ANNUAL REPORT 2024

AIBILI

AIBILI

association for
innovation and biomedical
research on light and image

ANNUAL REPORT 2024

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Message from the President

In 2024, AIBILI celebrated 35 years of excellence - a milestone that highlights the institution's sustained growth and impact. Over the years, AIBILI has evolved to tackle emerging scientific challenges and adapt to market demands, while establishing new partnerships, launching impactful projects, and gaining recognition, fueling the growing demand for new services. Founded on Professor Cunha-Vaz's dream to establish a reference ophthalmology research institution in Portugal, AIBILI's success is driven by a dedicated team and a strong organizational structure of Research Centres and Organizational Units working towards a common goal.

At the international level, AIBILI has a leading role in the coordination of the EVICR.net, a European network of 89 ophthalmology clinical research centres across 16 countries, with over 800 investigators. This network strengthens the EU's capacity for high-quality multinational ophthalmology clinical research. AIBILI's central role is further supported by the Coimbra Coordinating Centre for Clinical Research (4C) that also coordinates investigator initiated and industry sponsored clinical studies.

The Clinical Trials Centre (CEC) is actively engaged as a clinical site in several trials and studies, not only in Ophthalmology, given the recognized capacity for high-quality clinical research. The Coimbra Ophthalmology Reading Center (CORC) continues to be sought-after as a partner for large-scale multicentre trials, consistently known for its excellence and expertise. The Centre for New Technologies in Medicine (CNTM) continues to focus on developing innovative methods, including AI applications for early detection of retinal and cardiovascular disease, contributing to the advance of personalized medicine. The Data Centre (DC) plays a critical role on improving AIBILI's information security, cybersecurity, and privacy protection, ensures the safety and integrity of data collected for clinical research in compliance with both national and international regulations.

Additionally, Organizational Units are key to AIBILI's work, including the Quality Management Unit (QMU) for continuous improvement and quality assurance, the Translational Research and Technology Transfer Unit (UTT) that supports research and fosters collaboration, and the Information Technology Unit (IT), which manages IT networks and information systems.

At the national level, AIBILI maintains the recognition as a Technology and Innovation Center (CTI) by the Portuguese Ministry of Economy, emphasizing AIBILI's significant role in advancing innovation and promoting health in Portugal through translational research and knowledge transfer.

AIBILI implemented an integrated Strategic Scientific Research Plan 2020 – 2025 with five main research areas: Diabetic Retinopathy, Age-Related Macular Degeneration, Imaging Biomarkers, Drug Evaluation and Translational Vision. These core research areas remain our focus as we strive to transform knowledge into innovative solutions that enhance healthcare and human well-being.

Conceição Lobo
President


AIBILI
associação para
investigação biomédica e
inovação em luz e imagem

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Introduction

AIBILI, founded in 1989, is a non-profit Research Technology Organisation dedicated to clinical research and the development of new products for medical therapy and diagnostic imaging. It has been recognized by the Ministry of Economy as a Technology and Innovation Center in the health field, to support technology transfer and translational research.

AIBILI is located in the Coimbra University Health Campus since 1994 and has its own building with 1.454 m^2 and state-of-the-art equipment.

AIBILI main areas of activity are:

- Performance of Clinical Studies
- Planning, Coordination, Monitoring of Clinical Research Studies
- Pharmacovigilance, Pharmacoepidemiology and Pharmacoeconomics
- Grading of Eye Exams
- Research and Development in New Technologies for Medicine in the areas of Imaging, Optics and Photobiology
- Data Centre

AIBILI is ISO 9001:2015 certified for all its activities. Clinical research is performed in accordance with ICH-GCP Good Clinical Practice Guidelines and national and European regulatory requirements, as well as personal data protection legislation. AIBILI Data Centre is certified by ECRIN – European Clinical Research Infrastructures Network since 2016.

Regarding human resources it has a permanent staff of 60 people including medical doctors, researchers, engineers, pharmacologists, technicians, project managers, statisticians, data managers, quality managers, study coordinators and administrative personnel. Another 54 professionals collaborate regularly in research activities.

In order to promote science and technology advancement and to bring potential new treatments and diagnostic tools to the market, AIBILI has assumed an integrated Strategic Scientific Research Plan 2020-2025 with five main Research Programs: Diabetic Retinopathy; Age-Related Macular Degeneration; Imaging Biomarkers; Drug Evaluation; and Translational Vision. The outcome of this Strategic Scientific Research Plan will be a key element to enable AIBILI to maintain its excellence in health innovation. We aim to increase the number and quality of research projects, as well as their funding; to promote AIBILI as an added-value to clinical development and innovation; to promote technology transfer and translational research, and to stimulate novel national and international collaborations, focusing on the improvement of health research and life quality.

AIBILI closely follows current technological developments, particularly information technologies, artificial intelligence, and open science, opening new doors for AI research collaborations. These efforts aim to promote more inclusive and effective partnerships, while reinforcing its dedication to scientific progress and knowledge sharing.

AIBILI is dedicated to advancing translational research and innovation, with a clear focus on improving human health and enhancing overall wellbeing.

2024 Highlights

- AIBILI participated in the **ECRIN Training Program - Everything you need to know about submitting a European Multinational Clinical Study Proposal**, in Lisbon on 12/01/2024. Cecília Martinho was a guest speaker and presented the role of AIBILI's Lead Clinical Trial Unit in the MACUSTAR project;

- AIBILI participated in the presentation of the results of the **More Economy and Health Working Group**, on 05/02/2024 at the Ministry of Economy. AIBILI contributed to the different working groups to promote value creation in the health sector;

- AIBILI members took part in the **Ophthalmology Colloquia in Lisbon**, organized by the Centre for the Study of Vision Sciences of the Association for Research and Development of the Faculty of Medicine of the University of Lisbon (FMUL), on 9-10/02/2024. The **EUPO Course on Retinal Imaging** was moderated by Conceição Lobo and with presentations by Inês Marques and Luis Mendes;

- **Visit to AIBILI of the Minister for the Economy and the Sea**, António Costa Silva, on 28/02/2024. AIBILI's management had the opportunity to present the capabilities and capacities as a CTI - Technology and Innovation Center and to reinforce the importance that AIBILI plays in the national clinical research ecosystem;

- AIBILI Data Centre developed **two registries for the Portuguese Society of Ophthalmology (SPO)** on Keratoconus and Endophthalmitis, which are now available to ophthalmologists and will be used to carry out clinical studies;

- AIBILI participated in the kick-off meeting of the **EATRIS-CONNECT project**, in Utrecht, Netherlands, on 14/05/2024;

- The **Helen Keller Prize for Vision Research 2024** was awarded to Prof. José Cunha-Vaz on 07/05/2024 in Seattle, during the ARVO 2024 Congress. The prize was awarded in recognition of the excellence in research demonstrated by a significant number of contributions to vision science throughout his career;

- The **CIDMA Young Doctorate Award** was presented to Dr. Daniel Figueiredo. This biennial prize, awarded by CIDMA - Center for Research and Development in Mathematics and Applications at the University of Aveiro's Mathematics Department, recognizes young doctors with promising careers and high scientific merit in the field of mathematics.

- The organization of the **AIBILI Open Day** on 05/06/2024, featuring a program that included a presentation by Alexandra Vilela from ANI on the importance of CTIs - Technology and Innovation Centers, presentations from AIBILI Units, and a roundtable discussion on Clinical Research in Portugal, moderated by Cecília Martinho.

- AIBILI's Clinical Trial Centre Sub-director, Patrícia Barreto was invited by the **Portuguese Pharmaceutical Board** to join the **Interest Group on Clinical Trials**;

- The **Nascimento Leitão Prize** for the best presentation at the "6th Statistics on Health Decision Making: Artificial Intelligence" conference was awarded to work titled "Analysis of the progression of Age-related Macular Degeneration using the novel Variable Influence Analysis model", developed through a collaboration between AIBILI and the University of Aveiro;

- The organization of the **AIBILI Research Groups annual meeting**, which took place on 10/07/2024, provided a privileged forum for in-depth discussion and the exchange of ideas in the field of ophthalmology;

- **AIBILI celebrated 35 years** dedicated to the development and clinical research of new products for medical therapy and diagnostic image. This milestone was celebrated with company-wide team-building activities, emphasizing AIBILI's dedication to teamwork and acknowledgment of team contributions.

- AIBILI participated in Ophthalmology **national annual meetings**, including the Portuguese Society of Ophthalmology (SPO), the Portuguese Group of Retina and Vitreous, and the National Congress of Orthoptists;

- AIBILI strengthened scientific collaboration with Heidelberg through a visit by a Heidelberg Engineering representative on 16/10/2024;

- The webinar on **Data Management for Clinical Research** on 12/11/2024 was organized by AIBILI Data Centre with the support of AICIB, highlighting the critical role of data centers in clinical research and data management.
- The **SPO Plácido Prize** was awarded to Dr. Inês Figueiredo for her work "Influence of risk factors and individualized risk scores for age-related macular degeneration through a variable influence analysis model". This work was developed in collaboration between AIBILI and the University of Aveiro;
- AIBILI showcased **key interviews and opinion pieces** emphasizing significant achievements in vision research, clinical trials, and clinical research in Portugal were featured across various media outlets (RTP Program - Portugal em Direto, Exame Informática TV, Público, Lusa, Observador, Campeão das Províncias, Diário de Notícias);
- During 2024, AIBILI members participated actively through presentations and posters in the following **international congresses**: SIR 2024 - Italian Retina Society, February 15 - 17, 2024, Venice, Italy; San Raffaele OCT & Retina Forum, March 21 - 22, 2024, Milan, Italy; Imaging in the Eye Conference 2024, May 4, 2024, Seattle, Washington; ARVO 2024 Annual Meeting, May 5 - 9, 2024, Seattle, Washington; PARD 2024 - Pan American Research Day, June 1, 2024, Online; 34th EAsDEC Meeting, May 30 - June 1, 2024, Milan, Italy; E3 Consortium Meeting, August 27-29, 2024, Cambridge, UK; The Retina Society, September 11-15, 2024, Lisbon, Portugal; EURETINA 2024, September 19-22, 2024, Barcelona, Spain; ISoP Annual Meeting 2024, October 1-5, 2024, Montreal, Canada; FLORetina Meeting, December 6-8, 2024, Florence, Italy.

Technology and Innovation Center (CTI)

AIBILI is a Technology and Innovation Center (CTI) in the Health Sector of the National Technology Network of the Economy Ministry. This recognition identifies AIBILI as a key partner facilitating collaboration between scientific institutions, businesses, and industry to deliver innovative solutions to the healthcare market.

CTI CENTROS DE TECNOLOGIA E INOVAÇÃO

To promote research of excellence and scientific innovation, AIBILI has established the following priorities:

- To maintain a position of excellence in clinical and translational research, allowing the creation of new knowledge in collaboration with other reference institutions and participation in international consortia;
- To promote the integration of the different research programs through the application of different concepts under study and which make up the scientific strategy;
- To develop new imaging biomarkers in ophthalmology that support the diagnosis and identification of disease stages and facilitate the analysis for risk of development and progression of disease;
- To diversify the research carried out into the areas of diabetes, cardiology and neurology, benefiting from the link with primary health care units, and taking advantage of the skills and knowledge existing in the institution and their possible use in the study of the retina-brain relationship;
- To increase AIBILI's technological intensity by hiring qualified human resources, reinforcing and updating the knowledge/continuous training of its employees and acquiring state-of-the-art equipment.

