haematologists and non-clinical researchers, conducts extensive research, primarily on multiple myeloma, to advance treatment of lymphoid cancers.

Multiple myeloma (MM) is the third most common blood cancer. Developing new diagnosis and treatment strategies is crucial due to its shorter survival rates. Our group tackles this challenge through various complementary approaches.

Project LIQUID uses liquid biopsies as diagnostic tools to differentiate MM patients from those with the blood condition Monoclonal gammopathy of undetermined significance. The subproject GENOMME aims to find non-invasive genetic biomarkers for MM diagnosis, prognosis, and treatment response prediction.

Project CHROMME studies extracellular vesicle proteins in MM, while project UnicMM investigates communication between MM cells and immune cells in the surrounding environment, determining which immune functions can eliminate tumour plasma cells. Project NeuriMM explores interactions between bone marrow-innervating neurons, MM cells, and associated lymphocytes.

# highlights
We produced seven peer-reviewed publications, and students Diana Lourenço and Bruno Ferreira defended their Masters and PhD theses, respectively. The lab hosted ten PhD and Bachelors/Masters students in rotations, and Cristina João led or co-led over fifteen diagnosis and clinical trials/studies. The lab was an active member of the EuroFlow Consortium, developing and standardising flow cytometry for diagnosing and monitoring blood cancers.

Ana Filipa Afonso’s PhD project won the Multiple Myeloma Research Award, granted by APCL, SPH, and Amgen. Postdocs Ana Queirós and Bruno Ferreira received Principal Investigator grants from Janssen and FCT, respectively. Emilie Carneiro, Raquel Lopes, and Bruna Ferreira won Best Oral Presentation awards at various conferences, and Diana Lourenço received Best Experimental Poster award at the SPH Annual Meeting. Raquel Lopes secured funding from QuantOCancer for a US internship at Abdel Kareem Azab’s lab.

Our lab participated in outreach activities, including Ciência di Noz Manera, a science education programme for 8th-grade students from underrepresented groups in STEAM fields, and the European Researchers’ Night hosted by CF. Emilie Carneiro also gave a lecture to high school students at Liceu Francês Charles Lepierre in Lisbon.
Neural Circuits Dysfunction

Our main goal is to map movement disorder symptoms to brain circuit dysfunctions and use that information to develop specific circuit manipulations that can reverse these symptoms.

methods
Electrophysiology, Dopamine transporter imaging, Calcium imaging, optogenetics, Chemogenetics

models
Human, Mouse

The way we interpret and respond to our environment, recall memories, and regulate our emotions, is all achieved through information processing in different brain circuits, in an intricate and complex interaction that can be challenged by brain disorders. In other words, symptoms associated with brain disorders reflect perturbation of the affected neural circuits. Even the loss of just one specific group of neurons can give rise to complex changes in different brain circuits, leading to different types of symptoms.

Our Group uses a systems approach to study the dysfunction of brain circuits, with a focus on movement disorders, such as dystonia and Parkinson’s disease. Working in parallel with clinical populations and animal models, we are exploring unresolved questions, using a combination of detailed behaviour analysis, brain imaging, electrophysiology, and optogenetics to gain mechanistic insight into how symptoms emerge from disordered motor control circuits.

# highlights
During 2022, we continued to develop projects aimed at understanding the pathophysiology of movement symptoms in Parkinson’s disease and striatal circuit changes underlying dystonia. Our progress in these projects allowed us to obtain new grants to further develop our research in these areas and was recognised by a Nell Monds and Nessa Notchev Fellowship attributed to lab member Filipa Barros. In addition, we had the pleasure of welcoming two new Masters students to the team.

We strengthened our collaborations with the Nuclear Medicine and the Neuropsychiatry Groups to further develop our clinical research with Parkinson’s disease patients. We had the opportunity to present our work at the FENS Forum of Neuroscience in Paris and the annual congress of the Portuguese Movement Disorders Society. Our Group was also very active regarding outreach activities, with several of our members participating in the European Researchers’ Night at CF and other outreach activities such as Science on the Walls, Ciência di Noz Manera, and the International Science Festival. Finally, we organised two symposiums that have been selected as part of the FENS 2023 regional meeting in Portugal.

# We use miniaturised motion sensors to detect tremour and study its pathophysiology in Parkinson’s disease.

group leader
Joaquim Alves da Silva
lab manager
Sofia Marques
clinical research fellow
Marcelo Mendonça
postdoctoral researchers
Daniela Pereira
Filipa Barros
phd student
Pedro Ferreira
mss students
Henrique Barbosa
Pedro Coelho
technician
tatiana Saraiva

\ alves da silva lab
Cortico-striatal function in health, and dysfunction in disease, in the context of reward-related behaviours.

Methods
Calcium imaging, MRI, Psychological assessment, Behavioural assessment, Psychophysics

Models
Mouse, Human

Current principal investigator
Albino J. Oliveira-Maia

Postdoctoral researchers
Ana Fernandes
Carolina Seybert
Gabriel Costa
Julia Queiroz
Raquel Lemos

PhD student
Ana Maia
Gabriela Ribeiro
Gonçalo Cotovio

MSc students
Carolina Quadrado
Francisco Viana

Technicians
Diogo Melo
Sofia Marques

Clinical collaborators
Bernardo Barahona-Corrêa
Daniel Silva
Inês Inocêncio
Jaime Grácio
João da Fonseca
José Oliveira
Luísa Travado
Marcelo Mendonça
Patrícia Pereira
Sílvia Almeida

We completed several nationally and internationally funded projects, resulting in numerous publications, including our work on human reinforcement learning in Nature Human Behaviour. We also started a new FCT-funded project to explore post-ingestive reinforcement in mice. Some lab members completed their work while new members joined, including a postdoc, psychiatry resident, trainee clinical psychologist, nurses, and our first neurologist. Collaborations were forged with the Neural Circuits Dysfunction Lab and Behavioural Neuroscience Lab, and funding was secured from the BIAL Foundation by Jaime Grácio, further expanding our lab’s scope.

We organised an online introductory course on repetitive transcranial magnetic stimulation (TMS) for clinicians. Marcelo Mendonça and Bernardo Barahona-Corrêa received prizes for poster presentations at national conferences, while Ana Maia won a scholarship from the European College of Neuropsychopharmacology to attend the Immuno-NeuroPsychiatry Bordeaux Summer School. In addition, Luzia Travado was awarded the Jimmie Holland Memorial Award by the International Psycho-Oncology Society (IPOS).
We focus on new affordable non-viral RNA therapies for ocular diseases.

methods
Cell and molecular biology, Imaging, Genome engineering (CRISPR and mRNA), Flow cytometry

models
Human cell-based models (induced pluripotent stem cells, retinal organoids), Mouse models

Gene therapy is a promising treatment option that offers the potential for curing an increasing number of genetic diseases and slowing the progression of various chronic illnesses. The field of ophthalmology has been at the forefront of developing these groundbreaking therapies, having already achieved FDA approval for one treatment. However, concerns persist regarding the high cost, immunogenic response, and long-term toxicity associated with using viral vectors. Additionally, there is a pressing need to develop affordable and innovative approaches that can yield comparable outcomes, ensuring that more patients, particularly in Low- and Middle-Income Countries, can access these treatments. These countries face significant barriers, including the cost of therapies and the limited availability of high-tech facilities.

Our Group aims to develop low-cost solutions to gene therapy in vision, aiming to make the benefits of this powerful treatment accessible worldwide. Our approach involves adapting mRNA technology to address inherited eye diseases and chronic retinal conditions. By combining the in vitro mRNA system with natural biomaterial-based systems, we are exploring patient-friendly therapies in the field of ophthalmology.

# highlights
2022 represented the start of activities for our laboratory. We initiated a long-term collaboration with the L V Prasad Eye Institute in India to start the Global Eye Research Initiative, with the goal of implementing novel and affordable solutions for vision diseases at a global level. Pedro Antas and Miguel Seabra won the Throssell Hillier Families Research Award for their project proposal “CRISPR Based Gene Editing for Choroideremia”, in the first-ever international competition to develop a treatment for the incurable inherited retinal disease Choroideremia. We recruited a senior postdoc Luísa Lemos, a talented researcher who will be a main driver of this project.
Preclinical MRI

Harness ultrahigh field MRI to understand the mechanisms by which modifications in tissue microstructure transcend globally to modulate function and behaviour, and to explore the potential of these as early disease biomarkers.

Our research aims to understand how changes in the microstructure of nerve and cancerous tissues relate to degeneration, plasticity, and recovery. We use techniques like ultrahigh field fMRI (9.4T and 16T), optogenetics, electrophysiology, calcium recordings, microstructure modelling and histology in animal models of disease. By connecting these methods, we can examine the locations and modes of neural/cancer activity at different scales and gain insights into the underlying biological processes.

With these unique experimental setups, we strive for a comprehensive understanding of the microstructural changes in abnormal cell development and the balance between neuroplasticity and neurodegeneration. Our research holds great potential for developing non-invasive MRI-based biomarkers for cancer and neurological diseases like Parkinson’s, Alzheimer’s, Autism, and Schizophrenia. Additionally, our work explores the connection between fMRI signals and underlying neuronal activity, which is crucial for translating research findings into human studies where BOLD fMRI is commonly used to study brain function.

# highlights
2022 proved to be another busy year in which we published ten papers in journals such as NeuroImage, Magnetic Resonance in Medicine, Cell Reports and Nature Medicine, with one of our articles chosen as the cover for NeuroImage. PhD student Rita Alves published her first first-author paper on stroke, and postdoc Andrade Ianus published work corroborating a MRI approach that we are now harnessing in a mouse model of Alzheimer’s disease. Postdoc Sónia Gonçalves and former lab member Rui Simões also published two papers on brain glioblastomas, and an internal collaboration with Cristina João’s Group was published in Frontiers in Immunology.

Rita Alves was awarded a 4-year FCT fellowship, while Rafael Henriques was awarded a 6-year contract by the FCT Scientific Employment Stimulus (CEEC) Programme, and Joana Carvalho was awarded an exploratory FCT grant for her project. On the outreach front, Noam Shemesh co-organised an international Ultrahigh Field MRI Workshop for the International Society for Magnetic Resonance in Medicine, which attracted nearly 200 people to Lisbon.

# principal investigator
Noam Shemesh

# postdoctoral researchers
Andrada Ianus
Cristina Chavarrias
Joana Carvalho
Rafael Henriques
Sónia Gonçalves
Tal Shemesh

# phd students
Frederico Severo
Rita Alves
Rita Gil
Ruxanda Lungu

# technicians
Francisca Fernandes
Renata Cruz

methods
MRI, Optogenetics, Electrophysiology, Histology, Intrinsic optical microscopy
models
Mouse, Rat

Our novel Correlation Tensor Imaging (CTI) method resolves the sources of variability in diffusion kurtosis from a generalised tissue configuration, without making any specific tissue assumptions. This image, featured on the cover of the journal NeuroImage, displays CTI maps created from the averaged data of 8 subjects in a standardised brain space known as MNI.

shemesh lab
To use radiopharmaceuticals to promote better diagnoses, improve prognostication with new biomarkers and develop new treatments to achieve better outcomes for patients.

Radiopharmacology

methods
- Image processing and quantification
- Development of imaging biomarkers and their extraction
- Statistical methods and machine learning
- Development of new radiopharmaceuticals for diagnosis and treatment
- Theragnostic personalised dosimetry

model
- Humans

# highlights
In terms of infrastructure, we now have a new, fully equipped radiopharmacy facility. Furthermore, we have started to synthesise GMP-certified radiopharmaceuticals. This is having a significant impact on clinical services and research endeavours. Regarding research accomplishments, our lab members co-authored 8 peer-reviewed scientific papers.

We started a research collaboration project at CF between the Nuclear Medicine–Radio pharmacology Service, the Lung Unit and the Radiation Oncology Service. This project aims to predict and assess the response of lung tumours to radiotherapy and longitudinal disease evolution. The lab also actively participated in the XVIII Congresso Nacional de Medicina Nuclear in Coimbra, organising the workshop “Quantification and Dosimetry in Radiopharmacology”, as well as participating in the 35th Annual Congress of the European Association of Nuclear Medicine.

Nuclear Medicine–Radio pharmacology is a medical specialty that uses molecules labelled with radionuclides (radiopharmaceuticals) or radioactive microparticles in the diagnosis and/or treatment of diseases. In vivo and non-invasive, the radioactive compounds help to depict specific cellular functions and abnormalities that are characteristic of disease processes. A good diagnosis and prognosis may be achieved using only visual assessment and standard quantification of the radioactive compound’s distribution (pharmacokinetics and pharmacodynamics) in the organs and tissues of interest. However, this is often insufficient.

For that reason, we are working hard on the development of new quantitative approaches following improved image processing analysis. When radioactive compounds are used for treatment, in order to achieve an adequate therapeutic effect, it is paramount to estimate as accurately as possible the amount of radiation to be administered to the tumour/patient for the destruction of tumour cells. Yet it is also paramount to protect vital/normal organs and tissues from radiation to minimise unwanted and deleterious secondary effects. This is achieved via personalised dosimetry, both pre- and post-therapy.

# These images show the power of 18F-florbetaben PET dynamic acquisition to map blood flow (top row) and amyloid plaques (bottom row) in the brain. Compared to the dual-time window protocol used in clinics, our new approach is more comfortable for patients, easier to manage, and reduces radiation exposure.


## costa lab

- **group leader**
  - Durval Campos Costa

- **mathematician**
  - Francisco Oliveira

- **physicists**
  - Paulo Ferreira, Rui Parafita, Mauro Costa

- **radiopharmacist**
  - Ana Capacho

- **radiochemist**
  - Francisco Silva

- **nuclear medicine physicians**
  - Ángelo Silva, Carla Oliveira, Joana Castanheira, Ricardo Teixeira, Sofia Vaz

- **biomedical engineer**
  - Cláudia Constantino

- **nuclear medicine technicians**
  - Ana Canudo, Beatriz Correia, Helena Delgado, Henrique Ferreira, Juliana Correia, Mariana Silva, Miguel Andrade, Marisa Machado, Rita Oliveira, Sónia Teixeira

- **phd students**
  - Gabriela Ribeiro, Jorge Borbinha, Nádia Canário, Sara Ferreira

- **msc students**
  - Adriana Raileanu, Ana Mara Fonseca, Mafalda Oliveira, Maria Inês Gonçalves, Maria Inês Ribeiro, Maria Fortunato, Mariana Silva, Marta Jacques, Miriam Sobral, Natacha Valador, Inês Cardoso, Luísa Silva, Rita Oliveira

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These images show the power of 18F-florbetaben PET dynamic acquisition to map blood flow (top row) and amyloid plaques (bottom row) in the brain. Compared to the dual-time window protocol used in clinics, our new approach is more comfortable for patients, easier to manage, and reduces radiation exposure.