With these priorities, participation in international reference networks, following the Strategic Scientific Research Plan and the quality management system, AIBILI is positioned to achieve excellence in research and innovation contributing to improvements in clinical practice and bringing benefits to society

PRR Plano de Recuperação e Resiliência
REPÚBLICA PORTUGUESA
Financiado pela União Europeia NextGenerationEU
MI MISSÃO INTERFACE
ANI AGÊNCIA NACIONAL DE INOVAÇÃO

Associates

Founding Associates

- FLAD – Fundação Luso-Americana para o Desenvolvimento (Honorary Associate)
- IAPMEI – Instituto de Apoio às Pequenas e Médias Empresas e à Inovação
- José Cotta – EMS, S.A.
- José Cunha-Vaz
- Laboratório EDOL – Produtos Farmacêuticos, S.A.
- Biofísica da Faculdade de Medicina da Universidade de Coimbra
- Farmacologia da Faculdade de Medicina da Universidade de Coimbra
- Serviço de Dermatologia do Centro Hospitalar e Universitário de Coimbra
- SUCH – Serviço de Utilização Comum dos Hospitais

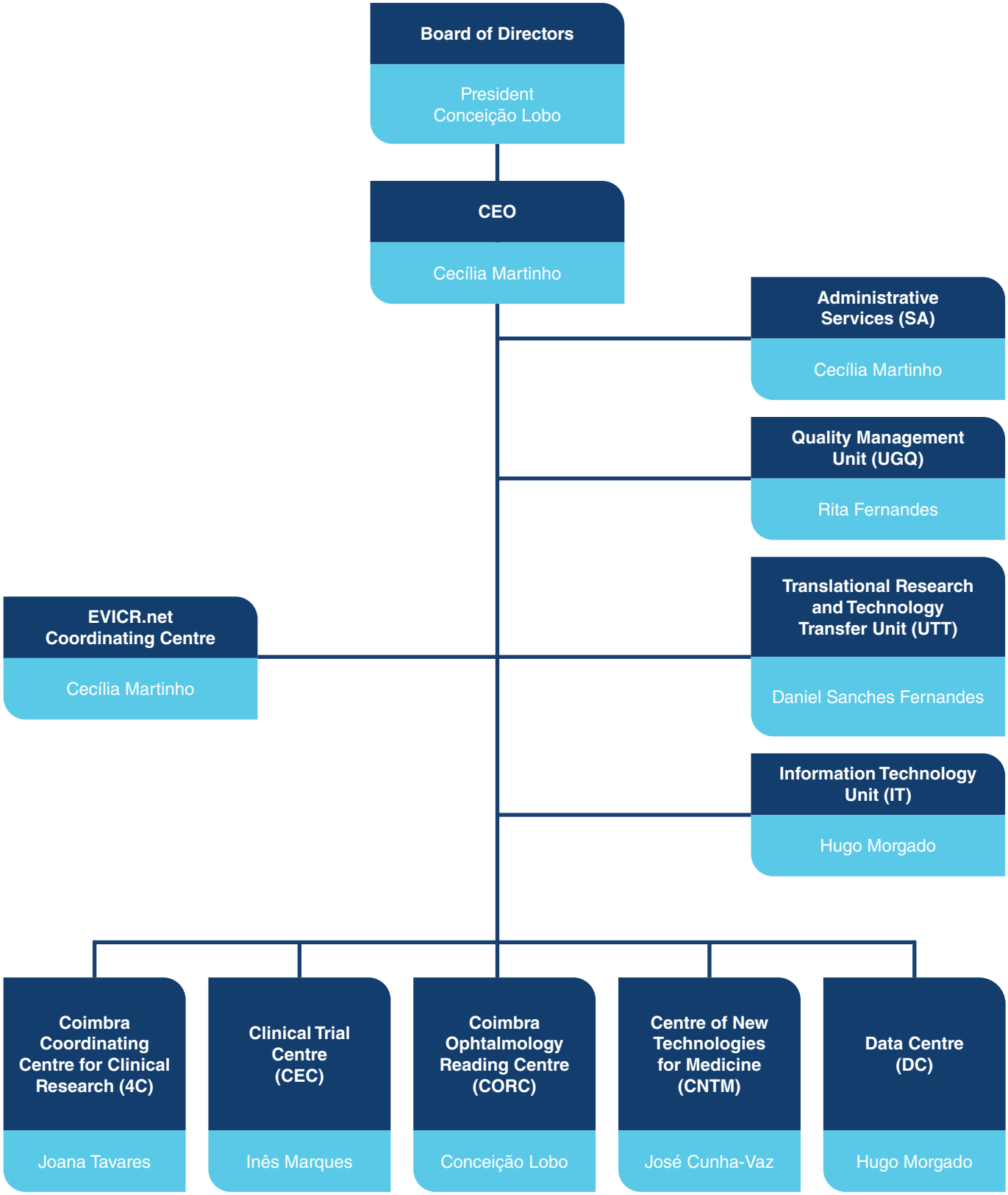
Other Associates

- Universidade de Coimbra (Honorary Associate)
- Fundação Champalimaud (Honorary Associate)
- Alcon Portugal - Prod. e Equip. Oftalmológicos, Lda.
- BIAL - Portela & Cª., SA
- Cecília Martinho
- Centro de Oftalmologia da Universidade de Coimbra
- Conceição Lobo
- Escola Superior de Saúde do Politécnico do Porto
- Francisco Batel Marques
- Hospital CUF Coimbra / José de Mello Saúde
- Laboratórios Pfizer, Lda.
- Novartis Farma, SA

Board of Directors (2023-2026)

- Conceição Lobo, President
- António Parreira (Rep. Fundação Champalimaud), Vice-President
- Nuno Pires (Rep. BIAL - Portela & Cª, SA)
- Gonçalo Pimpão (Rep. Laboratórios EDOL - Produtos Farmacêuticos, S.A.)
- Margarida Gonçalo (Rep. Serviço de Dermatologia do Centro Hospitalar e Universitário de Coimbra)
- António Cotta (Rep. José Cotta - EMS, Lda)
- Cecília Martinho, CEO
- José Cunha-Vaz, Honorary President

Organigram


Board of Directors
President
Conceição Lobo
CEO
Cecília Martinho
Administrative Services (SA)
Cecília Martinho
Quality Management Unit (UGQ)
Rita Fernandes
Translational Research and Technology Transfer Unit (UTT)
Daniel Sanches Fernandes
Information Technology Unit (IT)
Hugo Morgado
EVICR.net Coordinating Centre
Cecília Martinho
Coimbra Coordinating Centre for Clinical Research (4C)
Joana Tavares
Clinical Trial Centre (CEC)
Inês Marques
Coimbra Ophtalmology Reading Centre (CORC)
Conceição Lobo
Centre of New Technologies for Medicine (CNTM)
José Cunha-Vaz
Data Centre (DC)
Hugo Morgado

AIBILI in Numbers

1989

AIBILI Foundation

1991

Public Utility
Recognition

2010

European C-TRACER Member

2009

Expansion of AIBILI 4C
Retmarker ® – Official market launch

2016

Data Centre Certification

2017

Establishment of DruSER.net

Recognition as an Interface Center
by Ministry of Economy

Fulltime Staff	60
N° of PhD	20
N° of Consultants	54
N° of Ongoing studies, services, projects, contracts	135

N° Patents	2 (USA) + 1 (Europe)
N° of European Union funded projects (ongoing)	4
N° of Publications (2023-2024)	39
N° of Internships	6

1994

1ST Building in the Coimbra University Health Campus

1999

Good Laboratory Pratices Certification

2004

ISO 9001 Certification

EVICR.net Coordinating Centre

2008

Expansion of AIBILI CORC and CHAD

2021

Data Centre Recertification

2022

Recognition as a Technology and Innovation Center by Ministry of Economy

2023

Recognition of 4C as an EATRIS Expert Centre

2024

Celebration of 35 years

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Research Centres and Organisational Units

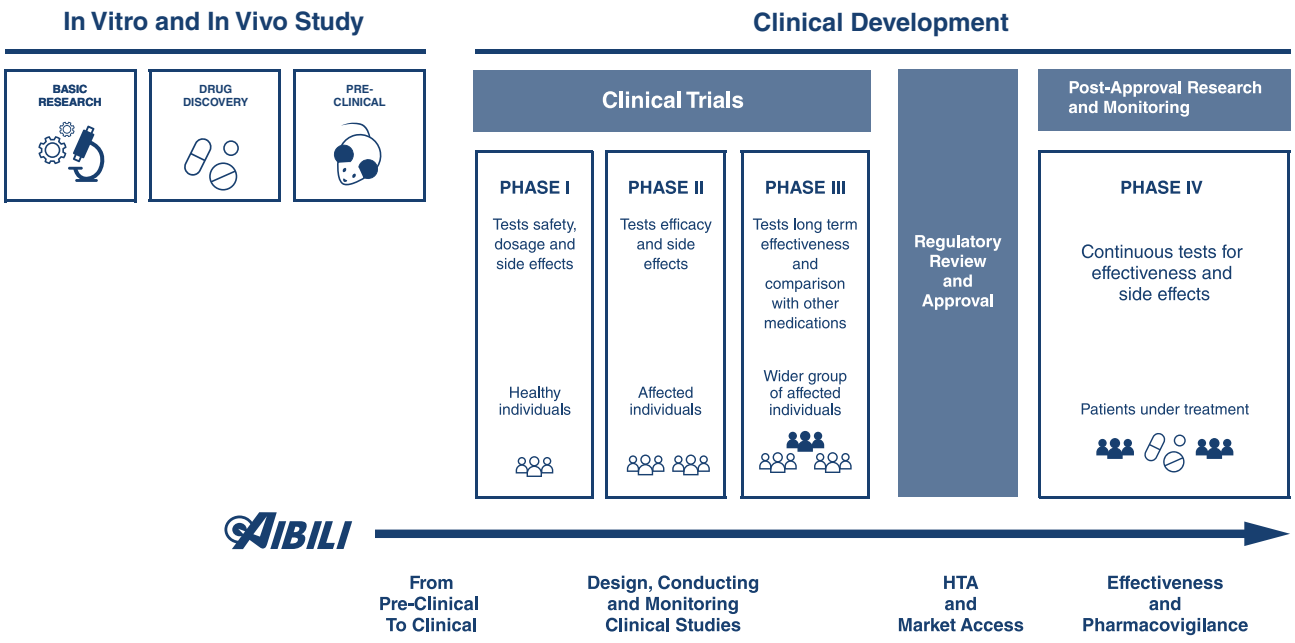
AIBILI is organised in Research Centres and Organisational Units.