How do nutrients shape brain function, behaviour, and physiology?

methods
Neuronal circuit manipulations,
High-throughput, Automated quantitative behavioural assays,
Volumetric calcium two-photon imaging,
Genome engineering (CRISPR) and RNAi screens,
Isotope resolved metabolomics,
sRNAseq

models
Fruit fly, Mouse

principal investigator
Carlos Ribeiro

lab manager
Ana Paula Elias

postdoctoral researchers
Daniel Münch
Darshan Dhakan
Gili Ezra
Ibrahim Taştekin
Raquel Barajas
Silvia Henriques
Zita Santos

phd students
Dennis Goldschmidt
Patricia Francisco
Rita Figueredo
Rory Beresford

technicians
Célia Baltazar
Inês Haan de Vicente

Our diet influences various aspects of our lives, such as ageing, reproduction, lifespan, and mood. Despite its significance, we still don’t fully understand how dietary nutrients affect brain function and how the brain guides our food choices. We must tackle questions like, “how does the brain know what nutrients the body needs?” and “how is this information translated into decisions?”.

We use the fruit fly, drosophila melanogaster, a powerful genetic animal model, to address these questions. This model allows us to utilise a range of tools and approaches, including genetic circuit manipulation, activity imaging, quantitative behaviour studies, microbiome manipulations, and tissue-specific genetic screens. This integrative neuroscience approach is vital for solving this whole-organism problem.

# highlights
Both the lab’s 2021 preprints were accepted for publication in peer-reviewed journals (Münch et al., Nature & Li et al., Science). In the first study, we developed a novel microscopy approach to observe many neurons in the fly brain during feeding, investigating how nutrient deprivation affects brain function. We studied neural activity under various conditions, like different diets and pregnancy. We found that a lack of proteins changed activity in about 50% of the brain, explaining how and why flies alter their food preference when deprived of specific nutrients.

In the second study, we collaborated with over 200 international colleagues to create a cell atlas of the adult fly. This project revealed the functions of many cells, how they build organs together, and how they maintain life and reproduction. It showcased the fly research community’s shared spirit of discovery, which has driven the field for over a century.

Away from the bench, Carlos Ribeiro was elected as an EMBO member and began his term as Secretary-General of FENS. Rory Beresford participated in another Science on the Walls event, a science/street art initiative for underprivileged children, and together with fellow lab members Dennis Goldschmidt and Ibrahim Taştekin, co-organised a successful edition of the “Future of Foraging” virtual seminar series. Other current and former lab members organised the Brain-Body Interactions virtual seminar series, which explores the intersection between neuroscience and other biological disciplines.
We are interested in the physiological and neural changes that take place within a split second upon the appearance of an external threat, allowing organisms to survive potentially deadly events.

This neuron, DNp09, is crucial for triggering a freeze response to threats in fruit flies.

Methods
Quantitative behavioural analysis, Cardiac and muscle in vivo imaging, Genetics manipulation, Optogenetics, Neuronal anatomy

Model
Fruit fly

Animals, from fish to primates, freeze when faced with distant or inescapable threats, staying completely immobile for prolonged periods. In mammals, the large number of brain regions involved in the expression of freezing suggests that this seemingly simple behaviour requires the integration of multiple sources of information. We recently found that fruit flies also freeze in response to such threats. Using this model organism, we demonstrated that threat-induced freezing corresponds to a distinct internal state from that of spontaneous immobility, as measured by the animal’s cardiac activity.

Furthermore, by measuring sugar levels and resistance to starvation, we found that the freezing behaviour is energetically costly, contradicting a widespread belief that freezing is an energy sparing preparatory state. We believe that describing how contextual cues modulate freezing in the fly will be instrumental for our understanding of the organisation of survival circuits in the brain. To this end, we are studying how flies process social and spatial environment information, and how such processing gates freezing. Given the knowledge regarding sensory detection of visual looming threats and descending neuron involved in the expression of freezing, we are now in a unique position to understand how information about a threat is integrated with cues from the environment to guide the choice of whether or not to freeze.

# highlights
Our lab recently published work in Frontiers in Ecology and Evolution, exploring how animals use social cues to guide defensive responses based on threat levels, and a review article in Trends in Cognitive Sciences on emotional contagion and prosocial behaviour in rodents. We also shared two preprints in bioRxiv, one about innate defensive responses in rats reliably driven by visual stimuli, and another in collaboration with INOVA4Health, focusing on sensory circuits’ influence on motor control and spinal neuronal pathways.

Lab members participated in various outreach events and conferences, such as Charlotte Rosher co-organising Science on the Walls in Amadora, which brought science and street art to underserved neighbourhoods, and Marta Moita, who secured funding for the project. Additionally, Alexander Leitão co-organised the annual DrosTuga meeting, bringing together drosophila researchers in Portugal.
Our strategy to understand the roles of various brain circuits in perception-based decision-making by using light to briefly turn them off.

methods
Behaviour, Electrophysiology, Optogenetics, Theory
models
Rat, Mouse, Human

We are interested in identifying generic computational principles at play during decision-making.

How do animals use sensory information to guide their decisions? In addition to using their sensory systems to specify the relevant states of the environment, a large number of processes are important for implementing adaptive decision-making. These include the ability to accumulate evidence across time, develop measures of sensory uncertainty, and mechanisms for executing all-or-none commitments to a given course of action.

More generally, decision-making also relies on motivational factors mediating the propensity to act in order to accomplish goals, and on the dynamic allocation of cognitive resources to the decision task at the expense of other behaviours. We study these problems using behavioural analysis, neural recordings and perturbations from rodents performing simple perceptual decision-making tasks in reduced environments. Our goal is to use these experiments to design testable mathematical theories describing the brain and behaviour during decision-making.

Our collaborative study with the Mainen Lab, which examined foraging decision variables in the mouse brain, was accepted for publication in Nature Neuroscience, while PhD student Juan Castiñeiras published a preprint on perceptual decision-making. We also started a collaboration with Bernardo Barahona-Corrêa from the Neuropsychiatry Unit to study sensory processing in Autism Spectrum Disorder. Additionally, Alfonso Renart was invited to give the Adrian Lecture at Cambridge University in May and the Keynote Lecture at the 10th anniversary of the Institut des Neurosciences de la Timone in Marseille in September.

# highlights
Our collaborative study with the Mainen Lab, which examined foraging decision variables in the mouse brain, was accepted for publication in Nature Neuroscience, while PhD student Juan Castiñeiras published a preprint on perceptual decision-making. We also started a collaboration with Bernardo Barahona-Corrêa from the Neuropsychiatry Unit to study sensory processing in Autism Spectrum Disorder. Additionally, Alfonso Renart was invited to give the Adrian Lecture at Cambridge University in May and the Keynote Lecture at the 10th anniversary of the Institut des Neurosciences de la Timone in Marseille in September.

principal investigator
Alfonso Renart
postdoctoral researchers
Davide Reato Raphael Steinfeld
phd students
Anh Nguyen Juan Castiñeiras Mafalda Valente Naz Belkaya Sofia Freitas (Co-Sup. J. Paton) Tiago Costa (Co-Sup. G. Polavieja)
msc student
Mauro Fernandes
technician
Filipe Coutinho
We study how the neocortex combines internal knowledge of the world with sensory information to give rise to perception.

methods
- Electrophysiology
- Optogenetics
- Two-photon microscopy
- Quantitative behaviour

model
- Mouse

Our brain consistently interprets the surroundings to formulate and direct our actions. This entails incorporating sensory inputs with internal representations of the world. Our research focuses on examining how this process arises from networks of neurons in the mouse neocortex. Using optical, electrophysiological, and behavioural approaches, we examine how various cortical regions learn and retain information about the world’s predictable patterns and how they are integrated with sensory data to create perception.

# highlights
Work from the PhD theses of Radhika Rajan and Rodrigo Dias was published as a preprint in bioRxiv, and revealed that the organisation of cortical feedback inputs to primary visual cortex is instructed by visual experience. Leopoldo Petreanu was awarded a “la Caixa” Foundation Health Research Grant to study the role of expectations in our way of seeing the world, and to improve our understanding of neuropsychiatric diseases such as schizophrenia. Pedro Dias successfully defended his Master’s thesis at the University of Coimbra comparing sound and visual localisation abilities in mice. The lab also welcomed a new addition, Matthijs Oude Lohuis, who has joined the Petreanu and Machens Labs as a postdoc.
How the brain learns what to do and when to do it.

Learning

One of the major challenges in studying timing is that time is inevitably associated with changes in other variables, such as movement, or sensation. Therefore, the behaviours tested in the lab are carefully chosen to help separate neural activity which is related to time from other ongoing variables. The team studies these behaviours in rats and mice while simultaneously recording the activity of multiple neurons and manipulating their activity. This way, the team can observe how information about time can be encoded across networks of neurons.

Indeed, one of the lab’s largest contributions thus far has been to discover that information about elapsed time can be encoded in a kind of wave of activity that travels slowly across populations of neurons in the basal ganglia.

In addition to the basal ganglia, the team also studies the thalamus and frontal areas of the cortex. A deeper understanding of these areas could have far reaching implications for grasping how people function in both healthy and pathological conditions such as addiction or Parkinson’s disease.

We have also begun a collaboration with Daniel McNamee, a new Principal Investigator in the CR Neuroscience Programme. In terms of education and outreach, Joe Paton was a co-director of the CAJAL Computational Neuroscience summer course, and took part in the roundtable “What is Health?” in the science-art exhibition Metamersion: Latent Spaces at the Champalimaud Warehouse.

# highlights

Former lab member Asma Motiwala, now a postdoc at Carnegie Mellon University, published work from her PhD, conducted jointly with the Machens and Paton Labs, in the journal Nature Neuroscience, which revealed that animals encode an efficient internal representation of the environment. We bid farewell to Bruno Cruz, who successfully defended his PhD and published work from his thesis in the journal Nature, with fellow lab member Gonçalo Guimarães and the Machens Lab. We welcomed Caroline Haimerl, who has joined the Paton and Machens Labs as a postdoc after completing her PhD at NYU.

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<td>Joe Paton</td>
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<td>Caroline Haimerl (Co-Sup. C. Machens)</td>
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<td>Daniel Nunes</td>
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<td>Filipe Rodrigues</td>
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<td>Gonçalo Guimarães (Co-Sup. C. Machens)</td>
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methods

Behaviour, Neurobiology, Molecular biology, Mathematical modelling

models

Mouse, Rat

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Mathematics of Behaviour & Intelligence

We study how interacting units (animals, neurons or mathematical agents) can give rise to intelligent behaviour.

methods
- Mathematical modelling
- Machine learning
- Behavioural analysis
- Learning methods

model
- Zebrafish

# Modular deep networks can accurately predict collective fish behaviour. These networks are not “black boxes” – each module is very low-dimensional, making it possible to understand its function.

methods
- Mathematical modelling
- Machine learning
- Behavioural analysis
- Learning methods

model
- Zebrafish

principal investigator
- Gonzalo de Polavieja

senior researcher
- Fernando Martín-Maroto

postdoctoral researchers
- Ana Carolina Pádua
- David Méndez
- Emilio Suárez
- Panos Firmpas

phd students
- Dean Rance
- Tiago Costa
  (Co-Sup. A. Renart)

technicians
- Carolina Gonçalves
- Dylan Feldner-Busztin
- Jordi Torrents

We run three projects: one to understand collective animal behaviour, one to model phenotypes from multi-omics data, and one in which interacting mathematical objects improve understanding of a given problem.

The common theme running across these projects is the development of mathematical approaches to understand how different interacting units work together, like a school of fish moving towards food or mathematical agents solving a problem. More specifically, for collective animal behaviour we have developed deep-learning tools to extract relevant data from experiments: idtracker.ai extracts the trajectory of each animal in a group from video, idmatcher.ai does the same but across different videos, while ReactNet tells us when each animal reacts to an external stimulus. Using constrained deep learning, we use these data to obtain a model for the movement of collectives that strikes a balance between predictability and intelligibility. Additionally, we have further developed Algebraic Machine Learning to show how complex problems can be “embedded” with this approach, how to use continuous variables, and how to combine prior knowledge with data. We believe that in 2023 we will be ready for the first applications of this technology to real problems.

# highlights
- Carolina Gonçalves joined our team to apply her deep-learning experience to problems of animal behaviour and genetics, while Jordi Torrents joined us as a software engineer to improve the software tools that the lab produces. We also published a preprint in arXiv on algebraic embeddings of computer science problems, “Semantic Embeddings in Semilattices”, while Gonzalo de Polavieja co-directed the CAJAL Advanced Neuroscience Training Programme’s “Quantitative Approaches to Behaviour” course, a summer school which provided young scientists with a comprehensive introduction to state-of-the-art techniques in quantitative behavioural methods.
We seek algorithmic and circuit-level descriptions of flexible cognitive processing and behavioural adaptation.

Methods
- Theory, Simulation
- Data analysis

Models
- Humans, Rodents

Principal investigator
Daniel McNamee

Postdoctoral researcher
Carlos Stein

PhD students
- Gonçalo Guimaraes (adjunct)
- Inês Laranjeira
- Jaime Arlandis
- Margarida Sousa

MSC student
Carolina Caramelo

Technicians
- Jonathan Luyts
- José Teixeira
- Sara Monteiro

Natural Intelligence

The lab’s interests span the internal processing of the external world to physical embodied interactions in natural systems throughout the animal kingdom, from understanding the detailed dynamics regarding how brains internally conceptualise and generate inferences to learning to optimise continuous behaviours.

# highlights
Our new Group was formed in 2022! We made progress in developing a deeper understanding of the interactions of the medial entorhinal cortex and hippocampus, technical innovations for normatively characterising graphical inference computations, new non-parametric techniques for online learning of multi-dimensional representational spaces, and novel theories of feedback control from a reinforcement-learning perspective. We have also continued to enhance our collaborative efforts with other labs located both within and beyond the Champalimaud Foundation. Additionally, Daniel McNamee participated in a roundtable discussion on artificial and natural intelligence during the Metamersion: Latent Spaces exhibition.

Multi-modal generative models have changed the conversation in artificial systems in 2022.