Research Centres

- Coimbra Coordinating Centre for Clinical Research (4C)
- Clinical Trial Centre (CEC)
- Coimbra Ophthalmology Reading Centre (CORC)
- Centre for New Technologies in Medicine (CNTM)
- Data Centre (DC)

Organisational Units

- Administrative Services (SA)
- Quality Management Unit (QMU)
- Translational Research and Technology Transfer Unit (UTT)
- Information Technology Unit (IT)



4C – Coimbra Coordinating Centre for Clinical Research

Director: Joana Tavares, PhD

Staff: Ana Silva, Cândida Dias, Cecília Martinho, Conceição Lobo, Daniela Cravo, Daniel Fernandes, Daniel Figueiredo, Débora Ferreira, Fábio Mesquita, Inês Aires, Inês Tavares, Joana Abrantes, José Cunha-Vaz, Laura Seco, Liliana Carvalho, Lisete Lemos, Mário Ribeiro, Pier Basile, Rita Coimbra, Rita Fernandes, Rita Ribeiro

The Coimbra Coordinating Centre for Clinical Research (4C) is a structure to support the development and coordination of Investigator-Initiated and Industry-Sponsored Clinical Studies, by providing the following services:

Contacts
Joana Tavares, PhD
Phone: +351 239 480 137
E-mail: jftavares@aibili.pt

PRE-STUDY

- Study Design
- Statistical Plan
- Protocol and Informed Consent development
- Clinical Centre selection
- Master File and Site File development
- SOPs development
- Regulatory Affairs
- Contracts and Insurance
- Monitoring Plan

IN-STUDY

- Study Coordination
- Investigational Medicinal Product/Medical Device Management
- Monitoring
- Pharmacovigilance and Risk Management

POST-STUDY

- Biostatistics
- Final Report
- Medical Writing
- Publication

4C uses the Clinical Management System (CMS) developed in house, for planning, management and monitoring of clinical studies. 4C has all the capacities to plan and implement/manage/coordinate multinational clinical studies, as well as medical devices clinical investigations.

4C is compliant with ICH GCP - Good Clinical Practice Guidelines and European regulations, namely Clinical Trials Regulation (Regulation (EU) No 536/2014), Medical Devices Regulation (Regulation (EU) No 2017/745) and ISO 14155 as well as national legislation.

4C is a useful resource to work closely with Pharmaceutical Industry and medical device sector, through all stages of drug development and medical device clinical investigations. It performs pharmacovigilance services necessary in clinical studies. It has a pharmacovigilance system fully compliant with the regulations, directives, and the general guidance related to electronic reporting of adverse events (US FDA 21 CFR part 11 and EMA's Good Pharmacovigilance Practice (GVP) Guidelines) for this purpose, as well as SOPs ICH compliant to perform pharmacovigilance clinical research. It has a license to use MedDRA, a standardised international medical terminology designed for use in safety monitoring of medicinal products through all phases of the development cycle (i.e., from clinical trials to post-marketing surveillance) that supports ICH electronic communication within the E2B Individual Case Safety Report.

Since 2008 AIBILI has been responsible for a Pharmacovigilance Unit (Unidade de Farmacovigilância de Coimbra, UFC) of the National Pharmacovigilance System which is contracted with the National Authority of Medicines and Health Products (INFARMED, IP).

N° OF CLINICAL STUDIES / PROJECTS AT 4C (2022-2024)

	Coordination of Clinical Studies (N°)					
Year	Investigator Initiated	Industry Sponsored	Drug Safety	Market Access	Other	Total
2022	18	2	8	8	4	40
2023	16	3	10	2	7	38
2024	**15**	**2**	**10**	**0**	**6**	**33**

REPRESENTATIVE PUBLICATIONS

Marques IP, Reste-Ferreira D, Santos T, Mendes L, Martinho AC, Yamaguchi TCN, Santos AR, Pearce L, Cunha-Vaz J. **Progression of capillary hypoperfusion in advanced stages of nonproliferative diabetic retinopathy: 6-month analysis of RICHARD study**. *Ophthalmol Sci.* 2024; 5(2):100632. doi:10.1016/j.xops.2024.100632

Barreto P, Farinha C, Coimbra R, Cachulo ML, Melo JB, Lechanteur Y, Hoyng CB, Cunha-Vaz J, Silva R. **Unveiling Statins and Genetics in Age-Related Macular Degeneration: The Coimbra Eye Study—Report 9**. *Invest Ophthalmol Vis Sci.* 2024;65(6):38. doi:10.1167/iovs.65.6.38

Rowen D, Carlton J, Terheyden JH, Finger RP, Wickramasekera N, Brazier J; MACUSTAR Consortium. **Development and Valuation of a Preference-Weighted Measure in Age-Related Macular Degeneration from the Vision Impairment in Low Luminance Questionnaire: A MACUSTAR Report**. *Value Health.* 2024; 27(5): 642-654. doi:10.1016/j.jval.2024.02.001

Marques IP, Ribeiro ML, Santos T, Reste-Ferreira D, Mendes L, Martinho AC, Santos AR, Figueira J, Lobo C, Cunha-Vaz J. **Patterns of Progression of Nonproliferative Diabetic Retinopathy Using Non-Invasive Imaging**. *Transl Vis Sci Technol.* 2024;13(5):22. doi:10.1167/tvst.13.5.22

Farinha C, Barreto P, Coimbra R, Machado MB, Figueiredo I, Cachulo ML, Cunha-Vaz J, Silva R. **Age-Related Macular Degeneration and Extramacular Drusen: Genetic Associations in the Coimbra Eye Study**. *Invest Ophthalmol Vis Sci.* 2024;65(35).doi:10.1167/iovs.65.5.35

CEC - Clinical Trial Centre

Director: Inês Marques, MD, PhD

Sub-Director: Patrícia Barreto, PharmD, MSc

Staff: Aida Vitorino, Ana Almeida, Ana Rocha, Catarina Eloy, Céu Simões, Cláudia Farinha, Conceição Lobo, Cristina Fonseca, Cristina Januário, Filipa Ponces, Filipe Martins, Filipe Mira, Guilherme Castela, Inês Pinto, Isabel Pires, João Figueira, João Pedro Marques, José Cunha-Vaz, Luísa Ribeiro, Marcela Pascoal, Maria da Luz Cachulo, Marta Lopes, Paulo Marques, Rufino Silva, Sandra Pardal, Tânia Mesquita

Contacts
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E-mail: ipmarques@aibili.pt

The Clinical Trials Centre (CEC) performs clinical trials and studies with special emphasis on ophthalmology, mainly diabetic retinopathy and age-related macular degeneration, focusing on patient's wellbeing. CEC also performs clinical studies in other medical areas such as neurology and diabetes.

Patient-oriented research involves characterizing disease progression and testing new discoveries by carrying out controlled research studies in patients, i. e., clinical trials. It also includes testing not only new drugs, but also new methods, devices, imaging and surgical procedures together with as well-designed prospective, non-interventional, longitudinal studies.

CEC has proven expertise with relevant scientific publications in these areas and is a certified Clinical Site of Excellence by the EVICR.net – European Vision Institute Clinical Research Network since 2006.
CEC has experienced, qualified staff and dedicated facilities to perform clinical research according to ICH-GCP Guidelines and Data Protection Regulation. In its daily routine, CEC uses an Electronic Medical Record (mediSIGHT) integrated with the equipment's imaging (OphthalSuite) allowing quicky access to structured data for clinical research.

Clinical Research: Diabetic Retinopathy; Age-Related Macular Degeneration; Glaucoma; Neurology; Diabetes

N° OF CLINICAL STUDIES AT CEC (2022-2024)

	Clinical Studies (N°)		
Year	**Investigator Initiated**	**Industry Sponsored**	**Total**
2022	11	8	18
2023	12	10	22
2024	**10**	**9**	**19**

INVESTIGATOR-INITIATED STUDIES

Diabetic Retinopathy

RECOGNISED - Retinal and Cognitive Dysfunction in Type 2 Diabetes: Unraveling the Common Pathways and Identification of Patients at Risk of Dementia
ClinicalTrials.gov ID: NCT04281186
Financial Support: European Union - H2020-SC1-BHC-01-2019-847749

PROGRESS 10 - Progression of Diabetic Retinopathy. Identification of Signs and Surrogate outcomes -10-year follow-up
ClinicalTrials.gov ID: NCT04650165
Financial Support: AIBILI

CHART - Characterization of Retinal disease progression in eyes with NPDR in diabetes Type 2 using non-invasive procedures
ClinicalTrials.gov ID: NCT04636307
Financial Support: IIR Grant from Bayer

RICHARD – Retinal Ischemia characterization in diabetes
ClinicalTrials.gov ID: NCT05112445
Financial Support: IIR Grant from Boehringer Ingelheim

PREDICTION – Prediction of Retinal Ischemia in Diabetes
ClinicalTrials.gov ID: NCT05581225
Financial Support: AIBILI

CLARUS DR - Diabetic Retinopathy Classification: ETDRS 7-fields vs Widefield Imaging
ClinicalTrials.gov ID: NCT05746975
Financial Support: IIR Grant from Zeiss

Age-related macular degeneration

MACUSTAR - Intermediate AMD: Development of novel clinical endpoints for clinical trials in patients with a regulatory and patient access intention
ClinicalTrials.gov ID: NCT03349801
Financial Support: European Union and EFPIA - Innovative Medicines Initiative 2 Joint Undertaking - Grant Agreement nº 116076

AMD_LifeGene - Diet, medication, and lifestyle in Age-related Macular Degeneration: can the genetic expression be modulated?
ClinicalTrials.gov ID: NCT05735730
Financial Support: EURETINA Clinical Research Award

Retinal Degenerative Diseases

STAR - Development of a Model for Advanced Screening for Timely Treatment of Age-Related Eye Diseases
Financial Support: AIBILI

EYEMARKER - Characterization of potential biomarkers of Eye Disease and Vision Loss
ClinicalTrials.gov ID: NCT02500862
Financial Support: AIBILI

INDUSTRY-SPONSORED CLINICAL TRIALS

Diabetic Macular Edema

Rhone-X - A Multicenter, Open-Label Extension Study To Evaluate The Long-Term Safety And Tolerability Of Faricimab In Patients With Diabetic Macular Edema
EudraCT Number: 2020-000402-29

NEON - A Phase 2 Randomized, Placebo-controlled, Double-masked Proof-of-concept Study to Investigate the Efficacy and Safety of Runcaciguat (BAY 1101042) in Patients with Moderately Severe to Severe Non-proliferative Diabetic Retinopathy
EudraCT Number: 2020-002333-15

BRUNELLO - A Randomized, Double-Masked, Multi-Center, 3-Arm Pivotal Phase 2/3 Study To Evaluate The Efficacy And Safety Of Intravitreal Eye103 Compared with Intravitreal Ranibizumab (0.5mg) In Participants With Diabetic Macular Edema
EudraCT Number: 2024-510944-30-00

Uveitic Macular Edema

MEERKAT - A phase III, multicenter, randomized, double masked, sham controlled study to investigate the efficacy, safety, pharmacokinetics, and pharmacodynamics of RO7200220 administered intravitreally in patients with uveitic macular edema
EudraCT Number: 2022-501793-19-00