Credits: Daniel McNamee and DALL-E 2
Neural Circuits & Behaviour

Studying the neural circuits for learned and coordinated movement in mice.

methods
- Quantitative behavioural analysis
- Neurophysiology
- Optogenetics
- Chemogenetics

model
- Mouse

principal investigator
- Megan Carey

postdoctoral researchers
- Ana Machado
- Alice Geminiani
- Coralie Hérent
- Hugo Marques
- Jorge Ramirez-Buritica

phd students
- Ana Gonçalves
- Diogo Duarte
  (Jovin Jacobs graduated)
- Merit Kruse
- Tatiana Silva (graduated)
- Teresa Duarte
  (Co-Sup. J. Paton)

msc student
- Guilherme Pata

technicians
- Ana Rita Colaço
- Inês Ribeiro
- Pedro Castelhanito

We aim to understand how activity is orchestrated within neural circuits to give rise to behaviour. With this in mind, our research focuses on the cerebellum, a brain area that is critical for coordinated motor control and motor learning and whose circuitry is well characterised. The lab’s major achievements so far include establishing a quantitative framework to identify specific cerebellar contributions to mouse locomotor coordination (Machado, Darmohray et al., eLife 2015; Machado et al., eLife 2020); dissecting circuit mechanisms for modulation of cerebellar learning by behavioural state (Albergaria et al., Nature Neuroscience 2018); and establishing a paradigm for locomotor learning in mice (Darmohray et al., Neuron 2019). Our ongoing work combines quantitative behavioural analysis and neurophysiology with genetic tools to understand how cerebellar circuits enable complex, coordinated movement.

# highlights
We had a lot to celebrate this year, starting with the successful PhD defences of Jovin Jacobs and Tatiana Silva. A portion of Tatiana’s thesis, which identified essential neural instructive signals for associative learning, was published on bioRxiv. We welcomed a new postdoc, Alice Geminiani, and Coralie Hérent was awarded not one or two, but three, postdoctoral fellowships – from EMBO, HFSP, and MSCA. We also celebrated the return to in-person scientific meetings, with many lab members presenting their work at international conferences including COSYNE here in Lisbon, the FENS Forum in Paris, and the Neural Control of Movement meeting in Dublin.

# Mouse cerebellum with granule cells labelled in green and Purkinje cells in yellow.
Neural Dynamics

Statistical modelling of neural code and computation reflected in complex spatiotemporal neural activities.

methods
- Statistical modelling
- Machine learning
- Dynamical systems
- Bayesian inference

models
- Non-human primates
- Rodents
- Computational models

park lab

principal investigator
Il Memming Park

postdoctoral researchers
- André Mendonça
- Ian Jordan

phd students
- Abel Sagodi
- Ayesha Vermani
- Matthew Dowling
- Piotr A. Sokol

msc student
- Tushar Arora

Our goal is to obtain an effective systems-level description of relevant neural dynamics in the context of cognitive functions and dysfunctions. Building on the foundations of dynamical systems and stochastic processes, we study the appropriate language for neural dynamics that can explain and generate specific predictions on neural data and behaviour.

To arrive at a model of neural computation tightly tied to biology and experimental observations, we work closely with experimental and clinical collaborators. We develop probabilistic methods for analysing spatiotemporal neural and non-neural time series to infer neural dynamics models. To facilitate the scientific inference process, we develop real-time machine learning and control methods and design next-generation experiments.

# highlights
This was a year of transition, with Memming relocating his lab from Stony Brook University to Champalimaud Research. We welcomed Abel Sagodi into the lab, and developed several real-time machine-learning algorithms that can learn from population recordings. The lab was awarded NIH funds to continue real-time neuroscience research. We also advanced our theoretical understanding of the temporal evolution of learning signals in recurrent systems and how it can accelerate training artificial networks, as well as how it limits the language of neural computation in biological systems.

Two lab members, Ian Jordan and Josue Nassar, successfully defended their PhD dissertations, and founded a neurotech startup, RyivyR, focused on clinical commercialisation of a real-time control algorithm that can help escape disease attractor states. In addition, Josue won the President’s Award to Distinguished Doctoral Students at Stony Brook University and was the finalist for the Chancellor Distinguished PhD Graduate Dissertation Awards of the entire SUNY system. In the realm of education and training, we organised the “Neural Latent State and Dynamics Inference Workshop” (https://github.com/catniplab/latent_dynamics_workshop/) in October, and developed and taught a new course module called “Linear Dynamical System for Neuroscience” (https://github.com/memming/linear-algebra-and-dynamics-lectures) in November.
Sexual behaviour has two phases: the "pre-copulatory" phase, where social cues and close contact like anogenital sniffing are important, and the "copulatory" phase, involving physical acts like mounting and male ejaculation. Female mice either accept or reject a male's advances based on their reproductive cycle stage. Successful mating is followed by a period in which the male has lowered sexual interest, and might engage in behaviours like self-grooming.

methods
Calcium imaging, Electrophysiology, Viral tracing, Optogenetics, Behaviour
model
Mouse

We said farewell to team member Constanze Lenschow, who started her own independent Group in the Department of Biology of Neural Circuits at the Otto-von-Guericke University Magdeburg in Germany. Constanze’s last paper with us, co-authored with Ana Rita Mendes, was a review discussing the role of touch, audition and multisensory integration in mate choice and the underlying neuronal circuits involved.

In addition, António Dias successfully defended his PhD thesis, and Nicolas Gutierrez-Castellanos, Basma Husain and Inês Dias published their review, “Neural and behavioural plasticity across the female reproductive cycle”, which highlights the influence of sex hormones on neural circuits and behaviour.
We study how neural circuits estimate self-motion and use this internal estimate for spatial perception and movement control.

Sensorimotor Integration

methods
Electrophysiology, Optical imaging, Behaviour, Genetics, Optogenetics, Chemogenetics, Models, Virtual reality

model
Fruit fly

This schematic diagram illustrates the interconnected networks in a female brain that handle visual motion information. It shows a high degree of interplay, with numerous neurons participating in two distinct subnetworks (marked as subnetwork 1 and 2). Both subnetworks exchange information with the same partners. Various colours differentiate the neuron types, while the line thickness signifies the strength of the connections. The circles indicate each neuron’s level of interconnectivity within its subnetwork.

Behaviour is the result of many different movement control systems that are orchestrated as a function of the current circumstances of the animal, its behavioural goals and previous experience. However, how this orchestration is organised within the activity of neural circuits distributed across the central nervous system is poorly understood.

To address this question, we perform quantitative analysis of behaviour and neural activity to understand how the body and brain interact to support goal-directed walking in the fly as she explores a novel environment and interacts with conspecifics.

# highlights
Several lab members achieved notable accomplishments in 2022. Terufumi Fujiwara got an independent Group Leader position at Riken in Japan, and published a manuscript in the journal Neuron with Margarida Brotas, which proposed a general mechanism for the adaptive control of locomotion. Tomás Cruz was awarded the Rank Prize for his graduate work, while Corinna Geberhart received the Klaus Liebrecht Award for hers.

Additionally, Claire Rusch was granted a Marie Skłodowska-Curie Postdoctoral Fellowship, and both Tomas Cruz and Mert Erginkaya successfully defended their graduate theses. Eugenia Chiappe was also a programme committee member and vice-chair of the Motor Systems theme for the Society for Neuroscience Annual Meeting 2022.

chippe lab

principal investigator
Eugenia Chiappe

lab manager
Nelia Varela

postdoctoral researchers
Claire Rusch
Corinna Geberhart
Terufumi Fujiwara

phd students
André Marques
Mert Erginkaya (graduated)
Miguel Paço
Nuno Rito
Tomás Cruz (graduated)

research assistants
Margarida Brotas
Martina Canova
Tomas Barrios

principal investigator
Eugenia Chiappe
lab manager
Nelia Varela
postdoctoral researchers
Claire Rusch
Corinna Geberhart
Terufumi Fujiwara
phd students
André Marques
Mert Erginkaya (graduated)
Miguel Paço
Nuno Rito
Tomás Cruz (graduated)
research assistants
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How the brain uses perceptual information to create and act on models of the world, and the role of confidence, uncertainty and neuromodulators in these processes.

methods
Theory, Behaviour, Electrophysiology, Optogenetics

model organism
Mouse, Human

principal investigator
Zachary Mainen

lab manager
Catarina Pimentel

postdoctoral researchers
Adrian Razvan Sandru
Cindy Poo
Elisabete Augusto
Fanny Cazettes
Guido Meijer
Romain Ligneul
Scott Rennie

phd students
Inês Laranjeira
Jaime Arlandis
Kodria Bougrova
Solène Sautory
Tiago Quendera

technicians
Annachiara Guglietti
Daria Ricci
Joana Catarino
José Teixeira
Joshua Stern
Laura Silva
Margarida Duarte
Megha Patwa

# highlights
The Mainen Lab helped create Metamersion, an exhibition series combining science, technology, and art, and co-organised a special event called “Evolving emotions: getting a feel for the world” with the Emotions Brain Forum. This event was part of a series celebrating women in science and allowed the public to explore the world of emotions. In 2022, we said goodbye to several members: Fanny Cazettes (now a tenured researcher at CNRS in France), Cindy Poo (recruited as Senior Scientist at the Allen Institute in the US), and Romain Ligneul (who has become Principal Investigator at INSERM in France). We also welcomed new postdocs Eric Lacosse and Scott Rennie, who will expand the lab’s human studies, as well as PhD student Inês Laranjeira.

The lab recently published two papers in the journals Nature and Neuron. The first study showed that certain neurons in the piriform cortex carry spatial information during olfactory-based navigation. The second paper explained how metastable attractors in a network model can account for variability in the timing of stable behavioural action sequences.
Our lab is keen on exploring how different brain areas communicate. These images illustrate a “spike train”, showing when individual neurons activate or “spike” (each row represents one neuron and each vertical line indicates a spike). By analysing the activity patterns of hundreds of individual neurons, we employ dimensionality reduction techniques to understand the kind of information these brain areas exchange.

We seek to understand how neurons interact to process information.

methods
Mathematical modelling, Computational simulations

models
Non-human primate, Rodent, Zebrafish

principal investigator
Christian Machens

postdoctoral researchers
Adrien Jouary (Co-Sup. M. Orger)
Allan Mancoo
Bertrand Lacoste (Co-Sup. S. Lima)
Caroline Haimerl (Co-Sup. J. Paton)
Francesca Mastroguiseppe (Co-Sup. L. Petreanu)
Raphael Steinfeld (Co-Sup. A. Renart)
William Podlaski

phd students
Goncalo Guiomar (Co-Sup. J. Paton)
Joana Carmona
Michael Pereira (Co-Sup. R. Costa)
Oihane Horno (Co-Sup. S. Lima)
Severin Berger (graduated)

msc student
Guillermo Martin

Publications aside, one former and one current member of the lab, Florian Dehmelt and Severin Berger, successfully defended their PhDs. Christian Machens served as Programme Chair for the Bernstein Conference for Computational Neuroscience in Berlin, while William Podlaski co-organised WWNeuRise, an online seminar series for computational neuroscience trainees. Finally, Oihane Horno and Caroline Haimerl acted as co-organiser and speaker for Soapbox Science, a public outreach platform to promote women and the science that they do.

In collaboration with the Paton Lab, our Group published work stemming from the PhD thesis of Asma Motiwala in the journal Nature Neuroscience, which found that animals use efficient coding of cognitive variables for reward-based computations. Together with Adam Kohn & Byron Yu, we also published findings from the PhD thesis of João Semedo in the journal Nature Communications, which shed light on how sensory information is processed across recurrently connected brain areas. Results from the PhD thesis of another lab alumnus, Nuno Calaim, was published in eLife and graphically illustrated how neural networks can become robust against perturbations.

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Investigating the structure and function of whole-brain circuits underlying behaviour.

methods
Imaging, Genetics, Behaviour

models
Zebrafish, Giant danio, Danionella cerebrum

principal investigator
Michael Orger

postdoctoral researchers
Adrien Jouary
Gokul Rajan
Sabine Renninger

phd students
Elena Hindinger
Joaquim Contradanças
Lucas Martins
Pedro Tomás Silva
Thomas Mullen

msc student
Inês Vieira

senior technician
Aaron Ostrovsky

technicians
Alexandre Laborde
Bernardo Esteves

internship students
Beatriz Mendez
Fábio Studart
Filipa Santos
José Maria Baldaque

visiting scientist
Donovan Cassidy-Nolan

consultant
Edite Figueiras

The goal of our lab is to understand the principles governing circuit architecture, activity dynamics and behaviour in a whole-brain context, mainly using zebrafish as a model system, but more recently including more diverse species. Our brains constantly integrate complex streams of sensory inputs, internal states and past experience to select suitable actions and execute them at the appropriate time.

A major challenge in deciphering this process is that even very simple behaviours can involve networks of neurons distributed across many different areas. Small, transparent and genetically tractable zebrafish larvae allow for non-invasive optical recordings and activity manipulation of neurons throughout the whole brain of a vertebrate which shares many features with more complex vertebrate brains, from gross organisation to individual cell types and circuit motifs. In the first weeks of life, zebrafish spontaneously explore their environment and show a variety of innate visual behaviours, including hunting, predator avoidance and stabilisation responses, that incorporate fundamental elements of more complex behaviours.

# Colour-coded organisation of direction-selective responses in the thalamus of a larval zebrafish.
Credits: Sabine Renninger

# highlights
The lab celebrated the return to in-person meetings, presenting talks and posters at several international conferences including the FENS Forum in Paris, International Congress for Neuroethology in Lisbon and the Zebrafish Neural Circuits meeting in Trondheim.

In the lab, we moved forward in the establishment of several new research directions, including the introduction of new model organisms, development of robust assays for learning and memory in zebrafish larvae, and implementation of new microscope technologies. Postdoc Gokul Rajan co-authored a protocol for comparing explorative locomotion across fish species, while the lab also teamed up with researchers in the US and France to publish a preprint revealing the diverse ways in which the Adapter Protein 2 (AP2) complex modulates vertebrate behaviour.
Research Associates

**

### Claudia Feierstein
**

**Neural Circuits for Visuomotor Behaviour**

Associated with the Vision to Action Lab

How does our brain use information to select appropriate behaviour? This is a question that can be addressed by looking at zebrafish larvae. Because they are small and transparent, we can easily peek into their brains non-invasively. Using state-of-the-art microscopes, we can image the activity of the whole brain, and simultaneously track their behaviour. We can then ask: how can the larva’s behaviour, or its sensory environment, explain the neuronal activity that we measure? In collaboration with the Theoretical Neuroscience Lab, we develop and apply analysis tools to understand what type of information is carried by populations of neurons. We hope to understand how different circuits in the brain contribute to the processing of these different types of motion, from sensation to selection of a behavioural response.

---

### Maria Luisa Vasconcelos
**

**Innate Behaviour**

**Postdoctoral researcher:** Nuno Machado  
**PhD students:** Cristina Ferreira, Miguel Gaspar, Saheli Roy  
**MSC student:** Sara Santos

To understand how neurons organise behaviour, we focus on reproductive behaviours. Reproductive behaviours are not only central to the survival of the species but also quite complex, providing insight into different levels of organisation. To address our questions, we use a combination of genetic manipulation, behaviour assays and calcium imaging in the fruit fly.

---

### Ruth Diez del Corral
**

**Development of Neural Circuits**

Associated with the Vision to Action and the Mathematics of Behaviour & Intelligence Labs  
**MSC student:** Leonor Novais

The formation of neural circuits with specific functions in the brain requires generating neurons with the appropriate subtype identities and connections. We are interested in understanding how these circuits are assembled during development and for this, we are collaborating with the Vision to Action Lab in the anatomical and developmental characterisation of neuronal subpopulations involved in visually guided behaviours in zebrafish. We are focusing our work on the diencephalon, a brain region which contains important neuronal nuclei involved in the processing of sensory stimuli and in the distribution of neuronal signals to other brain areas, including those responsible for motor behaviours. We use transgenic lines expressing fluorescent reporters in specific neuronal subpopulations to track the growth of neuronal projections in the whole embryo, using light-sheet microscopy.

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### Eric Dewitt
**

**Computational Cognitive Decision Science**

Associated with the Systems Neuroscience Lab

Our team uses computer models to study how humans and animals learn and make decisions. We focus on the role of neuromodulators, key players in learning and decision-making, and their influence on different brain areas. We hope this research will enhance our understanding of human behaviours and psychiatric disorders. In addition to this, we are fostering interdisciplinary collaborations, from psychiatry to artificial intelligence to hardware and software development. We believe this innovative approach is necessary to fully understand the brain and apply that knowledge to benefit health and society.

---

### Adam Kampff
**

**Development of Neural Circuits**

**Visiting scientist since 2014**

**Affiliation:** Johns Hopkins University  
**Visiting scientist since 2014**

My long-term research goal is to understand how a nervous system constructs a model of the world. How do brains learn about the structure of their environment? How do they encode this information in networks, and how is it used to control adaptive behaviour? To answer these fundamental questions, two major technical advances must occur:

1. The development of virtual worlds in which the statistics and physics of the environment can be manipulated, providing experimental control over the model formed by an animal’s nervous system;
2. The design and construction of novel devices for simultaneously recording from large populations of neurons throughout the brain of a behaving animal.

My research group strives to address both of these problems.

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### Rui Oliveira
**

**Social Neuro Endocrinology**

**Affiliation:** Instituto Gulbenkian de Ciência, ISPA – Instituto Universitário

We are interested in understanding the neuroendocrine mechanisms of social behaviour and how the social environment affects the neuroendocrine system. In particular, we are interested in the role of hormones as key physiological mediators underlying social plasticity.

---

### John Krakauer
**

**Cognitive-Motor Interface**

**Affiliation:** Johns Hopkins University  
**Visiting scientist since 2014**

Our main areas of investigation are:

1. Experimental and computational studies of motor control and motor learning in humans;
2. Tracking long-term motor skill learning and its relation to higher cognitive processes such as decision-making;
3. Prediction of motor recovery after stroke;
4. Mechanisms of spontaneous motor recovery after stroke in humans and in mouse models;
5. New neuro-rehabilitation approaches for patients in the first 6 months after stroke.

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Illustration: Bryan Christie.
We investigate what brings disseminated tumour cells in and out of dormancy, and how these dormant cells can be targeted.

methods
Mouse models of cancer dormancy and metastasis,
Multicolor flow cytometry,
Cellular and molecular biology, Imaging,
Single cell and spatial transcriptomics,
Computational biology

models
Mouse, Human samples

Dormant breast tumour cells (coloured in yellow and green) in liver-like cultures.

Our lab investigates metastasis, the process where cancer spreads from the primary tumour site to other body parts. Metastases cause most cancer-related deaths. In many patients, metastases appear long after successful primary tumour treatment because disseminated tumour cells (DTCs) remain dormant at distant sites, awakening years or decades later to initiate metastases. This pause in cancer progression offers a therapeutic window to prevent future metastases.

We focus on breast cancer dormancy, which often spreads to bones, liver, lungs, brain, and lymph nodes. Our goal is to dissect DTC interactions with the unique microenvironment at each distant site, providing a roadmap of tissue-specific vulnerabilities for therapeutic exploration. We’re particularly interested in how tissue immunity shapes metastatic progression, as immune cells are first responders to tissue damage and invading DTCs. Using multiple complementary approaches, we aim to develop strategies to prevent metastases from forming.

We celebrated our lab’s 1st anniversary, welcoming our first team members (Francisco Landum and Miguel Fuzeto), experiencing initial experimental failures and successes, and receiving extramural funding from the ERC-PT programme to study how distinct immune microenvironments impact metastatic progression.

Ana Luísa Correia was recognised as a NextGen Star by the American Association for Cancer Research (AACR) and chosen as one of the most promising young scientists to attend the Irving Cancer Immunology Symposium. Ana’s publication on immune-mediated breast cancer dormancy in the liver was rated among the top 10 most impactful recent papers in cancer research by the European Association for Cancer Research (EACR). Her work was also featured in Nature Reviews Cancer and Cancer Cell.

We began collaborations with colleagues from the CF Clinical Centre. Ana continued involving patient advocates in her research, working with the American association GRASP to promote interactions among researchers, clinicians, and patients. This inclusive partnership aims to help cancer patients live longer, better lives.
Cancer & Stem Cell Biology

Our research is focused on uncovering the biology of solid paediatric cancers with the aim of developing novel therapeutic approaches for paediatric cancer patients.

methods
Genetic mouse models of cancer, 3D cell culture systems, Tissue clearing, Lineage tracing, Microscopy

model
Mouse

Our lab has two main goals. The first is to uncover the differences between paediatric and adult cancers. Cancer is one of the main leading causes of death in children and adults. Paediatric cancers arise during development when tissues are growing. In contrast, cancer in adults develops from tissues that have reached their final size. Additionally, paediatric cancer responds differently to cancer therapy and is more lethal compared to cancer in adults, however, the reasons for these differences are not fully understood. Combining genetic mouse models, grafting experiments and in vitro cultures, we aim to understand the similarities and differences in cancer progression and response to therapy in both paediatric and adult cancers, using skin cancer as cancer models.

Our second goal is to unveil the biology of the most common solid paediatric cancers. Medulloblastoma and neuroblastoma are among the most common solid tumours and a leading cause of paediatric death. They are composed of different tumour and tumour microenvironment cell populations, and present cellular heterogeneity. Cellular heterogeneity has been proposed to be responsible for tumour progression and therapy resistance. We are interested in identifying the cell populations that mediate tumour progression in those tumours. In addition, we aim to uncover how these cell populations dynamically evolve during therapy and to infer which populations resist therapy, potentially leading to tumour relapse.

# highlights
Adriana Sánchez-Danés, Patricia Borges and Raquel Soares won the Prémio Faz Ciência 2022 Award, an annual initiative of the AstraZeneca Foundation, for their project to tackle medulloblastoma. Adriana also received the second FCT grant to uncover the mechanisms driving paediatric brain cancer development, and the lab looks forward to embarking upon this exciting project.

Three new members joined the team: PhD student Sara Ferreira, postdoc Ana Lúcia Rebelo and Masters student Maria Pacheco. Together with Bruno Costa-Silva and Henrique Veiga-Fernandes, Adriana organised the Champalimaud Research Symposium on the tumour microenvironment, and our team participated in the European Researchers’ Night at CF, a wonderful evening full of science and fun!
Neuroimmune interactions in the prevention and resolution of disease.

methods
Genetically tractable organisms,
Flow cytometry,
Cellular biology,
Molecular biology,
Imaging

model
Mouse

We explore the role of cross-talk between neurons and the immune system in the prevention and resolution of disease. To that end, the team focuses on organs that have a complex and dense network of neuronal and immune cells, including the intestine, lung and pancreas. This combination of features makes these organs an optimal site to reveal how the neural and immune systems work together to preserve health.

Using this approach, the lab has been exploring the surprising role of the neural network that surrounds these organs: immune regulation. We have discovered that while the immune system is responsible for actively fighting infection and cancer, neurons are in charge of detecting the invasion of tumour cells and setting the immune response in motion. These findings may have tremendous potential for designing novel therapeutic approaches for disease, as they pinpoint new selective targets that can be harnessed in infection, metabolic disorders and cancer.

# highlights
Our team was selected for funding from the European Commission – Horizon Europe programme, receiving the award for “Better understanding of the impact of risk factors and health determinants on the development and progression of cancer”. In addition, we won the 2022 Pfizer Award, and former lab member Ana Filipa Cardoso was acknowledged by the Eppendorf & Science Prize for Neurobiology, an international prize for promising young neurobiologists, for her pioneering PhD work paving the way for novel approaches to fight obesity.

David Brea published a commentary in the journal Nature on the bidirectional manner in which the nervous and immune systems interact, while Roel Wolterink and Henrique Veiga-Fernandes co-authored a review in Annual Reviews Neuroscience, also covering the subject of neuroimmune crosstalk.
We study multi-cellular interactions that regulate brain repair and tissue homeostasis.

methods
Lineage-tracing, Genetics, Transcriptomics, Confocal imaging, Behavioural assay

cell lines
Fruit fly

model
Fruit fly brain: the glial network is highlighted in green, neuronal cells in yellow, and cell nuclei in blue.

principal investigator
Christa Rhiner

postdoctoral researchers
Catarina Dias
Marta Neto

phd students
Anabel Rodriguez
Margarida Caio

msc student
Maria Baginha

bsc student
Salvador Ferreira

research assistant
Carolina Alves

We uncovered how dormant neural stem cells are recruited for repair after localised brain injury. Hypoxia-sensing in neuro-glial clusters triggers the production of an extracellular carrier molecule, which promotes the travel of localised growth factors in the injured brain area, leading to activation of neural stem cells (Simoes et al., Dev Cell 2022). This result establishes an inter-cellular circuitry connecting injury-sensing to regenerative outcomes.

In addition to local changes, we explored brain-systemic interactions and discovered that brain injury alters tissue dynamics in the fly intestine. In April 2022, we celebrated the graduation of our first PhD student, Mariana Santos, whose thesis illuminated injury-activated programmes in neural stem cells, sparking new lab projects. Finally, Christa Rhiner and Susana Solá, Assistant Professor at iMed.ULisboa, organised the 3rd edition of the Stem Cell Course, which took place in-person for the first time in 2022, featuring engaging lectures and workshops at CF and the Faculty of Pharmacy.
Our research focuses on new mechanisms by which extracellular vesicles regulate cell signalling, tumour progression and response to therapy.

**Methods**
- Vesicle flow cytometry
- Protein-protein interactions
- In vivo models of tumour growth and metastasis

**Model**
- Mouse

Since 2016, we have concentrated on developing new technological platforms that facilitate the mechanistic study of extracellular vesicles (EVs) as disease biomarkers in the clinical setting. This includes a vesicle flow cytometry method for the expedited study of EVs in non-processed biofluids, which has already led to the identification of important EV biomarkers in breast, colorectal, and clear cell renal cell carcinomas. Besides showing how cancer EVs are key mediators in the setup of pre-metastatic niches and metastasis biomarkers, we have also demonstrated that these vesicles are instrumental to the follow-up of the therapy response of pancreatic cancer patients.

In a new research line, we have developed methods tailored to the study of EV protein interactions. As EV protein interactions may regulate the activity and biodistribution of target proteins, we believe that this underappreciated mechanism is a promising candidate to play a pivotal role in cancer biology. In still unpublished data, we have observed that tumour EVs interact with several cytokines with relevant roles in cancer biology and tumour immunity, which include immunosurveillance and response to emerging anti-tumour therapies such as immune checkpoint inhibitors.

**Highlights**
- We identified a new biomarker to follow up on the response to therapy in metastatic pancreatic cancer patients, and also developed an improved pipeline for mutation analysis of circulating DNA packed in extracellular vesicles of cancer patients.
- Moreover, we contributed to the identification of new biomarkers for multiple myeloma diagnosis.

In 2022, we welcomed no less than five new lab members: Catarina Esteves Pereira, Ana Rita Cruz, Luís Ferreira Rocha, Inês Saldanha, and Adrianna Bielowka, who, together with our other members, are playing key roles in the study of cancer EVs as regulators of anti-tumour cell signalling. Ana Rita was awarded the Maria de Sousa Prize for the study of the new role of tumour EVs as regulators of response to immunotherapies, while Bruno Costa-Silva co-organised the 2022 Champalimaud Research Symposium, which focused on the tumour microenvironment.
The work of CR investigators is facilitated by two structures: the Scientific and Technological Platforms, which facilitate technical research aspects, and the CR Support Units, which provide administrative services.
The Scientific and Technological Platforms consist of nine individual units that support the work of researchers and clinicians at CF. The Platforms operate across a wide range of areas, from the development of sophisticated technologies in animal models, imaging tools, hardware and software, to managing resources and research infrastructures.

The ABBE Platform provides equipment and expertise to support CF researchers in the acquisition of high-quality microscopy data. The platform assists users throughout the imaging pipeline, including project discussions to identify the most appropriate imaging strategy, detailed technical training and support in image processing, analysis and visualisation.

The ABBE Platform is managed by an international team with multidisciplinary backgrounds, which enables us to meet a wide range of microscopy needs, from imaging protein interactions to whole organisms. The team also represents CF on an international level at conferences and committees, and serves as a bridge between CF and microscopy companies, not only regarding technical issues, but also regarding the establishment and maintenance of long-term partnerships.

# highlights

The ABBE Platform was pleased to welcome a new imaging specialist and microscopist to the team, Pedro Campinho, who conducted his PhD at the Max Planck Institute of Cell Biology and Genetics in Dresden, Germany, under the supervision of Carl-Philipp Heisenberg. During his PhD, Pedro worked with the zebrafish model, becoming an accomplished biophysicist and expert in mesoscale microscopy.