SANDCAT - A phase III, multicenter, randomized, double-masked, sham-controlled study to investigate the efficacy, safety, pharmacokinetics, and pharmacodynamics of RO7200220 administered intravitreally in patients with uveitic macular edema
EudraCT Number: 2022-501794-39-00

Thyroid Eye Disease

SatraGO-2 - A Phase III, Randomized, Double-Masked, Placebo-Controlled, Multicenter Study To Evaluate The Efficacy, Safety, Pharmacokinetics, And Pharmacodynamics Of Satralizumab In Participants With Moderate-To-Severe Thyroid Eye Disease
EudraCT Number: 2023-503669-50-00

Macular Edema Secondary to Retinal Vein Occlusion

QUASAR - Randomized, Double-Masked, Active-Controlled, Phase 3 Study of the Efficacy and Safety of Aflibercept 8 mg in Macular Edema Secondary to Retinal Vein Occlusion
EudraCT Number: 2022-502174-16-00

Neurological Disorders

OPTIMUM-LT - Multicenter, non-comparative extension to study AC-058B301, to investigate the long-term safety, tolerability, and control of disease of ponesimod 20 mg in subjects with relapsing multiple sclerosis
EudraCT Number: 2016-004719-10

PALOMA - A Multicenter Longitudinal Study to Evaluate the Correlation between Oculometric Measures and Clinical Assessment in Patients with Idiopathic Parkinson's Disease
ClinicalTrials.gov ID: NCT05862649

REPRESENTATIVE PUBLICATIONS

Barreto P, Farinha C, Coimbra R, Cachulo ML, Melo JB, Lechanteur Y, Hoyng CB, Cunha-Vaz J, Silva R. **Unveiling Statins and Genetics in Age-Related Macular Degeneration: The Coimbra Eye Study-Report 9.** *Invest Ophthalmol Vis Sci.* 2024;65(6), 38. doi:10.1167/iovs.65.6.38

Farinha C, Barreto P, Coimbra R, Machado MB, Figueiredo I, Cachulo ML, Cunha-Vaz J, Silva R. **Age-Related Macular Degeneration and Extramacular Drusen: Genetic Associations in the Coimbra Eye Study.** *Invest Ophthalmol Vis Sci.* 2024;65(5):35. doi.org/10.1167/iovs.65.5.35

Marques IP, Ribeiro ML, Santos T, Reste-Ferreira D, Mendes L, Martinho AC, Santos AR, Figueira J, Lobo C, Cunha-Vaz J. **Patterns of Progression of Nonproliferative Diabetic Retinopathy Using Non-Invasive Imaging.** *Transl Vis Sci Technol.* 2024;13(5):22. doi:10.1167/tvst.13.5.22

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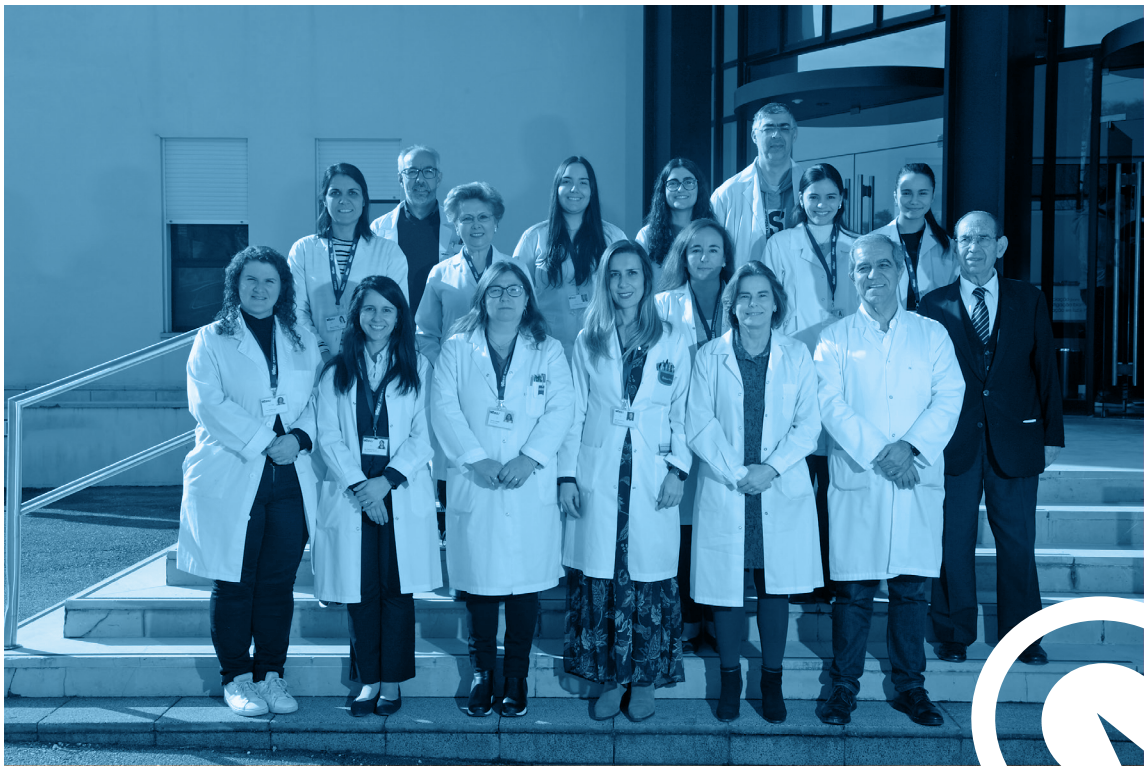

CORC – Coimbra Ophthalmology Reading Centre

Director: Conceição Lobo, MD, PhD

Staff: Alda Baltar, Ana Catarina Almeida, Ana Cláudia Rocha, Ana Francisca Almeida, Ana Raquel Branco, Ana Sousa, André Rocha, Andreia Carvalho, António Martinho, Beatriz Lopes Maia, Beatriz Pereira, Cátia Sousa, Carla Sofia Gomes, Carolina Ramalho, Catarina Neves, Christian Schwartz, Cláudia Farinha, Cláudio Ferreira, Daniel Figueiredo, Diana Ramos, Emmanuel Neves, Francisco Pereira, Inês Marques, Inês Pais, Inês Pinto, Isa Sobral, Isabel Pires, Joana Providência, João Bernardes, João Gil, João Pedro Marques, José Cunha-Vaz, José Filipe Costa, Judite Ribeiro, Keissy Sousa, Lia Correia, Luisa Cardoso, Luisa Ribeiro, Márcia Ferreira, Maria Filipa Ponces, Maria Inês Figueiredo, Maria da Luz Cachulo, Marta Fernandes, Marta Lopes, Matheus Matos, Miguel Raimundo, Nuno Gouveia, Pedro Pereira, Petra Gouveia, Telma Machado, Thomas Almeida, Tiago Baptista, Rúben Magalhães

The Coimbra Ophthalmology Reading Centre (CORC) is a qualified provider for central reading and grading of ophthalmology exams for multinational and multicentric clinical studies, as well as for the Diabetic Retinopathy Screening Programmes of the Central and South Regions of Portugal. It receives and grades exams from all over the world, contributing to standardized results and high quality data to ophthalmic research, by grading several features in different imaging modalities, focusing its activities in the characterization and quantification of ophthalmic diseases.

CORC has all the necessary human resources for its activities, namely Medical Project Coordinators, a vast team of Graders, Study Coordinators, Data Manager and IT Specialist for software/applications development.

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CORC AREAS OF EXPERTISE

Posterior segment / Retinal Diseases

- Diabetic Retinopathy (DR) and Diabetic Macular Edema (DME)
- Age-related Macular Degeneration (AMD)
- Inherited Retinal Diseases (IRD): Retinitis Pigmentosa (RP), Stargardt Disease (STGD)
- Retinal Vein Occlusion (RVO)

Anterior Segment Diseases

- Neurotrophic Keratitis (NK)

OPHTHALMIC EXAMS GRADED BY CORC

Ophthalmic Exams

- Retinal fundus images
  - Fundus Photography (FP)
  - Fluorescein Angiography (FA)
  - Ultrawide field (UWF) imaging (UWF FP and UWF FA)
  - Indocyanine-green Angiography (ICG)
  - Fundus Autofluorescence (FAF)
- Optical Coherence Tomography (OCT)
- Optical Coherence Tomography Angiography (OCTA)
- Anterior Segment Photography
- Functional examinations: Perimetry, Microperimetry, Electrophysiology

CORC SERVICES

Study Development

- Consultancy support for study design (before study start-up activities)
- Project set-up and management
- Scientific and technical support before and during the service
- Study-specific Acquisition Protocols development
- Providing Web-based platform for exams' submission
- Study-specific Grading Forms database development and validation
- Study-specific Grading Protocols development
- Study-Specific Reading Centre Manual development
- Participation in Investigators meeting(s)

Training and Certification

- Equipment
- Technicians
- Support and management of Sites' difficulties
- Training sessions for Sites

In-study Services

- Grading of ophthalmic exams
- Eligibility criteria review and confirmation
- Quality check of functional objective examinations
- Management and monitoring of exams received and results
- Data management for data quality monitoring, data validation and data transfers
- Exploratory analysis
- Data backup procedures and a Disaster Recovery Plan
- Secure long-term archiving of study materials, both digital and hardcopy

CORC IT SYSTEMS*

*hosted on AIBILI's Data Centre certified by ECRIN.

Transmission of images from Clinical Sites to CORC

- CORC Online Platform (https://www.studies.corc.pt), a secure custom-designed web-based tool for both certification activities and study exams submission

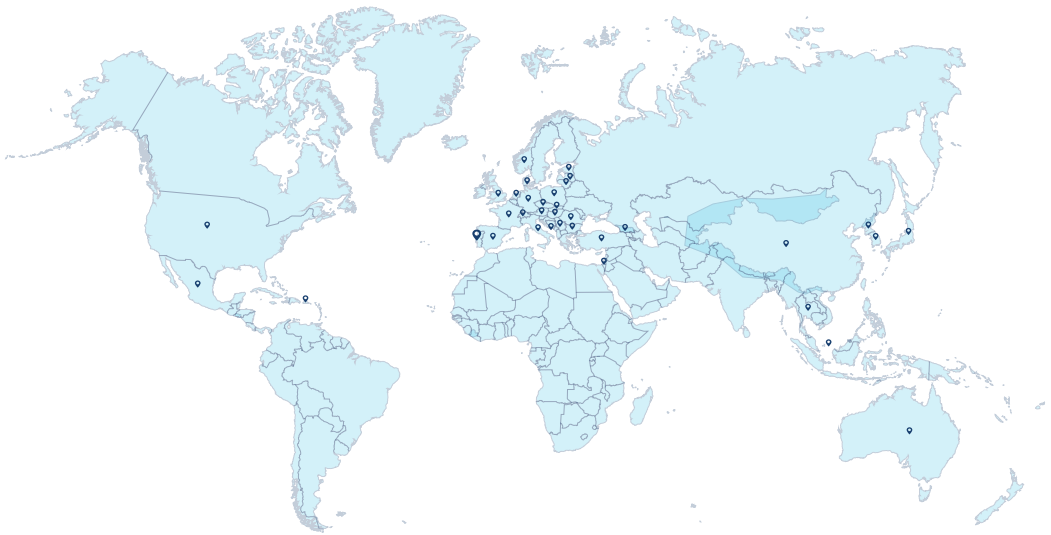
Grading

- REDCap software, used as CORC Digital Grading Forms Platform to record grading results (Digital Grading Forms)
- Licensed software from the equipment suppliers (e.g., Cirrus (Carl Zeiss Meditec), EyeSuite (Octopus, Haag-Streit), Heidelberg Eye Explorer (Heidelberg Engineering), Topcon (Topcon Corporation), ReVue/iVue software (Optovue), Navis-EX (Nidek CO), Optopol OCT (Optopol), OptosAdvance (Optos), Zeiss CLARUS Review (Carl Zeiss Meditec), etc)
- Common applications for imaging edition and analysis (e.g., GIMP, XnViewer, ImageJ, etc)