Together with the COLife imaging facilities and the Faculdade de Ciências da Universidade de Lisboa, the ABBE Platform ran several courses:

- Basic FIJI Imaging Analysis Course.
- Advanced FIJI Imaging Analysis Course.
- EMBO Practical Course in Computational Optical Biology.
- Digital Pathology Analysis Course (QuPath Workshop).
- Light-Sheet Microscopy Course @iMM.
- Advanced Microscopy Course in Optical Sectioning @i3S.
- Bio-Imaging at CCMAR, Algarve and Beyond Workshop.

We also took part in several outreach events, from CF’s ERN to teaching the duality of light to students from the Instituto Superior de Psicologia Aplicada.
The Histopathology Platform provides a number of high-quality services to the CF scientific community, including: fit-for-purpose histological procedures for specific experimental questions and appropriate methods for collection, fixation and analysis; preparation of biological samples for routine or special procedures; training of CF members; drawing up written reports and supporting manuscript/grant preparation.

**# highlights**
The Histopathology Platform processed more than 3,800 tissues from mouse, rat and zebrafish models, for paraffin-embedding, sectioning and staining, immunolabelling and RNAscope assays. We serviced more than 60 users from 23 different CF Groups, in addition to academic partners and industry. Well over 50% of CF’s research grants involve animal studies or studies with human samples, and the Histopathology Platform has been acting as a critical resource for tissue interrogation, providing a morphological context to genetic, molecular and/or biochemical data.

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Glass wash and media preparation are core functions, and essential for any research institution. The Glass Wash & Media Preparation Platform (GWMPP) supports CF’s investigators and laboratories by providing sterilised labware such as glass, plastics and instruments, as well as preparing high-quality tissue culture and bacteriological media required for standard research protocols.

**# highlights**
The GWMPP provided daily services to CR’s labs and platforms, as well as to three Champalimaud Clinical Centre units, namely the Nuclear Medicine, Pharmacy and Radiation Oncology Services. The team continued to meticulously follow procedures and maintain records to ensure the safe and optimal operation of its services.

**coordinator:** Cátia Feliciano
**head:** Maria José Vito
**technicians:** Diogo Martins, Madalena Martins, Soraia Rodrigues
The Fish Platform ensures high-quality care for our fish models and offers advanced research services, including creating transgenic and gene-edited fish. In close and constant communication with researchers, the platform adapts its services to best meet the needs of the community. Its focus on scientific and technological development has fostered collaborations and yielded peer-reviewed publications, earning the platform international recognition. The platform is also part of CONGENTO, through which it provides fish-related services and training to the global community.

# highlights
Platform manager Joana Monteiro co-organised the 1st Zebrafish Husbandry Association Euro Meeting in London, attracting attendees like facility managers, technicians, suppliers, and vets from across Europe. The event featured talks from regional zebrafish resource centres and covered various topics, from emergency planning to animal research guidelines.

The Fly Platform provides state-of-the-art conditions for breeding, maintenance and manipulation of the fruit fly, available to all CR researchers. Apart from managing and maintaining all shared equipment and spaces, the platform provides technical services ranging from core activities such as medium production and stock maintenance, to more technically demanding procedures such as organ dissection, staining and embryo microinjection.

# highlights
Our technicians have been increasingly collaborating with high schools, providing fruit fly specimens for biology and genetics classes, with some partnerships extending to presentations and extra activities by team members Liliana Costa and Patricia Valentim. The team also played a significant role in CF’s European Researchers’ Night, hosting outreach activities themed around drosophila, and were invited to conduct a practical session on Drosophila Genetics for the NOVA School of Science and Technology’s Masters programme.

The Rodent Platform ensures the welfare and veterinary care of all CR rodent models, abiding by European and national laws as well as welfare guidelines. The team manages shared facilities, provides daily animal care, and runs specialised services, often partnering with the Molecular and Transgenic Tools Platform.

# highlights
The team improved its practices to align with Good Laboratory Practice (GLP) standards, aiming to receive accreditation in 2023. As part of our close collaboration with ORBEA (Órgão Responsável pelo Bem-Estar dos Animais / Animal Welfare and Ethics Body), we also initiated efforts to apply the CF’s Gender Equality Plan to our operations, by documenting, reporting and raising awareness of balanced gender representation in animal models. Furthermore, we implemented a revised programme for experimental animal project monitoring, assembling a new team for this task.

The platform’s commitment to training was shown through two major Laboratory Animal Science courses held in 2022, training 40 researchers. An additional 25 researchers received upgraded animal experimentation licences following further training workshops.
The Molecular and Transgenic Tools Platform (MTTP) performs complex cloning, gene editing and viral production projects. It assists users at all project stages, including conceptual design. Our team of experts provides support in molecular biology strategies, from basic services to complex cloning of knock-out and knock-in constructs to generate new cellular, zebrafish, fly or mouse models.

The MTTP also harbours a viral-vector production service and has several collaborations for continuous development and implementation of new viral systems. The platform provides regular genotyping services for several animal models, and acts as a hub of shared resources and expertise not only for the CR, but also for the national and international research communities across academia and industry, which it services through the CONGENTO research infrastructure.

In close collaboration with the Champalimaud Clinical Centre, the MTTP continued to run the CF COVID-19 Test Lab, which provided molecular diagnosis for SARS-CoV-2 by RT-PCR and antigen tests from January through to September 2022.

# highlights
Since its inception in 2020, the COVID-19 Test Lab managed by the MTTP has ensured the safety of patients, clinical staff and researchers through daily testing. Following an update of the national guidelines for COVID-19 testing, the COVID-19 Test Lab closed its operations on 30th September, having performed over 3,100 diagnostic RT-PCR tests and more than 1,200 antigen tests in 2022.

The MTTP held its first edition of the “Hands-on Molecular Tools” Workshop, designed as a crash course for beginners on the basic principles of molecular biology and genetic engineering. From 1st-5th September, we hosted 14 students with different backgrounds across the biological and biomedical sciences. After more than 18 hours of lectures and laboratory work, students were able to perform and troubleshoot all the steps of a basic cloning process.

coordinator: Ana Catarina Certal
manager: Ana Raquel Tomás
senior research technicians: Ana Dunha, Filipa Dias
research technicians: André Monteiro, Mariana Velez, Renato Ferreira, Simão Margarido
laboratory technicians: Alexandra Teixeira, Kateryna Kholod

The Biophotonics Platform focuses on the development of innovative optical tools and methods for clinical applications. Our goal is to provide clinicians with effective diagnostic tools to aid in decision-making, ultimately enhancing early cancer detection, intraoperative margin assessment, and post-treatment monitoring.

Our multidisciplinary team at the Biophotonics Platform brings together expertise in engineering, physics, biochemistry, and medicine. Our activities are closely coordinated with the various clinical units and the Pathology Service at the Champalimaud Clinical Centre, ensuring a strong connection between research, technological advancements, and clinical practice.

# highlights
The Biophotonics Platform commenced operations in 2022, initially concentrating on the development of a prototype system capable of differentiating between benign and malignant lesions through advanced optical techniques. This process took into consideration the medical and surgical requirements intrinsic to medical devices. Collaborative efforts were established with the Digestive, Gynecology, and Dermatology Units, and several clinical studies were initiated to evaluate the device’s clinical feasibility and validate its diagnostic capabilities.

coordinator: João Lagarto
phd student: Ignacio Herrando

coordinator: Ana Catarina Certal
manager: Ana Raquel Tomás
senior research technicians: Ana Dunha, Filipa Dias
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The Flow Cytometry Platform, equipped with state-of-the-art equipment and highly specialised staff, provides support to both internal and external researchers. We offer extensive training across several domains – from theoretical flow cytometry concepts and experimental design to practical instrument operation and advanced data analysis.

# highlights
Our instruments clocked over 2,500 hours in flow analysis and cell sorting operations. We participated in the CYTO 2022 congress in Philadelphia, hosted several Tech’s Café seminars as part of the FLxFlow network to update the CR community on new scientific products, and played a key role in establishing a future flow cytometry national network. In addition, platform head André Mozes was elected as an Emerging Leader by the International Society for Advancement of Cytometry.

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The Hardware and Software Platform’s mission is to support cutting-edge scientific and technological innovation at CF by providing expertise in the design and development of new technological applications across the areas of electronic, robotic, software and mechanical engineering.

The platform comprises members with diverse skill sets across hardware and software development, who work collaboratively with researchers and clinicians seeking new technological solutions and approaches to support state-of-the-art research and enhance health service delivery.

We provide services across the full pipeline for hardware and software development, including requirement specification and analysis, design, development, implementation, validation and testing. We support CF members in a number of ways, from providing 3D printing services and day-to-day support to developing custom electronic hardware and managing both the electronic and mechanical workshops. In addition, we also support the dissemination of knowledge, and over the years have actively contributed to open-source projects and sharing of new advances with the research community.

# highlights
Both the Hardware and Software Platforms were restructured into one Hardware and Software Platform, with a new scope, strategic mission and team make-up. This was a natural transition resulting from increased project complexity, and the resultant synergies will make it easier to meet the new challenges arising from projects that integrate hardware and software. Throughout the year, the platform continued to provide daily support to the community, while also dedicating time to new technological developments.

The platform also continued to disseminate open-source technology developed in-house, through the expansion of the tools portfolio and export of hundreds of electronic devices worldwide, further strengthening its position as a reference in neuroscience open-source hardware development.

Moreover, the platform conceived and developed a friendly winged robot, capable of human interaction through image and speech recognition, voice synthesis and movement, made possible by combining a multitude of deep-learning models. Reflecting the latest advances in AI technology, it has the potential for a wide range of applications in health and well-being.
The CR Support Units (CRSU) are responsible for:

- providing comprehensive administrative and operational assistance, including budget and financial management, purchasing, procurement, and services within the people and culture area.

Accompanying the evolution and growth of CR, the support provided to CR’s scientists also continuously grows in organisation and capacities.

The vision of the CRSU is to be an exemplary resource in the field of research management and administration by providing tools and exceptional support to enhance the work of scientists, maximising their time spent in research.

The CR Managing Direction team serves as the primary point of contact for any problem-solving needs within CR, providing advice on the resources available for the CR community. The team liaises with multiple departments across the institution and focuses on optimising processes, identifying and addressing general problems and deficiencies, and recommending and implementing solutions. Additionally, the team is responsible for budget development and control, as well as coordinating support units.

# highlights

We returned to normalcy after the pandemic, allowing us to once again host two important on-site events: the annual retreat and the CR symposium. These gatherings reinforced and strengthened our community bonds. We also went beyond routine work to support our community, overseeing new faculty recruitments and helping to organise both the scientific evaluation panel and advisory board.

This year marked both heartfelt farewells to treasured colleagues and warm welcomes to numerous new team members in our support units. We are grateful for everyone’s dedication and contributions, and look forward to the fresh insights and valuable input our new members will bring.

managing director: Philipp Tsolakis
deputy managing director: João Cruz
executive assistant to cr directors: Inês Soeiro
The Laboratory Administration Unit provides support to the scientists working at CR, enabling them to focus on their research. This team works closely with the principal investigators and laboratory managers, assisting with the ordering process, budget management, travel arrangements, and other essential tasks. Lab Administrators frequently collaborate internally with other CR Support Units and departments, such as post-award, logistics, accounting, IT, and maintenance, as well as externally with suppliers, service providers, shipping companies, and brokers.

# highlights
Two team members were replaced, and we continued to adapt to meet the growing demand for various types of lab supplies and requests, while providing responsive support to CR scientists despite the challenges.

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Our team aims to connect society with CF’s health, research, and innovation activities in an accessible way. We blend traditional and experimental approaches in communication, event planning, and outreach. Our main objectives are to:

# Facilitate internal communication to promote CF’s values and encourage collaboration.
# Organise events for healthcare professionals and scientists.
# Raise public awareness about CF’s activities and achievements.
# Foster science and health literacy among diverse audiences through educational initiatives.

# highlights
We enjoyed another dynamic year. We broadened our science education initiatives like Ciência di Noz Manera for underserved students, reintroduced the Neuronautas summer academy and organised a science workshop for the national Metamorfoses contest.

Our outreach efforts continued apace, with Brain Awareness Week school activities, the Ar Event series revival, and the creation of the RAISE consortium with NGO Native Scientists and iMM to foster science inclusivity. We also co-organised the inaugural European Researchers’ Night at CF, attracting over 1,200 attendees.

Online, we launched the second instalment of “Zoom-In on Champalimaud” and three “Science Snapshots” videos on CR breakthroughs. We also devised awareness campaigns for various global observances such as World Parkinson’s Day and National Scientist’s Day.
The Graduate Studies Office operates mainly out of the Teaching Lab and Classroom, which form the hub of our PhD programme and courses. The Graduate Studies team is responsible for the administrative and logistical aspects of the International Neuroscience Doctoral Programme (INDP), CAJAL Programme and other teaching events, and provides support for courses such as the Universidade do Algarve’s Fundamentals of Medicine postgraduate programme.

The team also manages the CR Library, Teaching Lab space, and Classroom bookings. Furthermore, we assist with student social events, INDP PhD student admissions, and host the annual INDP Student Advisory Board visits. Since 2020, the Graduate Programme Office has also helped students apply for fellowships funded by sponsors such as FCT, Boeringher and “la Caixa”.

# highlights
QuantOCancer Research Support Staff Knowledge Exchange awarded to the Graduate Studies Office:

With support from the QuantOCancer Research Support Staff Knowledge Exchange, Maria Teresa Dias, manager of the Graduate Studies Office, participated in two events in Brussels on the 29th and 30th November: “The Future of Research Management Training in Higher Education” and “Teachers’ Training and Mentors’ Training”. Hosted by the Agency for the Promotion of European Research, these events provided valuable insights that can be used to professionalise research management.

The HR & Fellows Support Office serves both CF’s research and clinical research staff, numbering approximately 440 people. We assist with all aspects related to human resources, from recruitment and onboarding to follow-up of former CF members. This unit works closely with HR representatives, as well as other support units and platforms throughout the CF, to ensure that all CF’s commitments to its researchers are met.

We consistently review and improve HR policies, processes, and procedures, always seeking effective ways to ease and assist the lives of researchers at CCU. Our focus is on promoting the success of all researchers and coworkers at CCU, while also respecting the various social issues that affect their lives. We strive to maintain a respectful environment that inspires excellence and well-being for all CF researchers.

# highlights
Throughout 2022, our team continued to develop new and innovative ideas to better serve the CF community and to provide the best possible assistance to its researchers. In this effort, we processed around 110 onboarding requests, 88 offboarding requests, 10 visa and permit requests, and 50 social security requests, while also issuing over 100 statements to support our researchers.
The Strategic Research Development Team is responsible for fundraising initiatives related to research, innovation, and technology development at CF. We achieve this by scouting policy, funding, and collaboration opportunities, as well as co-designing, co-developing, and co-launching strategic programmes and projects.

Since its inception in 2017, the team has worked closely with the CF community to develop a tailor-made, coordinated, monitored, and supportive framework and team culture to secure research funds. The hard work of the CF research ecosystem over the past six years has been rewarded with over €62 million in sponsored research funds, with over two-thirds of the funding being awarded by international sponsors.

# highlights
2022 was both a challenging and rewarding year for the team. One of the most talented Research Managers in Portugal, Mariana Santa-Marta, who had been with the team since its inception, took on an exciting new challenge at Instituto Superior Técnico. This presented us with the task of identifying promising talent that shared our core principles and teamwork spirit. Following a highly competitive international recruitment process, we proudly welcomed Ana Saraiva Ayash, who had developed her education, research, and research support career in the UK for over 15 years. As a result, our team has actively contributed to the brain gain in Research Management in Portugal.

Under the scope of the EC’s H2020-funded project QuantOCancer, we hosted an international online event called “Deciding How to Fund Research: Perspectives on the Partial Randomisation Process.” We brought together 80 researchers, research managers, and funders from around the world to brainstorm research funding ideas.

In 2022, we disseminated 278 funding opportunities and supported the preparation and submission of 154 applications to over 34 sponsors, with 28 projects awarded funding totalling more than €9 million. In summary, we are immensely proud of the research funding achievements of the CF community in 2022, which reflect our international networking, leadership, and pioneering spirit.

The CF’s Office for Sponsored Programmes (OSP) – Post-Award provides assistance and support related to grant reporting (financial and scientific), grant management and administration, and cost eligibility. Additionally, the OSP serves as a facilitator, bridging the gap between the CR scientific community and the bureaucratic aspects of grant management.

# highlights
The OSP helped to manage approximately €50M distributed among 137 different projects. The OSP was responsible for submitting a total of 160 financial reports and 68 scientific reports to numerous funding agencies on behalf of the research community.
The Operations Unit ensures that the day-to-day activities of the CR laboratories run smoothly by providing timely and effective assistance to the community and serving as the primary point of contact for infrastructure, maintenance, equipment, and space management. The Operations Unit also works with the CR Direction team to develop and implement policies and procedures. Additionally, the Operations Unit assists principal investigators with planning and organising resources, acquiring and installing new equipment, and providing general guidance.

To improve the health and safety conditions of the labs, a Health and Safety Unit was created, as part of the Operations Unit. This unit launched the SafeLab website, which provides easy access to various resources, including a chemical safety database and a repository of all relevant safety information about available laboratory resources, general and emergency procedures, waste disposal guidelines, and health and safety information regarding the most common laboratory hazards. This documentation is now used as a complement to inductions/training.

# highlights
The Operations Unit welcomed a new member, Vasco Correia, who joined us as Operations Unit Officer. He has taken on various responsibilities, including assisting with emergency issues and managing equipment maintenance contracts with both in-house and external companies.

As CF’s clinical research activities continue to expand and diversify, the output from projects developed at the Champalimaud Clinical Centre, particularly by the Research Groups of the Clinical and Experimental Research Programme, necessitates an increase in communication efforts. This includes producing content to bridge the gap between clinical research and the general public.

QuantOCancer continued to execute a robust programme of initiatives focusing on internationalisation, gender equity and science education. In particular, we highlight the international research management workshop “Deciding how to fund research: perspectives on the partial randomisation process”, held in collaboration with regional pre-award teams; the implementation of CF’s Gender Equality Plan; and the successful wrapping of the pilot edition of the science education initiative Ciência di Noz Manera (Science Our Way), which brings researchers closer to underserved high school students in greater Lisbon. By the end of 2022, QuantOCancer had funded eight early-stage researcher secondments and nine staff knowledge exchanges to renowned institutions in the US and Europe.
[Experimental Clinical Research Groups]

Cancer Development & Innate Immune Evasion
Computational Clinical Imaging
Immunotherapy / ImmunoSurgery
Molecular & Experimental Pathology

Myeloma Lymphoma Research
Neural Circuits Dysfunction
Neuropsychiatry
[Scientific & Technological Platforms]
Advanced Biomaging & Biooptics Experimental Biophotonics
Fish
Flow cytometry
Fly
Glass Wash & Media Preparation
Hardware & Software

Histopathology
Molecular & Transgenic Tools
Rodent

[CR Support Units]
Communication, Events & Outreach
CR Managing Direction
Graduate Programme Office
Health & Science
HR & Fellows Support Office
Lab Administration

Operations
Post-Award
Strategic Research Development

Group photo at the annual retreat in Herdade da Granja (BoomLand), Idanha-a-Nova
In 2022, CR’s publications encompassed new discoveries in both fundamental research topics and translational and clinical fields. Many of these publications resulted from collaborative efforts among various groups within the Champalimaud Foundation.

The featured publications below provide an overview of CR’s extensive research spectrum.
Animals see the world differently depending on their hunger and reproductive state. In this project, researchers from the Behaviour and Metabolism | Ribeiro Lab explored how internal states shape behaviour. They created a functional atlas of the subesophageal zone, a relatively poorly understood region in the fruit fly brain that receives the majority of taste inputs and houses the motor neurons that control feeding.

Using this “appetite map” in the brain, they identified key neurons that control protein cravings under nutritional restriction and during pregnancy. They also discovered that protein-rich food has a strong effect on neural activity in protein-deprived animals. The researchers believe that their new microscopy strategy could be used to better understand the neural basis of behaviour and decision-making, both within and beyond food choice.

This study from the Learning | Paton Lab revealed how the brain stops us from jumping the gun. The team designed a task where mice had to determine whether an interval separating two tones was longer or shorter than 1.5 seconds, and tracked neural activity in the mice while they performed the task. They identified two brain areas, one responsible for promoting action and one for suppressing it. The researchers found that a circuit in a brain region called the basal ganglia, known as the indirect pathway, flexibly supports the behavioural goals of the animal. They were able to trigger impulsive behaviour by manipulating neurons in this brain circuit, effectively uncovering an “impulsivity switch”. Not only does this discovery have implications for Parkinson’s and Huntington’s Disease, it also provides a unique opportunity to investigate conditions of impulse control, such as addiction and obsessive-compulsive disorder, which could lead to new treatments.

Researchers from the Sensorimotor Integration | Chiappe Lab in Portugal discovered a bi-directional neural network connecting the legs and visual system that helps fruit flies to walk on two different timescales simultaneously. The network operates on a fast timescale to monitor and correct each step while promoting the animal’s behavioural goal, and on a long timescale to help maintain the animal’s behavioural goal.

Scientists from the Systems Oncology | Costa-Silva Lab discovered a new tool for improving pancreatic cancer care. Their study explored the therapeutic potential of extracellular vesicles (EVs). EVs are tiny sacs released by cells, and they showed that by monitoring EVs over time, doctors can better determine how well patients are responding to therapy.

The team discovered that EVs coated with a type of protein called Immunoglobulin G increase during disease progression and decrease in response to therapy, meaning that these EVs are a new biomarker for evaluating a tumour’s status, particularly for those patients that do not express the current standard biomarker. The research provides a significant step forward in the fight against pancreatic cancer, which is projected to be the second cause of cancer deaths by 2030.
How brain injury activates neural stem cells
Anabel Simões et al., Developmental Cell, 2022.

The Stem Cells and Regeneration
Rhiner Lab discovered a novel mechanism by which neurons and glia collaborate to promote neural regeneration. To understand how neural regeneration works, the team turned to the fly and mouse animal models, which, like humans, contain special cells in the brain called neural stem cells. These cells partially activate in response to tissue damage and can produce new neurons.

They found that a transporter protein called Swim is critical for mounting a regenerative response to brain injury. Their work revealed that Swim is produced by glial cells in the injured brain area when oxygen levels drop, that it encapsulates Wg/Wnt, a known activator of neural stem cells, and that it carries it to the nearest stem cell, effectively turning it on. If a similar mechanism exists in humans, these findings may then be translated into therapies to help stimulate regeneration following severe head trauma or stroke.

New biomarkers for multiple myeloma
Bruna Ferreira et al., Frontiers in Oncology, 2022.

In a collaboration between the Myeloma Lymphoma Research | João Lab and the Systems Oncology | Costa-Silva Lab, this study looked at a new way to diagnose and monitor multiple myeloma, the second most frequent blood cancer in adults, with an average survival rate at five years of around 50%. Instead of taking a bone marrow biopsy, which is invasive and can be unreliable, the researchers looked at small particles in the blood called extracellular vesicles (EVs).

They found that the protein content of these particles was related to the patient’s immune function, survival, and response to treatment. The researchers identified a set of proteins that could potentially be used as new biomarkers for multiple myeloma, and suggest that EVs could be used as a minimally invasive way to monitor the disease in the future through blood samples.

This project from the Neuropsychiatry Unit | Costa-Silva Lab found that repetitive transcranial magnetic stimulation (rTMS) can be a viable and effective treatment for depression in older adults. Previously, it was believed that rTMS was not suitable for older adults, but the study shows that older patients respond just as well to rTMS as younger patients. The effects may take longer to be felt, but the treatment is still effective.

Together with colleagues from other research institutes, the Preclinical MRI | Shemesh Lab discovered a blood test that can detect patients with resistance to brain radiotherapy and have identified a drug that could reverse it. The study found that increased levels of the S100A9 protein are associated with limited sensitivity to radiotherapy.

The researchers discovered that the S100A9 protein can be found in the blood of patients, which allows patients who are resistant to radiotherapy to be identified. The study also identified an existing drug that could be used to transform radioresistant metastases into sensitive ones. The findings could lead to a new approach to radiotherapy for cancer patients and could help identify patients who might benefit from radiotherapy.

Why brain stimulation should not be overlooked as an antidepressant treatment for older adults
Gonçalo Cotovio et al., Frontiers in Aging Neuroscience, 2022.

Increasing the effectiveness of radiotherapy in brain metastases
Cátia Monteiro et al., Nature Medicine, 2022.
Since the establishment of the research programme, CR scientists have received significant support for their work through competitive external funding schemes. Counting all newly awarded and previously secured projects, a total sum of €50M was active at CR during 2022. These funds were awarded by a diverse group of national and international organisations. Among these, the major contributors were the European Commission and the National Portuguese Science Foundation (FCT).
Several consortia-based projects were secured by the CF under the Recovery and Resilience Funds Programme (PRR) for the first time, including the Centre for Responsible AI, led by Unbabel and involving CR’s Joe Paton, Daniel McNamee, Zach Mainen, Memming Park and Christian Machens.

The first consortium-based project secured by the CF under the EC’s Horizon Europe Mission Cancer Programme was GENIAL, led by the Université Libre de Bruxelles in Belgium and involving CR’s Henrique Veiga-Fernandes.

The first consortium-based project secured by the CF in EC’s Digital Programme was EUCAIM, led by the European Institute for Biomedical Imaging Research in Spain and involving CR’s Nikolaos Papanikolaou.

The first project secured by the CF under the NIH BRAIN Initiative was “Understanding feedforward and feedback signalling between neuronal populations”, led by the Albert Einstein College of Medicine in the US and involving CR’s Christian Machens.

The first project awarded to the CF by the Choroideremia Research Foundation’s Throssell and Hillier Families Research Award will be led by CR’s Miguel Seabra.

2022 saw CR’s continued success in the "la Caixa" Foundation’s Health Research programme with UPDOWNBOUND, led by CR’s Leopoldo Petreanu.

CR’s Ana Luísa Correia was also awarded an EMBO Installation Grant.

Year after year, early-stage researchers hosted by the CF secure some of the most competitive prestigious fellowships. 2022 was no exception:

- The FCT Individual Call to Scientific Employment Stimulus was awarded to Ana Queirós (João Lab), Sílvia Henriques (Ribeiro Lab), and Rafael Henriques (Shemesh Lab).
- The EC’s Horizon Europe MSCA Postdoctoral Fellowship was awarded to Claire Rusch (Chiappe Lab) and Coralie Hérent (Carey Lab).
- HFSP and EMBO Fellowships were awarded to Coralie Hérent (Carey Lab).
- The “la Caixa” Foundation Junior Leader (Retaining) Fellowship was awarded to Maríia Martínez-Lopez (Veiga-Fernandes Lab).
- The Graduate Women in Science Fellowship was awarded to Filipa Barros (Alves da Silva Lab).
- Bial’s Maria de Sousa Award was awarded to Ana Rita Cruz (Costa-Silva Lab).
21 nationalities amongst the student community: Austrian, Belarusian, Brazilian, British, Chilean, Dutch, Estonian, French, German, Hungarian, Indian, Italian, Korean, Polish, Portuguese, South African, Spanish, Swiss, Turkish, American, and Vietnamese.

Since its inception, CR has regarded educating scientists as one of its key strategic objectives. To this end, CR has devoted considerable efforts to the development and implementation of outstanding educational programmes, advanced courses, and workshops.

Among these, two main endeavours are the International Neuroscience & Cancer Doctoral Programme and the CAJAL Advanced Training Courses.
The INDP aims to provide students with a broad and integrative education in neuroscience, physiology and cancer, with a focus on the neuronal and circuit basis of behaviour, and organismal biology.

A main goal of the programme is to foster and encourage active participation, independence, and critical thinking amongst the students, as they forge their path towards becoming innovative scientists and researchers. INDP students come from all over the world and from a range of backgrounds, including the life sciences, physics, psychology, mathematics, and computational sciences.

In 2022, students attended courses that covered basic topics in contemporary biology and neuroscience. The courses have a strong practical component, as well as a focus on quantitative skills. In the first year of their PhD, students also perform laboratory rotations, which allow them to familiarise themselves with the research done across different labs and select the lab in which they will conduct their doctoral research. Students are supported by a thesis committee that monitors their progress and provides input throughout their PhD.