Management

- CORC Management System (CORCMS), an internal custom-designed web-based tool to support managing activities of CORC and of CORC studies/services. Planned modules: Grading Tracker, In Grading, Statistics, Certification Tracker, In Certification, Exams Quality [work in progress]

CORC RECEIVES AND GRADES EXAMS FROM ALL OVER THE WORLD:



- AUSTRALIA
- AUSTRIA
- BULGARIA
- CZECH REPUBLIC
- CHINA
- DENMARK
- ESTONIA
- FRANCE
- GERMANY
- GEORGIA
- HUNGARY
- ISRAEL
- ITALY
- JAPAN
- KOREA
- LATVIA
- LITHUANIA
- MALAYSIA
- MEXICO
- MONTENEGRO
- NETHERLANDS
- NORWAY
- POLAND
- PORTUGAL
- PUERTO RICO
- ROMANIA
- SERBIA
- SLOVAKIA
- SPAIN
- SWITZERLAND
- THAILAND
- TURKEY
- UK
- USA

N° OF PROJECTS PER SCIENTIFIC AREA AT CORC (2022-2024)

	N° of Projects			
Year	DR & DME	AMD	Others (RVO, RP, STGD, NK)	Total
2022	11	3	6	20
2023	12	3	8	23
2024	**14**	**3**	**10**	**27**

REPRESENTATIVE PUBLICATIONS

Farinha C, Barreto P, Coimbra R, Machado MB, Figueiredo I, Cachulo ML, Cunha-Vaz J, Silva R. **Age-Related Macular Degeneration and Extramacular Drusen: Genetic Associations in the Coimbra Eye Study**. *Invest Ophthalmol Vis Sci*. 2024;65(5):35. doi:10.1167/iovs.65.5.35

Lobo C, Santos AR, Marques IP. **Moving Forward to a Wider Retinal Field of View**. *JAMA Ophthalmol*. 2024;142(9):863-864. doi:10.1001/jamaophthalmol.2024.3071

Pereira PN, Simão J, Silva CS, Farinha C, Murta J, Silva R. **Imaging characterization of the fellow eye in patients with unilateral polypoidal choroidal vasculopathy**. *Int Ophthalmol*. 2024;44(1):122. doi:10.1007/s10792-024-03048-2

Santos AR, Ghate S, Lopes M, Rocha AC, Santos T, Reste-Ferreira D, Manivannan N, Foote K, Cunha-Vaz J. **ETDRS grading with CLARUS ultra-widefield images shows agreement with 7-fields colour fundus photography**. *BMC Ophthalmol*. 2024;24(1):387. doi:10.1186/s12886-024-03537-z

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CNTM - Centre for New Technologies in Medicine

Director: José Cunha-Vaz, MD, PhD

Staff: António Martinho, Celine Cangueiro, Francisco Ambrósio, Luís Mendes, Nicole Duarte, Raquel Santiago, Rufino Silva, Telmo Miranda, Torcato Santos

Contacts
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The Centre for New Technologies in Medicine (CNTM) develops new medical diagnostic techniques with special emphasis in the area of eye fundus imaging.

CNTM main areas of research of CNTM are diabetic retinopathy and age-related macular degeneration, both major causes of blindness. CNTM has been able to contribute extensively to the present state of knowledge of these two diseases. It has participated actively in major European multicentric studies such as EUROCONDOR, RECOGNISED and MACUSTAR.

The eye offers unique opportunities to obtain, in a non-invasive manner, information on the body in general and of the retina and brain in particular. It is, in fact, a window to the body. CNTM is particularly interested in developing non-invasive methodologies that allow repeated observations and measurements in order to identify early alterations that may allow timely therapeutic interventions, e.g. precision medicine, as well as the identification of eye at risk of developing vision threatening complications.

CNTM has been able to patent novel biomarkers of disease progression, such as microaneurysm turnover in diabetic retinopathy identified automatically by the Retmarker® software, developed in-house, in a partnership with Retmarker SA. (Meteda Group, Rome, Italy), and fluid quantification in the retinal diseases by identifying noninvasively changes in the Blood-Retinal Barrier in the retina, using a novel algorithm, the OCT-Fluid, formerly known as OCT-Leakage.

AI methods are also being applied to develop techniques that identify eyes at higher risk of diabetic retinopathy (DR) progression and those with the greatest potential to respond to treatment. These methods also aim to enhance the characterization of DR pathophysiology and associated complications. This research is expected to pave the way for the development of AI systems that can be used in diabetic retinopathy screening programs and primary care units, revolutionizing clinical practice in global diabetes care.

CNTM is also engaged with EVICR.net in the development of the EVICR.net Eye Platform. This Cloud-based platform, composed of several components and microservices, is exploring Cloud's computing capabilities for gathering high-quality ophthalmology data generated in Europe to allow secondary use of data and foster clinical research. After the success of the pilot study focused on AMD, it is now entering its second phase and expanding to use available data in Diabetic Retinopathy. EVICR.net Eye Platform is a platform designed to gather high quality ophthalmology data across Europe, enabling the secondary use of this data for large-scale analyses. It aims to advance clinical research, including research studies and application/development of data-driven technologies such as artificial intelligence.

CNTM has a collaboration with Carl Zeiss Meditec (Dublin, CA, USA) through a clinical research agreement for the identification of biomarkers of diabetic retinopathy using non-invasive modalities such as optical coherence tomography angiography (OCTA) and ultrawide field fundus imaging. A major effort is also being made in the validation and development of OCTA for diagnosing progression of diabetic retinopathy and to develop methods involving artificial intelligence.

RESEARCH FOCUS

- Multimodal imaging of retinal disease
- Characterization of capillary closure to identify diabetic retinopathy progression
- OCT-Fluid. Layer by layer fluid analysis of the retina and identification of extracellular fluid accumulation
- Characterization of prognostic biomarkers of retinal disease progression
- Identification of the eyes that are at higher risk of DR progression and with the greatest potential to respond to a given treatment using artificial intelligence
- Studying the role of microaneurysms as a tool for characterizing DR progression based on modern image acquisition techniques in a real-word setting-based data
- Characterization of response to treatment in Diabetic Macular Edema

N° OF PROJECTS AT CNTM (2022-2024)

	N° of Projects		
Year	Imaging / Artificial Intelligence	Diabetic Retinopathy	Total
2022	11	6	17
2023	12	8	20
2024	**9**	**9**	**18**

REPRESENTATIVE PUBLICATIONS

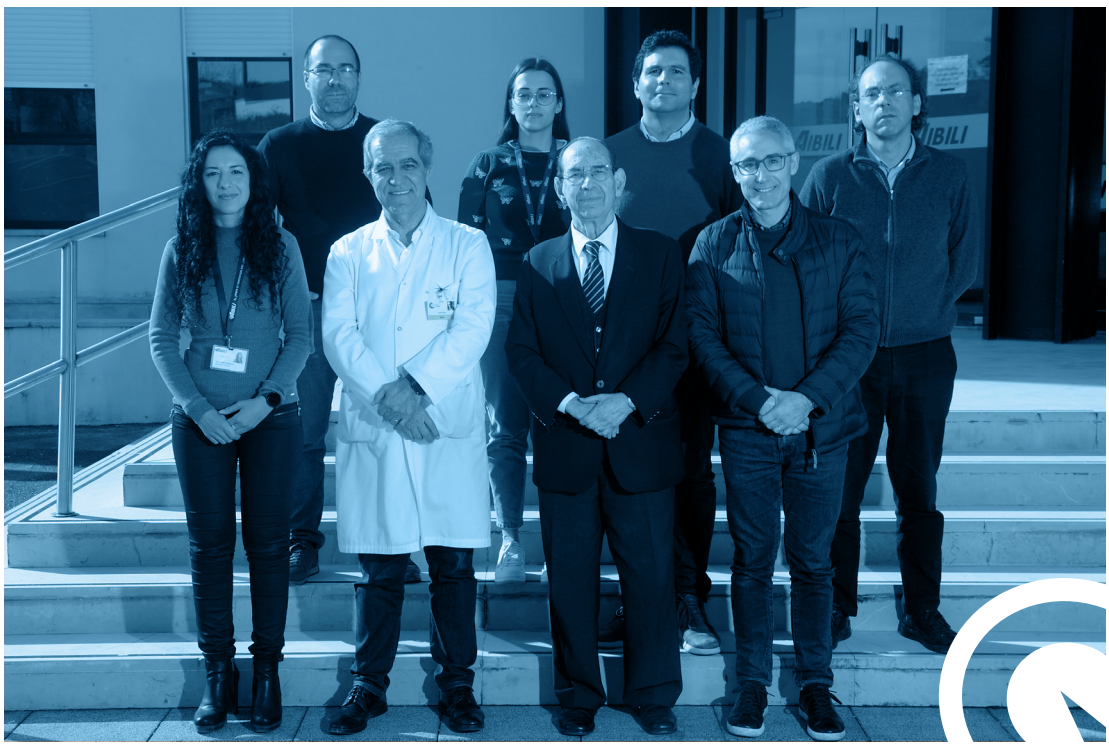
Marques IP, Reste-Ferreira D, Santos T, Mendes L, Martinho AC, Yamaguchi TCN, Santos AR, Pearce E, Cunha-Vaz J. **Progression of capillary hypoperfusion in advanced stages of nonproliferative diabetic retinopathy: 6-month analysis of RICHARD study**, *Ophthalmol Sci.* 2024;5(2):100632. doi:10.1016/j.xops.2024.100632

Mendes L, Ribeiro L, Marques I, Lobo C, Cunha-Vaz J. **Characterization and Automatic Discrimination between Predominant Hypoperfusion and Hyperperfusion Stages of NPDR**. *J Pers Med.* 2024;14:977. doi:10.3390/jpm14090977

Reste-Ferreira D, Marques IP, Santos T, Ribeiro ML, Mendes L, Santos AR, Lobo C, Cunha-Vaz J. **Retinal neurodegeneration in eyes with NPDR risk phenotypes: A two-year longitudinal study**. *Acta Ophthalmol.* 2024;102(4):e539-e547. doi: 10.1111/aos.15787