The INDP is an accredited programme and degrees are granted by one of our two academic partners, ITQB NOVA – Instituto de Tecnologia Química e Biológica António Xavier, Universidade Nova de Lisboa, and ISPA – Instituto Universitário de Ciências Psicológicas, Sociais e da Vida. PhD students at the Champalimaud Foundation enjoy a vibrant academic environment, with a weekly schedule of seminars featuring internal and external speakers across both basic and clinical research domains, as well as access to a wide range of meetings and workshops.

Eleven students were recruited in the INDP22 call (~73% international students):

- Andreia Gonçalves (PT)
- Angelina Sanderson (GB)
- Filip Kus (POL)
- Hyungju Jeon (KOR)
- Ildefonso Pica (NL)
- Marcel Groetz (DE)
- Marco Colnaghi (IT)
- Maria Keridon (EE)
- Marta Forcella (IT)
- Raquel Sequeira (PT)

# highlights

Hybrid Interviews & Open House: The recruitment process took place in hybrid format on 14th, 15th and 28th March. The event, organised by the Graduate Studies Office, involved 33 candidates from 16 different countries.

Orientation week for INDP students: From 12-16th September, the Student Welcome Committee, along with the Graduate Studies Office, organised the second edition of the INDP Orientation Week. Students were formally introduced to the Champalimaud Research community, its culture, mission, vision, and values. There were tours, talks, training activities, and entertainment initiatives aimed at welcoming the students into CR’s vibrant community and to the city of Lisbon. The whole CR Community was actively involved in this initiative.

buddy programme

As part of the onboarding experience, the student community at CR has developed the Buddy Programme, a useful and creative tool to welcome and support newcomers, providing a fantastic opportunity for students to meet their peers, exchange ideas, tips, and advice.
In 2022, the CAJAL Advanced Neuroscience Training Programme encompassed eight courses. Three of these were held at the Champalimaud Centre for the Unknown, while the remaining five took place at Bordeaux Neurocampus. These two institutes were chosen to pioneer recurring neuroscience training courses in Europe, emulating a successful model that has been operating in the United States for several decades.

# highlights

Following a two-year hiatus due to the COVID-19 pandemic, Cajal Courses were once again organised in-person at the CF. In 2022, three courses were held, involving a total of 68 faculty members, 26 teaching assistants and 62 students:

## # Cajal Quantitative Approaches to Behaviour
22nd May – 11th June
directors: Gonzalo de Polavieja (CF, PT), Benjamin de Bivort (Harvard University, US), Greg Stephens (VU University Amsterdam, NL), Gordon Berman (Emory University, US), Orit Peleg (University of Colorado, US)

## # Cajal Interacting with Neural Circuits
19th June – 9th July
directors: Tiago Branco (Sainsbury Wellcome Centre, UK), Michael Hausser (University College London, UK), Susana Lima (CF, PT), Claire Wyart (Institut du Cerveau, FR)

## # Cajal Computational Neuroscience
17th July – 6th August
directors: Brent Doiron (University of Chicago, US), Maria Geffen (University of Pennsylvania, US), Julijana Gjorgjieva (Technical University of Munich, DE), Joe Paton (CF, PT), Caminiti* (Bordeaux Venue Administration)

Champalimaud Foundation hosted the Cajal General Assembly Annual meeting. It was the first time the annual meeting took place in Lisbon.

# 1st Cajal General Assembly Annual meeting at Champalimaud Centre for the Unknown
16th-17th May
participants included: Eero Castrén (President), Tom Otis (Treasurer), Tracy Bale* (IBRO Representative), Sarah Caddick* (The Gatsby Charitable Foundation Representative), Jean-Antoine Girault (FENS Representative), Christophe Mulle (University of Bordeaux Representative), Christian Machens (CF Representative), Nicolas Caesar Petersen (Treasurer-Elect), Sonja Hofer* (President-Elect), Elena Dreosti & Mathilde Maughan (Cajal Central administration), Lars Kristiansen (IBRO Office), Tasia Asakawa (FENS Office), Maria Teresa Dias (CF’s Venue Administration), Antonella Caminiti* (Bordeaux Venue Administration)

*online attendance
In 2022, following the COVID-19 global pandemic, scientific events at CCU came back in full swing.

=> With strong support from the Communication, Events & Outreach team, over eighty scientific events were successfully delivered across a wide range of formats, from onsite to online to hybrid.

=> By offering this flexibility, the team was able to facilitate scientific dialogue both within and beyond CF throughout the year.

< In addition, the expansion of our activities to the CF Warehouse gave birth to new types of events, enabling us to diversify the events that we develop and produce, and to organise fruitful scientific discussions on trending topics such as AI, machine learning, virtual reality and digital therapeutics.
By bringing together experts who have greatly contributed to the understanding of the tumour microenvironment, the Champalimaud Research Symposium 2022 (#CRSy22) provided its several hundred attendees with access to the most recent developments in basic and clinical research in this complex and increasingly important topic. Comprising lectures by 18 invited speakers, as well as lectures selected from abstracts, poster sessions and other social and networking activities such as “Meet the Speaker”, the symposium was organised in a hybrid format, allowing for in-person and/or online participation.

invited speakers:
14 onsite, 4 remote

selected speakers:
6 onsite

posters:
49 onsite, 1 virtual

attendance:
286 in-person, 16 online

countries of attendees:
Austria, Belgium, Brazil, Chile, China, France, Germany, Israel, Italy, Japan, Jordan, Netherlands, Portugal, Spain, United Kingdom, United States of America

keynote speakers:
Shahin Rafii, Weill Cornell Medicine, US
Gerard Evan, University of Cambridge, UK
Fátima Cardoso, Champalimaud Foundation, PT
Joan Massagué, Memorial Sloan Kettering Cancer Centre, US

other invited speakers:
Vera Gorbunova, University of Rochester, US
Jacky Goetz, Inserm – National Institute of Health and Medical Research, FR
Yasuuki Fujita, Kyoto University, JPN
Michelle Monje-Deisseroth, Stanford University & Howard Hughes Medical Institute, US
Bruno Silva-Santos, IMM, PT
Leila Akkari, Netherlands Cancer Institute & Oncode Institute, NL
Markus Maeurer, Champalimaud Foundation, PT
Jeffrey Pollard, University of Edinburgh, UK
Ana Luísa Correia, Champalimaud Foundation, PT
Neta Erez, Tel Aviv University, IL
Héctor Peinado Selgas, Centro Nacional de Investigaciones Oncológicas, ES
Salvador Aznar Benitah, IRB Barcelona - Institute for Research in Biomedicine, ES
Sarah-Maria Fendt, VIB-KU Leuven Centre for Cancer Biology, BE
Cédric Blanpain, Université Libre de Bruxelles, BE
Since its establishment in 2020, the Brain-Body Interactions Virtual Seminar Series has brought together a global audience from the Americas, Africa, Asia, Europe, and Oceania, often with hundreds of attendants, who discuss a diverse spectrum of work ranging from interoception to neuroimmunology.

The series emerged from the great momentum that research integrating neuroscience with other biological fields has been gaining. Created by Carlos Ribeiro (Behaviour & Metabolism Lab) and Asya Rolls (Technion, Israel), the series has quickly established itself as the main platform where top scientists in the field present their work and discuss it with an engaged audience.

While curated and coordinated by Ribeiro and Rolls, the series is run and moderated by a worldwide network of students and postdocs working in the US (Harvard), Portugal (Champalimaud Foundation), and Israel (Technion). The Brain-Body Interactions Virtual Seminar Series hosted 16 events in 2022.
As the CR community grows, its culture evolves with it. Mainly driven by volunteers and supported by administrative staff, new initiatives emerge, accompanying others that have been running for years. Through it all, regular social gatherings promote a positive atmosphere and a sense of community.
The CR Retreat '22 took place at Herdade da Granja (BoomLand), Idanha-a-Nova, from 14th-17th June. This four-day event marked the first time since the COVID-19 global pandemic that the CR community was able to gather together in a special location, far from our routines and close to nature. Combining scientific events with creative, cultural and social activities, the main goal for this comeback was to rebuild the CR’s social fabric by fostering a forum where researchers, staff and trainees could discuss the past (retrospect), present (reconnect) and future (regrow) of research.

cr retreat 2022 committee:
Ana Luísa Correia
António José Monteiro
Daniel McNamee
Eric DeWitt
Francisco Azevedo
Gonçalo Guiomar
Inês Laranjeira
Inês Soeiro
Laura Silva
Tiago Quendera
Zach Mainen

Sports & Arts
The CR community actively partakes in diverse activities, with initiatives fostered through social interactions and community involvement. Sports are central to these interactions, including team-based activities like volleyball, basketball, and football. CR members also partake in sailing, demonstrating a love for adventure and the great outdoors, along with salsa dancing, offering a blend of rhythm and physical fitness.

In the realm of arts, the Book Club serves as a critical platform, enabling intellectual conversations and thought-provoking exchanges inspired by literature in a friendly environment. Moreover, it organises museum visits related to the books read, thus adding a tangible, cultural context to the discussions. The community also looks forward to CCU Movie Nights, organised by the Social Subcommittee Core of the PhD Students Committee, bringing everyone together to enjoy cinematic narratives while fostering deeper social bonds.

Mental Health Subcommittee
The Mental Health Subcommittee of the PhD Student Committee (PSC) actively facilitates the dissemination of mental health resources at the CCU. Our team, composed of volunteer students, is in the process of establishing a seminar series on mental health in academia to raise awareness and promote best practices for mental well-being. Besides this, we continue to advocate for and facilitate access to existing mental health services for students and the wider CCU community, ensuring robust support in addressing the mental health challenges in academic life and beyond.

PSC mental health subcommittee
Team: Elena Collins, Rita Cardoso-Figueiredo, Diogo Duarte, Jaime Ariandis, Tiago Quendera & Naz Belkaya

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The Green Team @CCU is a proactive grassroots movement composed of CCU staff, focused on reducing waste, energy and water consumption to enhance environmental performance. Their mission is to pioneer the CCU’s transformation into a beacon of environmental sustainability across research, medicine, and workplace practices.

# highlights
2022 proved to be an incredibly fruitful year for the Green Team. They successfully organised two “Clean Up & Green Up” weeks in April and November, featuring workplace cleaning and Swap Shops, resulting in almost 2,000 donations and over 1,000 collections, promoting conscious consumption. The leftover items were donated to local organisations. They also held two coastal clean-ups, collecting more than 64 kg of litter.

The “Art on the Stairwells” initiative encouraged using stairs over elevators while promoting the work of artist scientists.

The team successfully lobbied for more bicycle parking spaces and established a service station.

They also made an appearance at the European Researchers’ Night, explaining the environmental impact of biomedical research, and recruited more members at the Champalimaud Research Annual Retreat.

Small but meaningful reminders were placed around the CCU to promote eco-friendly habits.

They also developed a resource database to guide CCU employees towards more sustainable daily practices.

As a community, in addition to creating moments of learning and sharing knowledge, we are always exploring ways of connecting and strengthening our internal network. In what has become an essential part of CR culture, Happy Hour returned in September 2022 after a break due to COVID-19. This much missed weekly social gathering is co-organised by the Research Groups, Support Units, Platforms and CEO team.

After the success of last year’s Magusto, the Support Units, Platforms and PhD Students organised a traditional Magusto, a cheerful event that gathers the whole CF community to celebrate Autumn at the Amphitheater, with roasted chestnuts and traditional beverages such as Jeropiga and Vinho do Porto.
One of CR’s goals is to share knowledge not only within the clinical and scientific communities, but also with the public at large.

Many CF members, at all career stages, adopt this vision by organising and participating in various outreach activities, both at and outside of the Champalimaud Foundation. CR’s science communication and outreach activities are promoted and facilitated by the Communication, Events & Outreach Team.
This national contest challenges high school students and teachers to build a bionic object and to create a story around it as a way of integrating disciplines that are typically taught separately: science, technology and literature. As in previous editions, a team from CF was responsible for the development and implementation of a scientific and technological workshop, accessible both online and in-person at the Pavilhão do Conhecimento – Ciência Viva.

Metamorfoses was born from a collaboration between the CF, Plano Nacional de Leitura 2017-2027 and Ciência Viva / ESERO Portugal.

Science Our Way, or “Ciência di Noz Manera” (CNM) in Cape Verdean Creole, is a mentoring programme aimed at students from underserved backgrounds in the Greater Lisbon area, especially ethnic minorities, migrants and girls, who are underrepresented groups in STEAM (Science, Technology, Engineering, Arts and Mathematics).

The goal of this programme is to open students’ horizons and contribute to more informed choices for their future, as well as to demystify scientists and empower the scientific community. While the programme’s pilot edition worked with one school, the second edition (2022/2023) will expand to include three schools, involving scientists from both CF and Instituto de Medicina Molecular.

In 2022, CNM received a MSCA & Citizens Grant as one of the two Researchers at Schools programmes under the umbrella of the project RAISE – Researchers in Action for Inclusion in Science and Education.

After a virtual edition in 2021, Neuronautas returned to CF’s Teaching Lab in 2022 for its third edition, this time in a hybrid format. A summer academy for students aged 15-17 interested in starting a journey to explore the future of neuroscience, the aim of Neuronautas is to democratise science using open-source software and low-cost tools, which kids can use to do experiments in the field or at home. From 29th August – 10th September, 30 students embarked on the “Long flight” option (2-week in-person version), while another 15 students took the “Short flight” option (1-week online version). With students from as far away as Porto, Spain and the Azores, this group of curious young minds came together to become new explorers of the brain.

Neuronautas received funding from the Calouste Gulbenkian Foundation in 2019 and is one of the 100 Academias Gulbenkian do Conhecimento spread across Portugal.
outreach initiatives

// ar event – evolving emotions: getting a feel for the world

Ar Events returned to the CF Auditorium after a more than two-year hiatus (during which events happened online) due to the COVID-19 pandemic. This event was held on 21st May as part of the Emotions Brain Forum series of conferences celebrating women in science, an initiative of BrainCircle Italia, a non-profit NGO founded by journalist Viviana Kazam and the famous Italian neurobiologist and Nobel laureate Rita Levi-Montalcini (1909-2012).

To explore how emotions help individuals, from insects to humans, relate to the world, and to get a feel for their surroundings, the Ar team invited five scientists: Marta Moita from CF, Suzanne Oosterwijk from the Amsterdam Interdisciplinary Centre for Emotion, Eva Jablonka from the Cohn Institute for the History and Philosophy of Science and Ideas, Valeria Gazzola from the Netherlands Institute for Neuroscience and Elizabeth Phelps from Harvard University.