Marques IP, Ribeiro ML, Santos TP, Mendes LG, Reste-Ferreira D, Santos AR, Lobo CL, Cunha-Vaz JG. **Different Risk Profiles for Progression of Nonproliferative Diabetic Retinopathy: A 2-Year Study**. *Ophthalmol Ther.* 2023;12(1):485-500. doi:10.1007/s40123-022-00623-7

Santos T, Santos AR, Almeida AC, Rocha AC, Reste-Ferreira D, Marques IP, Cunha-Vaz Martinho A, Mendes L, Foote K, Cunha-Vaz J. **Retinal Capillary Nonperfusion in Preclinical Diabetic Retinopathy**. *Ophthalmic Res.* 2023;66(1):1327-1334. doi:10.1159/000534553



DC – Data Centre

Director: Hugo Morgado, BSc

Staff: Carlos Domingues, Celine Cangueiro, Fábio Mesquita, José Monteiro, Pier Basile, Rafael Santos, Telmo Miranda, Tiago Baptista

Consultant: Torcato Santos

Contacts
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Phone: +351 239 480 150
E-mail: hmorgado@aibili.pt

The AIBILI Data Centre was specifically built to support AIBILI's information systems, as well as to store clients and partners data. Inside the Data Centre, the server racks are connected to two separate power circuits, protected by redundant Uninterruptible Power Supplies (UPS). These redundant power supply units ensure that a failure of one power supply unit does not cause any problems, ensuring continuous power to all equipment, including servers, switches and storage. The UPS also ensures that the power quality remains constant. It compensates for voltage and frequency fluctuations and thereby effectively protects sensitive computer electronic components and systems. Block batteries ensure that all operating applications can run for almost three hours. For cooling, the Data Centre has implemented a cold air container solution with redundant air conditioning units. Cold air is directed to the container through the floor and flows through the racks, effectively dissipating the heat produced by servers and maintaining optimal temperature and humidity for electronic equipment. Water detection sensors on the floor and an automatic fire extinguisher (based on gas-based suppression system FM200) complement the Data Centre asset protection.

The Information Technology Unit (IT) maintains more than 70 servers, either virtual or physical, supported by various operating systems and technologies. There are specific Standard Operating Procedures (SOPs) in place, developed according to IT best practices, such as Information Technology Infrastructure Library (ITIL), and project management standards, as recommended by the Project Management Institute (PMI). All changes in the production environment are preceded by testing and validation processes, following the GAMP5 V-model methodology. The Data Centre Unit is responsible for guaranteeing the safety and integrity of data and images collected in compliance with GCP Guidelines and applicable national legislation.

In recognition of the critical importance of information security in today's digital landscape, AIBILI has been implementing the best practices, server management and information system security, aligned with ISO 27001 (Information Security Management). Regular internal audits and penetration tests are performed to ensure the safety and integrity of data. Furthermore, AIBILI Data Centre has a Security Operation Center (SOC) that was implemented and is managed by Visionware, a specialized company in cybersecurity.

All this information is categorized with specific backup policies defined according to information value. Long-term storage procedures are in place to ensure the whole information lifecycle. Information Technology Unit manages more than 90 TB of useful information/data (clinical images and databases, administrative information, project information and long-term storage) and has the capacity for further expansion.

AIBILI Data Centre is certified by ECRIN – European Clinical Research Infrastructure Network (www.ecrin.org) version 3 since April 2016, with the recertification (for version 4) obtained in February 2021. AIBILI Data Centre is the only one certified in the Iberian Peninsula. ECRIN certification confirms AIBILI capacity to provide compliant, effective, and efficient data management services for multinational, randomized controlled clinical trials as well as for clinical studies.

In 2024, AIBILI developed and provides data management, maintenance and support to two registries, one in Keratoconus and another in Endophthalmitis for the SPO – Portuguese Society of Ophthalmology.

MAIN ACTIVITIES

- CDMS (Clinical Data Management System) implementation, validation and support
- eCRF (Electronic Case Report Form) development and management
- eCRF users training and helpdesk
- Data Management, data export and biostatistics support
- CORC platform support
- Development of Digital Grading Forms and support
- Cybersecurity activities
- Long Term Storage

N° OF SERVICES AT DC (2022-2024)

Year	Design & Development of CDMA/eCRF and Data Management	Development of Grading Forms	Development of Registries	Others	Total
2022	10	10	0	6	26
2023	11	12	2	7	32
2024	**12**	**18**	**1**	**7**	**38**

Organisational Units

ADMINISTRATIVE SERVICES

CEO: Cecília Martinho, BSc

Staff: Laura Seco, Mara Miraldo, Marco Santos, Paulo Barros, Sandra Jesus, Tânia Melro

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The Administrative Services (SA) are responsible for the management of AIBILI and for performing all the necessary administrative tasks, including finances and accountability, human resources management, as well as maintenance of infrastructure according to the institution's needs and in compliance with national legislation and requirements. The Administrative Services establishes a direct liaison between the Board of Directors and its Research Centres and Organisational Units. They also provide secretariat support to AIBILI Ethics Committee.

QUALITY MANAGEMENT UNIT (QMU)

Quality Manager: Rita Fernandes, BSc

Staff: Marta Ventura

Contacts
Rita Fernandes, BSc
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E-mail: anarf@aibili.pt

The Quality Management Unit (QMU) is responsible for the Quality Management System (QMS), which is in accordance with ISO 9001:2015, Principles of Good Clinical Practices, requirements for Certification of ECRIN Data Centre and General Data Protection Regulation (EU) 2016/679, Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use, Regulation (EU) 2017/745 on medical devices, as well as other regulatory requirements applicable to AIBILI activities, to ensure continual improvement through regular support to Unit´s activities and internal audits. ISO/IEC 27001 is being implemented since 2023.

AIBILI is currently incorporating in its AIBILI's Quality Management System several standards to meet the current Organizational context, namely for Data Centre services the ISO/IEC 27001 — Information security management systems - Requirements to improve its information security, cybersecurity, and privacy protection, the NIS 2 Directive(EU) 2022/2555) to enhance AIBILI cybersecurity; EU GMP Annex 11 and FDA 21 CFR Part 11 regulations for computerised systems and electronic data in clinical trials.

Internal auditing is a guarantee that procedures are followed and the QMS is in continual improvement to enhance Client's satisfaction by meeting Clients´ requirements. Information security internal audits have been also performed by QMU to assess the employees´ conduct regarding data protection and security issues and their compliance with the internal Policies, as well as to prepare them for the current implementation of stricter procedures.

The QMU assures that the Quality Management System (QMS) is maintained effective and efficient, permitting continual improvement and has the necessary resources to provide the services and meet the needs of its Clients and interested parties. AIBILI QMS is in digital format streamlining approvals, records and archiving, as well as giving permanent access to all information.

AIBILI is ISO 9001 certified for all its main activities, namely for: Performance of Clinical Studies, Planning, Coordination, Monitoring of Clinical Research Activities, Pharmacovigilance, Pharmacoepidemiology and Pharmacoeconomics, Grading of Eye Exams, Research and Development in New Technologies for Medicine in the areas of Imaging, Optics and Photobiology, Data Centre Activities. The certification renewal is foreseen in 2025.

AIBILI Data Centre is certified by ECRIN Data Centre requirements and the certification renewal is foreseen in 2025.

The QMU provides internal and external Quality Assurance (QA) services. The QMU also performs internal and external training on quality and regulatory requirements applicable to clinical research activities.

The QMU, as Personal Data Privacy Committee, is responsible for promoting compliance and awareness of applicable personal data protection laws, advising on the implementation of data protection standards and monitoring compliance in AIBILI.

The QMU has also a Compliance Committee, which is responsible for managing and processing whistleblower breach reports in a work-related context submitted through an internal channel available at www.aibili.pt.

The QMU has also a Data Access Committee (DAC) responsible for evaluating Data Access Requests to AIBILI in order to re-use data for scientific research (via DAC@aibili.pt).

QMU has been actively participating with EVICR.net Coordinating Centre in the development and implementation of the EVICR.net Eye Platform, namely in compliance with regulatory requirements, as well as in the development of SOPs for its implementation.

TRANSLATIONAL RESEARCH AND TECHNOLOGY TRANSFER UNIT (UTT)

UTT Manager: Daniel Fernandes, BSc

Staff: Cecília Martinho, Isabel Ferreira

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The Translational Research and Technology Transfer Unit supports the development of research activities and promotes translational activities by establishing the connection between the different stakeholders. It identifies opportunities for generating new knowledge and transferring technology, while also facilitating contracts with industry, research collaborations, and the pursuit of funding programs.

The UTT is also responsible for promoting and disseminating AIBILI activities, being the main point of contact for partnerships and collaborations.

Following the implementation of the AIBILI Strategic Scientific Research Plan 2020-2025, UTT coordinates the activities of the different lines of research, supporting the conceptualization and elaboration of different projects and applications.

INFORMATION TECHNOLOGY UNIT (IT)

IT Manager: Hugo Morgado, MSc

Staff: Carlos Domingues, Celine Cangueiro, José Monteiro, Rafael Santos, Telmo Miranda, Tiago Baptista

Consultant: Torcato Santos

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Hugo Morgado, MSc
Phone: +351 239 480 150
E-mail: hmorgado@aibili.pt

The Information Technology Unit (IT) is responsible for AIBILI IT support and maintenance, management and maintenance of AIBILI Data Centre, IT network and information systems. The Data Centre, built in 2014 for storing AIBILI's critical information, houses all AIBILI servers and systems, including: the Electronic Medical Record that is daily used to collect patient clinical information at CEC; the custom-designed web based platform used for the transmission of images form Clinical Sites to CORC (https://studies.corc.pt/); the Clinical Data Management System that is used in the development of eCRFs and Grading Forms for each clinical study; as well as the Clinical Management System (CMS) used for the management of multiple multinational clinical studies by 4C.

Additionally, the AIBILI Data Centre supports other business related information systems. It also hosts the EVICR.net website (www.evicr.net) and EVICR.net Eye Platform (https://www.evicr.net/eyeplatform/) as well as other administrative/office information systems.

IT has been implementing the best practices in accordance with ISO 27001 for server management and information system security ISO 27001. Furthermore, IT is incorporating several standards to meet the EU GMP Annex 11 and FDA 21 CFR Part 11 regulations for computerized systems and electronic data in clinical trials.

Ethics Committee

AIBILI has an Independent Ethics Committee (IEC) that is responsible for protecting the rights, safety and wellbeing of human subjects involved in clinical studies (not involving Investigational Medicinal Products (IMP) or medical devices classified as Class IIb or III) performed by AIBILI according to the Portuguese Decree Law nº 80/2018 of October 15th.

AIBILI Ethics Committee is available to be called upon National Ethics Committee for Clinical Research (CEIC) request, in case it is needed for the review of ophthalmology clinical trials or studies since it has expertise in this scientific area.

For more information regarding the AIBILI Ethics Committee: https://www.aibili.pt/units-centres/ethics-committee/.

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MEMBERS

President

André Dias Pereira, PhD

President of the Board of Directors of the Centre for Biomedical Law of the University of Coimbra

Associate Professor at the Faculty of Law of the University of Coimbra

Vice-President of the National Council of Ethics for Life Sciences

Vice-President and Secretary

Margarida Duarte Ramos Caramona, PhD

Emeritus Professor at the Faculty of Pharmacy, University of Coimbra

Members

José António Moura Pereira, MD

Ophthalmologist at the University Hospital of Coimbra

Maria Elizabete Batista Geraldes, MD

Endocrinologist at the University Hospital of Coimbra

Paulo Simões, BSc

Former Chaplain of the University of Coimbra, Master's Student in Philosophy

Filomena Maria Ferreira Ramos Mena, BSc

Nurse at the National Institute of Forensic Medicine, Coimbra

Maria Cecília Martinho, BSc

AIBILI CEO

Technology and Innovation Center

3

Research and Innovation

Throughout its thirty-five years of existence, AIBILI has created an excellence track record in ophthalmology clinical research, being internationally recognized for its innovation in the area of imaging biomarkers and diagnostics.

With the huge acceleration in novel imaging methodologies in the past years, and the increased complexity in medical needs, it has become crucial for science to escort this acceleration. Researchers must provide more insight on disease understanding and deliver more healthcare solutions to promote and protect human health. Likewise, AIBILI also needs to keep up its pace in innovation.

In order to promote science and technology advancement and bring potential new treatments and diagnostic tools to the market, AIBILI has assumed an integrated Strategic Scientific Research Plan 2020 - 2025 with five main research areas:

- Diabetic Retinopathy
- Age-Related Macular Degeneration
- Imaging Biomarkers
- Drug Evaluation
- Translational Vision

AIBILI Strategic Scientific Research Plan aims to achieve four main goals, to stimulate the complementarity of our main research areas:

INTEGRATE SCIENCE AND MEDICINE DEVELOPMENT

- Support the development of precision medicine, biomarkers
- Create integrated evaluation pathways for assessment of medical devices and innovative products

IMPROVE RESEARCH QUALITY

- Foster innovation in clinical trials
- Exploit digital technology and artificial intelligence (AI)
- Expand benefit-risk assessment and communication

ADVANCE IN PATIENT-CENTRED ACCESS TO MEDICINE

- Contribute to HTA decision-making in innovative medicines
- Promote high-quality real-world data
- Deliver improved products, targeted on earlier stages and precision medicine

LEVERAGE RESEARCH AND INNOVATION

- Foster collaboration between academia and other research institutes to address critical research innovation questions in our dedicated Research Programs
- Contribute to better healthcare and personalized medicine

2024 Publications

Baptista FI, Ambrósio AF. **Tracing the influence of prenatal risk factors on the offspring retina: Focus on development and putative long-term consequences**. *Eur J Clin Invest.* 2024;54(10):e14266. doi:10.1111/eci.14266

Barreto P, Farinha C, Coimbra R, Cachulo ML, Melo JB, Lechanteur Y, Hoyng CB, Cunha-Vaz J, Silva R. **Unveiling Statins and Genetics in Age-Related Macular Degeneration: The Coimbra Eye Study-Report 9**. *Invest Ophthalmol Vis Sci.* 2024;65(6), 38. doi:10.1167/iovs.65.6.38

Farinha C, Barreto P, Coimbra R, Machado MB, Figueiredo I, Cachulo ML, Cunha-Vaz J, Silva R. **Age-Related Macular Degeneration and Extramacular Drusen: Genetic Associations in the Coimbra Eye Study**. *Invest Ophthalmol Vis Sci.* 2024;65(35). doi:10.1167/iovs.65.5.35

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Franca M, Providência J, Castela G, Patrício D, Sousa IS, Ambrósio AF, Alves CH, Marques JP. **Clinical and Histopathologic Findings in Jalili Syndrome**. *Ophthalmol Retina.* 2024:S2468-6530(24)00531-1. doi:10.1016/j.oret.2024.11.002. Epub ahead of print.

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Diabetic Retinopathy Research Program

Coordinators: João Figueira, Inês Marques and José Cunha-Vaz

Research Team: Ana Rita Santos, Conceição Lobo, Inês Laíns, Débora Ferreira, Inês Aires, Joana Tavares, Luís Mendes, Luísa Ribeiro, Pier Basile, Rita Coimbra, Torcato Santos, Marta Lopes, Ana Cláudia Rocha, Ana Almeida, Inês Pinto

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Diabetic retinopathy (DR) remains a major cause of blindness as the prevalence of diabetes is expected to approximately double globally between 2000 and 2030. DR progresses over time at different rates in different individuals with only a limited number developing significant vision loss due to the two major vision-threatening complications, clinically significant macular edema and proliferative diabetic retinopathy.

Good metabolic control is important to prevent and delay progression, but whereas some patients escape vision loss even with poor control, others develop vision loss despite good metabolic control. Our research group has been able to identify three different DR phenotypes characterized by different dominant retinal alterations and different risks of progression to vision-threatening complications.

Microaneurysm turnover (MAT) has been validated as a prognostic biomarker of development of clinically significant macular edema, whereas subclinical macular edema identified by Optical Coherence Tomography (OCT) and more recently OCT angiography metrics appear to be also good candidates as an organ-specific biomarker of DR. Hemoglobin A1c (HbA1c) remains the only confirmed systemic prognostic biomarker of DR progression.

MAIN GOALS

To identify new biomarkers of DR progression and their correlation with different risks for development of vision-threatening complications, offering new perspectives for understanding DR and for its personalized management.

ONGOING PROJECTS

PROGRESS 10 - Progression of Diabetic Retinopathy. Identification of Signs and Surrogate outcomes -10-year follow-up
ClinicalTrials.gov ID: NCT04650165
Sponsor: AIBILI

PROGRESS 10 is the continuation of the PROGRESS study (NCT 03010397), a prospective non-interventional longitudinal clinical study designed to follow type 2 diabetic individuals with non-proliferative diabetic retinopathy, in a 10-year period of follow-up.
Patients have a complete annual ophthalmological examination, including standard methodologies as color fundus photography (CFP), visual acuity, optical coherence tomography, and also taking advantage of recent and innovative approaches as Spectral domain OCT-angiography (SD-OCTA) and Swept-source OCT-angiography (SS-OCTA)

RECOGNISED - Retinal and cognitive dysfunction in type 2 diabetes: unraveling the common pathways and identification of patients at risk of dementia.
ClinicalTrials.gov ID: NCT04281186
Sponsor: VHIR, Barcelona, Spain
Financial Support: European Union – H2020-SC1-BHC-01-2019-847749

RECOGNISED is a multicentre, multinational study that aims to investigate the common mechanisms involved in the pathogenesis of DR and cognitive impairment in the type 2 diabetes (T2D). The main goal is to use the retina as a tool to identifying individuals with T2D at a higher risk of developing cognitive decline or dementia.

CHART - Characterization of Retinal disease progression in eyes with NPDR in diabetes Type 2 using non-invasive procedures
ClinicalTrials.gov ID: NCT04636307
Sponsor: AIBILI
Financial Support: IIR funding from Bayer

CHART is a multicentric two-year observational study that aims to better characterize the retinal changes that occur during a 2-years follow-up period in patients with the initial stages of NPDR and at higher risk for sight-threatening complications (ETDRS 35, 43, 47 and 53), allowing better characterization of eyes at risk of progression (phenotypes B and C).
The main aim is to identify biomarkers, obtained using non-invasive procedures, that can predict disease progression and progression to sight-threatening stages of the disease and to characterize the retinal changes that occur in NPDR.

RICHARD - Retinal ischemia characterization in diabetes
ClinicalTrials.gov ID: NCT05112445
Sponsor: AIBILI
Financial Support: IIR funding from Boehringer Ingelheim

RICHARD uses state-of the art imaging methodologies to perform a complete, accurate and noninvasive evaluation of retinal ischemic events associated with diabetes, aiming for a more precise characterization of Diabetic Macular Ischemia (DMI) and its microvascular mechanisms, which can have critical importance in clinical practice allowing a more precise medicine and essential for development of new drugs and treatments.

PREDICTION - Prediction of Progression of Retinal Ischemia in Diabetes
ClinicalTrials.gov ID: NCT05581225
Sponsor: AIBILI

PREDICTION is a non-interventional observational cross-sectional and prospective study that aims to better characterize disease progression in patients with moderate to severe disease (ETDRS DRSS grade 43, 47 or 53) and to investigate the progression of microvascular changes in the diabetic retina in a 4-year prospective study, using OCTA metrics as potential biomarkers of progression of NPDR to VTDR. This study was also designed to explore functional biomarkers of DR disease.

REPRESENTATIVE PUBLICATIONS

Marques IP, Reste-Ferreira D, Santos T, Mendes L, Martinho AC, Yamaguchi TCN, Santos AR, Pearce E, Cunha-Vaz J. **Progression of capillary hypoperfusion in advanced stages of nonproliferative diabetic retinopathy: 6-month analysis of RICHARD study**. *Ophthalmol Sci*. 2024;5(2):100632. doi:10.1016/j.xops.2024.100632

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Age-Related Macular Degeneration Research Program

Coordinators: Rufino Silva

Research Team: Cláudia Farinha, Inês Laíns, Joana Tavares, José Cunha-Vaz, Luís Mendes, Patrícia Barreto, Rita Coimbra

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Age-related Macular degeneration (AMD) is the leading cause of adult blindness in developed countries, which affects almost 30% of the older population. In fact, with the aging of population, AMD will become globally an increasingly important and a prevalent disease worldwide.

The hallmark of the early phases of AMD are macular drusen and pigmentary changes, and it progresses slowly from early AMD to intermediate AMD (iAMD) and, ultimately, late-stage AMD with severe manifestation and frequently irreversible lesions. Of note, it is probable that the early and intermediate forms of AMD do not represent a single disease, but rather a collection of subtypes, which ultimately progress to the advanced forms. Therefore, elucidating these subtypes and their underlying pathogenesis will be critical in developing effective therapies for these earlier stages of AMD.

The ethiology of AMD is complex, and although genomewide and gene-candidate studies have been enabled to identify genetic variants associated with AMD pathogenesis, studies on gene-environment interactions have gained increased relevance on the disease onset. Hence, maintenance of healthy diet, with the use of nutritional supplements, has raised as a strategic preventive measure for personalized medicine in AMD.

The AMD multifactorial nature is currently well-established; however, how these factors interact to promote the development and progression of this condition remains largely unknown. This leads to a current lack of treatments for dry AMD and to halt its progression to AMD late blinding forms. Identification of progression biomarkers would be a major advance that could greatly improve patient care.

MAIN GOALS

To contribute to the understanding of the pathophysiology of AMD, and to identify novel targets for future treatments of this condition and innovative diagnosis methods.

In order to achieve this, our research is focused on:

- Structure and function relation in AMD
- Genomics and metabolomics of AMD
- Lifestyle and genetics interplay in AMD onset and progression
- Drug safety and effectiveness in AMD
- Development of innovative approaches, based on AI, to facilitate AMD diagnosis and progression
- Correlation of genetics, pathophysiology and phenotype

ONGOING PROJECTS

COIMBRA EYE STUDY - Epidemiological study of the prevalence and incidence of Age-Related Macular Degeneration in Portugal
ClinicalTrials.gov ID: NCT01298674, NCT02748824 and NCT01715870

AMD_LifeGene - Age-Related Macular Degeneration: Genetic susceptibility, Nutrition and Lifestyle
ClinicalTrials.gov ID: NCT05735730
Sponsor: AIBILI
Financial Support: EURETINA Retinal Medicine Clinical Research 2022

The purpose of this project is to determine the effect modification on the risk of AMD onset and progression of high-risk-patients due to nutrition and lifestyle. It will assess on what grounds food, nutrients and lifestyle protect or not patients at genetic risk for AMD.