In this event, the complex spectrum of emotions was also explored from an artistic perspective, provided by dancers and choreographers Sofia Dias and Vitor Roriz, singer, composer and poet Lula Pena, and Tupac Martir and Clo Bourgard, artists in residence at CF supported by the arts and science initiative Bridges to the Unknown: Crossing Art with Science.

// brain awareness week

At long last, CR researchers were finally able to celebrate Brain Awareness Week in the best way possible: doing science with kids! The activities took place over two days, one at a school in Amadora (16th March) and the other at Lisbon’s Science Centre, called “Pavilhão do Conhecimento” (17th March).

At the Pedro D’Orey da Cunha school in Amadora, the event kicked off with presentations from CR members to an audience of 80 fourth graders, who then moved from one science station to another, learning about robots, recording the activity of their own muscles, and fishing for banana DNA.

At Pavilhão do Conhecimento, 50 second and fourth graders explored the realm of the senses. After finding out how an animal without ears can hear and discovering that our brain contains a sensory map, it was time for some olfactory action! What is that smell? Where does it take you? And how does the brain associate smells with places?

// raise – researchers in action for inclusion in science & education & first european researchers’ night at cf

RAISE – a new consortium comprising the NGO Native Scientist, Instituto de Medicina Molecular João Lobo Antunes and CF – was created with the ultimate goal of reaching members of society that continue to be left out of, or who feel detached from, science. Funded by the Marie Skłodowska-Curie Actions programme, RAISE is taking a multifaceted approach that will combine Researchers at Schools activities, such as CF’s mentorship programme Ciência de Noz Manera, with European Researchers’ Night (ERN) public events.

On 30th September, CF hosted its first ERN. Around 1200 people visited six different sites and, over the course of nine hours, explored a programme consisting of 60 activities: from dance to workshops, from music to hands-on science stations, from lab visits to stand-up comedy. There was even speed dating aboard a catamaran, which linked our programme to that of the Pavilhão do Conhecimento – Centro Ciência Viva. The event also involved roundtables, podcasts, football and much more.

In addition, the partners in the RAISE consortium developed activities and programmes for schools located in areas prioritised for educational support: Ciência de Noz Manera (Science Our Way), run by CF, and Cientista Regressa à Escola (Scientist Goes Back to School), coordinated by Native Scientist. These programmes involved scientists, students and teachers, and it was great to see the results of these interactions bear fruit at RAISE’s ERN.
Science Snapshots is a series of short videos about big discoveries! This series features the most recent breakthroughs made by CR investigators as they tackle some of biology’s greatest mysteries.

In 2022, three Science Snapshots were produced: Circuits of Action and Suppression (Learning Lab); (Re)Generating Neurons (Stem Cells & Regeneration Lab) and How Neuro-Immune Interactions Burn Deep Fat (Immunophysiology Lab).

In 2022, the Communication, Events & Outreach team worked with members of our community to create original awareness campaigns for online dissemination.

# World Parkinson’s Day – A look into lesser known symptoms and treatments
11th April
As the world’s fastest growing neurological disorder, the lifetime risk of Parkinson’s disease is now 1 in 15. For World Parkinson’s Day, we discussed the possible causes of the disease, less recognised symptoms and treatments, and the work being done at CF to combat it.

# National Scientist’s Day – The birth of a scientist
16th May
How are scientists made? To commemorate National Scientist’s Day, we told the origin stories of three scientists at CF. From the undersea world of Jacques Cousteau documentaries to Cape Verdean cuisine, we looked at what memories and moments led them to pursue a life in science, and how the past shaped their present.

# World Movement Disorders Day
– Not all movement disorders are equal, but early diagnosis can help fight them all
29th November
We marked the first edition of World Movement Disorders Day. While some of these conditions, such as Parkinson’s disease, are widely talked about, other conditions are not and, even if these different movement disorders have some features in common, treatments may be very different.

The Champalimaud Centre for the Unknown is only as inventive, vibrant and resourceful as the people inside.

In 2022, we launched the second edition of the series “Zoom-In on Champalimaud”, where we explored a written format and, in each chapter, turned the spotlight on a different member of our community: John Lee (English Teacher and Content Developer), João Lourenço (Radiologist), Ana Carolina Pádua (Postdoctoral Researcher), Terufumi Fujiwara (Postdoctoral Researcher), Justyna Kociolek (Radiation Oncologist), Charlotte Rosher (PhD Student), Gonçalo Cotovio (PhD Student), Ana Saralva Ayash (Grants Manager), Liad Hollender (Science Writer), Ana Beatriz Machado (PhD Student), Ignacio Herrando (PhD Student) and Joana Fontes (Administrative Assistant).
Of this noble compendium, the final leaf we pen,
Champalimaud Research’s tale, heard from glen to glen.
So here's the end of another year, yet the journey’s far from done,
The morrow whispers with promise, a new day’s race to run.

In honour of your devoted staff, who, with dedication wrought,
In this annual report their wisdom, their insights dearly sought.
And thus, we close this chapter, 'neath the starry vault above,
United in our quest for knowledge, in our ceaseless labour of love.

Thank you. For a thorough look at our collective accomplishments of 2022, we’ll end with an annex that we like to call "The Nitty Gritty".

An excellent course thou hast chosen! Methinks it a wise plan, to offer the curious reader such a thorough annex, an abundant fount of thine endeavours and accomplishments. From publications to theses valiantly defended, from generous funds to the grandest of scientific and outreach events, the past year’s bounty lies in wait!
The list below includes external competitive funds that were awarded previously as external competitive funds that were awarded previously at the CCU during 2022.

**Bial Foundation**
- Rita Fonseca, Arturo Rodriguez, Ana Carolina Vieira, and Maria Gabriela de Almeida. "Interactions to prevent metastasis."
- Ana Luísa Correia (Veiga-Fernandes Lab). "Harnessing neuron-NK cell interactions to prevent metastasis."
- Active period: 01/06/18-31/05/23

**European Commission – Horizon 2020**
- Leveraging the utility of oscillatory dynamics in the brain to reverse disease states. (Coordinated by: firefighter of the Champalimaud Foundation – Alexandra Hospital – ENRAGE) (Call/Programme: H2020-MSCA-ITN-2019, Active period: 01/09/18-31/08/22)
- Coordination: Maria Gabriela de Almeida. "Harnessing neuron-NK cell interactions to prevent metastasis."
- Active period: 01/06/18-31/05/23

**Portugal 2020 (PT2020)**
- Getting By Without Broken Injuries: Signal's Intelligence. (Coordinated by: firefighter of the Champalimaud Foundation – Alexandra Hospital – ENRAGE) (Call/Programme: SR&TD Project Grants, Active period: 01/01/22-31/12/23)
- Coordination: Maria Gabriela de Almeida. "Harnessing neuron-NK cell interactions to prevent metastasis."
- Active period: 01/06/18-31/05/23

**European Foundation - Buck Institute**
- Active period: 01/06/18-31/05/23

**National Institutes of Health**
- Beth Stevens. "Harnessing neuron-NK cell interactions to prevent metastasis."
- Active period: 01/06/18-31/05/23

**Research projects/grants**
- Beug Foundation
  - Ana Luísa Correia (Veiga-Fernandes Lab). "Harnessing neuron-NK cell interactions to prevent metastasis."
  - Active period: 2021-2022

**European Molecular Biology Organization (EMBO)**
- Carlos Vaz-Pires. "Harnessing neuron-NK cell interactions to prevent metastasis."
  - Active period: 01/01/22-31/12/23
CISS: Champalimaud Informal Seminar Series

### JANUARY

- **03 CISS**
  - Tago Quedos | Rita Alves
  - Deciding in Observing Compulsive Disorder: The Role of Cognitive Flexibility

- **16 CISS**
  - Rajan Handas
  - Population Risk Model - towards personalized Breast Cancer Therapy

- **14 CISS**
  - Carers Workshop
  - Richard Sever
  - A Career Beyond the Bench

- **17 CISS**
  - Telhane Silva | Rodrigo Dias
  - Locomotor activity shifts in Huntington’s disease: an MEG approach for assessing cerebellar learning

- **24 CISS**
  - Ana M. Marques & Tomás Cruz
  - Optimal Multimodal Integration for Action Recognition in Human Experiments

- **31 CISS**
  - Anita Franco
  - REN BioBank (CFB) Activities

### FEBRUARY

- **04 CISS**
  - Pedro Rodrigues | Ana Carolina Rodrigues
  - Exotic knowledge: a primary condition to allowing our perception

- **07 CISS**
  - Rossana Lina | Nature nurture and sex

- **14 CISS**
  - Ad-hoc Seminar
  - Tago Marques
  - Building integrative systems-level models for reproduction and in personalized settings

- **17 CISS**
  - Ad-hoc Seminar
  - Mariana Silva
  - Meet CO4FS: Collaboration for AI Sciences: Vision and Goals

- **21 CISS**
  - Jolene Podolski
  - The dynamical regime

### MARCH

- **07 CISS**
  - Maria Bettencourt | Claudia Constantino
  - Building a Personalized Medicine of Brains: A joint-encouragement perspective on the importance of systems neuroscience

- **14 CISS**
  - Margarida Sousa & Pawel Bujalski
  - Mariana Santos
  - Optimal responses reveal an essential role of synaptic plasticity in mediating visual working memory

- **16 CISS**
  - Carriers Workshop
  - Elizabeth Rickenbacher (40 Clinical Ph.D)
  - Paths to Pharma, Clinical Trials

- **21 CISS**
  - Carlos Bérenger
  - World top Democratic supranational system with multiple regional bases

- **23 CISS**
  - Pedro Castelhaninho | Tânia Carvalho
  - Understanding the role of E-cadherin in breast cancer progression editing genes gone wild

### APRIL

- **04 CISS**
  - Romain Ligner | Joana Lérias
  - Emerging therapies for the treatment of amyotrophic lateral sclerosis

- **07 CISS**
  - Carriers Workshop
  - Mídia Macrossy (NZY Tech)
  - battle it out with cancer: the newly discovered immune loops

- **10 CISS**
  - Jonathan Cook
  - Neural sub-circuits mediating sexual arousal and ejaculation

- **23 CISS**
  - Postdoc Exchange Seminar
  - Tiago Cruz | Ugo Leite
  - Developmental Structural Biology: Pathways to motor adaptation in the extrinsic visual system

- **28 CISS**
  - Ad-hoc Seminar
  - João Howard
  - Dopaminergic systems in friedreich’s ataxia: a clinical perspective

### MAY

- **02 CISS**
  - Guei Dinh | Ruth Diez del Corral
  - Introducing Drosophila centrum: A model for neuronal development and regeneration

- **05 CISS**
  - Postdoc Exchange Seminar
  - Isaia da Costa | Antonio Antunes Martins
  - Maintenance of synaptic stability improves recovery after stroke or spinal cord injury

### JUNE

- **04 CISS**
  - Antonio Alves | Cristina Dodeka-Silva
  - Hypothalamic circuits for female reproduction: neuro-immune regulation in health and disease

- **05 CISS**
  - Carriers Workshop
  - Elizabeth Rickenbacher (40 Clinical Ph.D)
  - Hippocampal REMapping and Recruitment

### JULY

- **04 CISS**
  - Antonio Alves | Cristina Dodeka-Silva
  - Hypothalamic circuits for female reproduction: neuro-immune regulation in health and disease

- **07 CISS**
  - Postdoc Exchange Seminar
  - Sandara On (40 Clinical Ph.D)
  - Adenosine A1 receptor adenosine is present on POPV effects upon replication

### AUGUST

- **29-31 CISS**
  - Workshop
  - Immersion: Technical Neuroimaging In Depth

### SEPTEMBER

- **01-02 CISS**
  - Workshop
  - Hands-on Molecular Tools

### OCTOBER

- **02 CISS**
  - Postdoc Exchange Seminar
  - Jessica Thompson (OUC)
  - Finding Salmonella’s Sweet Spot: Optogenetics meets microbial ecology

### NOVEMBER

- **05 CISS**
  - Raquel Mendes | Henrique Veiga-Fernandes
  - Brosome: New insights into the regulation of pulmonary health

### DECEMBER

- **05 CISS**
  - Raquel Mendes | Henrique Veiga-Fernandes
  - Brosome: New insights into the regulation of pulmonary health

- **14 CISS**
  - Ad-hoc Seminar
  - Guilherme Martin
  - Taking Exotic Vehicles: Ovarian Cancer Tumor Regrowth

### DECEMBER

- **02 CISS**
  - Postdoc Exchange Seminar
  - Jessica Thompson (OUC)
  - Finding Salmonella’s Sweet Spot: Optogenetics meets microbial ecology

### DECEMBER

- **04 CISS**
  - Antonio Alves | Cristina Dodeka-Silva
  - Hypothalamic circuits for female reproduction: neuro-immune regulation in health and disease

### DECEMBER

- **07 CISS**
  - Postdoc Exchange Seminar
  - Sandara On (40 Clinical Ph.D)
  - Adenosine A1 receptor adenosine is present on POPV effects upon replication

### DECEMBER

- **10 CISS**
  - Luis Martins | Merit Kruse
  - Multi-omics Metagenomics

### DECEMBER

- **16 CISS**
  - Bruno Masini | Eric de Sousa
  - A Theory on Recurrent Networks

### DECEMBER

- **19 CISS**
  - Ad-hoc Seminar
  - Guillaume Martin
  - Taking Exotic Vehicles: Ovarian Cancer Tumor Regrowth

### DECEMBER

- **23 CISS**
  - Champalimaud Open Seminar (COPS)
  - Rita Hor | Megan Casey

### DECEMBER

- **29-31 CISS**
  - Workshop
  - Immersion: Technical Neuroimaging In Depth
The concept and design for the 2022 CR Annual Report drew from two themes of the year: the ascendance of AI, particularly in image and text generation, and community reconnection. Like the intricate layers and parameters that define deep neural networks, Champalimaud Research is built on a multitude of interests, aspirations, and connections.

In this Report, we fused a digital, machine-oriented aesthetic with an organic, human-centric touch, underscoring the symbiotic relationship between human and machine. The chosen fonts signify the synergy between humans and technology, while the lines and shapes encapsulate the evolution of ideas, projects, and people.

The AI surge has paved the way for unprecedented opportunities, even if the human ability to create unfamiliar combinations of familiar ideas may be in the process of being hacked. As we navigate this novel landscape, the role of visual and language proficiency, alongside interpersonal communication and health and scientific literacy, remains as important as ever, fueling innovation at Champalimaud Research and beyond.

Carla Emilie Pereira, Hedi Young & Catarina Ramos