MACUSTAR - Intermediate AMD: Development of Novel Clinical Endpoints for Clinical Trials in Patients with a Regulatory and Patient Access Intention
ClinicalTrials.gov ID: NCT03349801
Sponsor: UKB, Bonn, Germany
Financial Support: European Union and EFPIA – IMI 2 Joint Undertaking - Grant Agreement nº 116076

MACUSTAR is a multinational clinical study which the major objective of is to develop novel clinical endpoints for clinical trials with a regulatory and patient access intention in the area of functional, structural, and patient-reported outcome measures in patients with intermediate age-elated macular degeneration (iAMD). MACUSTAR will also characterize visual impairment in iAMD and its progression, as well as identify risk factors for progression to late-stage AMD.

REPRESENTATIVE PUBLICATIONS

Barreto P, Farinha C, Coimbra R, Cachulo ML, Melo JB, Lechanteur Y, Hoyng CB, Cunha-Vaz J, Silva R. **Unveiling Statins and Genetics in Age-Related Macular Degeneration: The Coimbra Eye Study-Report 9**. *Invest Ophthalmol Vis Sci*. 2024;65(6), 38. doi:10.1167/iovs.65.6.38

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Imaging Biomarkers Research Program

Coordinators: Conceição Lobo and José Cunha-Vaz

Research Team: Ana Rita Santos, Débora Ferreira, Inês Marques, João Figueira, Luís Mendes, Torcato Santos

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The eye offers unique opportunities to obtain, in a non-invasive manner, information on the body in general, and of the retina and brain in particular. It is, in fact, a window to the body. The retinal circulation and the retina can be examined using a variety of methods. Fundus Digital Photography, Optical Coherence Tomography (OCT) and Optical Coherence Tomography Angiography (OCTA) are non-invasive examinations that offer extremely promising perspectives as the data collected can be analysed automatically. The analysis of the data can also be tailored to specific purposes, allowing validating imaging biomarkers of disease. Our group has been able to identify biomarkers of disease progression, such as microaneurysm (MA) turnover in diabetic retinopathy (DR) identified automatically by software developed in-house the Retmarker®, and identify non-invasively changes in the Blood-Retinal Barrier (BRB) in the retina, using also a novel AIBILI patented algorithm, the OCT-Leakage.

MAIN GOALS

To develop new imaging techniques of the eye fundus for diagnosis and risk progression, with particular interest in non-invasive methodologies allowing repeated observations and measurements to identify early alterations and degree of activity.

ONGOING PROJECTS

Optical Coherence Tomography Angiography and Widefield Fundus Photography as tools to evaluate capillary closure and disease severity level
Sponsor: AIBILI
Financial Support: Study performed in partnership with Carl Zeiss Meditec (CA, USA)

Ultra-widefield CFPs devices are now commonly available at clinical practices as they allow to image more than 80% of the retinal surface area, providing detailed visualization of the retinal periphery. OCTA has also begun to play a relevant role in DR management, by offering non-invasive, three-dimensional mapping of the retinal microvasculature. This technology enables the quantification of capillary closure, which correlates with the progression of DR. Furthermore, understanding the regional distribution of retinal capillary changes, showing that changes in the periphery may be indicative of retinopathy progression. This insight enables our understanding of DR progression and helps to create more accurate risk progression profiles.

OCT-Leakage. Layer by layer fluid analysis of the retina
Sponsor: AIBILI

Our group is developing applications that result to advanced imaging algorithms to enable analysis of OCT data, focusing on the segmentation of the different layers of the retina and to evaluate the alterations of permeability of the BRB. In a recent publication, our research group reported an association between abnormal retinal fluid accumulation, BCVA loss and increased perfusion in the deep capillary plexus in eyes with CI-DME.
A European Patent nº 3289565 was attributed to the “Method and device for the non-invasive indirect identification of sites of alterations of the Blood–Retinal Barrier” by the EPO - European Patent Office as well as by the USPTO – United States Patent and Trademark Office, with nº US 11,234,591 B2.

Artificial intelligence for characterization of retinal biomarkers
In recent years, the availability of huge amounts of data and the development of disruptive deep learning techniques are pushing artificial intelligence (AI) to another level. One of the main goals of this Research Group is the development, testing, and validation of cognitive computing methods applied to state-of-art imaging data to be used in the screening and management of eye disease.

Another related goal is the creation of a multimodal imaging dataset suitable for the training and validation of automatic methods.

Window Body Management of diabetes and associated complications by incorporating AI models based on retina images at the different stages of the medical care
Sponsor: AIBILI

Ophthalmological data can be used for the identification and prediction of vascular and neurodegenerative changes associated with type 2 diabetes. This project aims to go a step further in the characterization of the pathophysiology of the DR and associated complications based on modern image acquisition techniques in a real-word setting-based data. It is expected that all the knowledge and data integration generated in this project will open a door to the development of an AI system to be used in DR screening programs and that will revolutionize the clinical practice of diabetes care worldwide.

Risk Profiles - Identification of the eyes that are at higher risk of DR progression and with the greatest potential to respond to a given treatment.
Sponsor: AIBILI

The progression of NPDR to vision-threatening stages with vision loss varies from individual to individual. It is, therefore, of major relevance to identify the presence of retinopathy and, when present, to identify the eyes that have the greatest risk of progression and greatest potential to benefit from treatment. Special attention was given to the development of interpretable AI models using multimodal features and studying the role of microaneurysms as a tool for characterizing DR progression.

EVICR.net Eye Platform
Sponsor: AIBILI
Financial Support: Boehringer Ingelheim International GmbH

The Eye Platform is a cloud-based software solution that allows the collection, organization, and sharing of well-characterized multimodal ophthalmological data to foster and accelerate clinical research using AI tools. The project included the development of the platform and already includes a study, with another study commissioned to be included. The study with data already included focuses on intermediate AMD with and without early atrophy, aiming to predict disease progression. The newly commissioned study, expected to run during 2025, aims to identify the progression of retinal disease in the more severe stages of DR at risk of progression to vision-threatening complications.

Ultra-widefield CFP vs 7-fields at 30° for ETDRS severity level evaluation
Sponsor: AIBILI
Financial Support: In partnership with Carl Zeiss Meditec (CA, USA)

To identify and compare the ETDRS severity level of diabetic patients using 3 different images modalities: the standard 30° ETDRS 7-fields CFP and two wide-field techniques (Clarus 500TM and OptosTM). Our group published a paper showing a nearly perfect agreement between 7-Filed CFP and Ultra-widefield CFP on ETDRS grading. In addition, Ultra-widefield CFP helped with a finer evaluation of retinal lesions. Our goal is to demonstrate that ETDRS severity level can be accurately evaluated using only two ClarusTM high quality images with wider amplitude, while improving the quality and identification capability of key disease features with less artifacts than other WF systems.

REPRESENTATIVE PUBLICATIONS

Marques IP, Ribeiro ML, Santos T, Reste-Ferreira D, Mendes L, Martinho AC, Santos AR, Figueira J, Lobo C, Cunha-Vaz J. **Patterns of Progression of Nonproliferative Diabetic Retinopathy Using Non-Invasive Imaging**. *Transl Vis Sci Technol.* 2024;13(5):22. doi:10.1167/tvst.13.5.22

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Drug Evaluation Research Program

Coordinators: Joana Abrantes

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The demand on healthcare services and the challenges of drug development, in the light of increased aging of population, changing patterns of disease and increased costs of drugs, creates the need for research on the effectiveness, safety and economics of medical research and development (R&D), as well as the complexities of reimbursement. Our research is, through several interconnected ongoing projects, aimed at real world outcomes, safety, economics and market access of drugs.

MAIN GOALS

To strengthen the evaluation of drugs for the benefit of public health, through research and development of methodologies to assess their safety, effectiveness and efficiency as well as the corresponding costs for either the national Health agencies or the patient itself.

ONGOING PROJECTS

DruSER.Net – Drug Safety and Effectiveness Research Network
Sponsor: AIBILI

The DruSER.Net is a research network of Hospitals and Primary Healthcare Centers, which is coordinated by the Pharmacovigilance Unit of Coimbra. The main objective of the DruSER.Net is to investigate and monitor safety and effectiveness of drugs used in routine clinical practice and therefore contributing for patient safety through the conduction of research projects using real-world data. In addition, DruSER.Net promotes collaboration among healthcare professionals and researchers to enhance evidence-based decision-making in clinical settings.

Hypersensitivity Adverse Drug Reactions
Sponsor: AIBILI

The purpose of this project is to collect well-characterized hypersensitivity adverse drug reactions reported by allergist/immunologist physicians from specialized departments in hospitals collaborating within the DruSER.Net. The aim of collecting those cases is to increase knowledge about culprit drugs, types of hypersensitivity reactions and risk factors for such reactions in the real-world clinical practice.

Post-Authorisation Safety Studies
Sponsor: AIBILI
Financial Support: INFARMED I.P.

Post Authorisation Safety Studies (PASS) are essential to obtain further information on a medicine's safety or to measure the effectiveness of risk-management measures. The MARVEL study, completed in 2023 and funded by INFARMED, I.P., focused on assessing the effectiveness of educational materials for healthcare professionals and patients/caregivers for three Ophthalmology drugs. Building on this collaboration, a new study protocol, ARTEMIS (Aflibercept: Estudo de Monitorização Intensiva de Segurança), has been designed for 2024. This study aims to investigate the safety profile and potential adverse drug reactions associated with two dosages of the antiangiogenic agent aflibercept (Eylea®) in clinical practice in Portugal. The ARTEMIS study will also compare the safety data of the newly approved 8 mg dosage (114.3 mg/ml), granted marketing authorization by the European Medicines Agency in January 2024, with findings from the Bayer® PULSAR and PHOTON studies, while continuing to monitor the long-established 2 mg dosage (40 mg/ml).

Probabilistic Models for Health Technologies Assessment (ProMoHTA)
Sponsor: AIBILI

ProMoHTA studies analytical and symbolic methods for the analysis of economic models, with a special focus on Markov models. For this purpose, it uses the software PRISM – Symbolic Probabilistic model checker. This tool allows the specification of a model and facilitates its symbolic study. Estimation tools using the Monte Carlo method are also implemented in this software, allowing to compare the performance of both approaches. Finally, the specification of Markov models through the PRISM tool allows the researcher to use the temporal logic language embed in the software, along with other functionalities.

A case study was developed and published under the title "Probabilistic Model Checking in HTA: A Case Study for Ranibizumab", showcasing the practical application of these methods in health technology assessment.

Signal Detection and Monitoring
Sponsor: AIBILI

Signal detection involves the identification of potential signals or patterns that may indicate an adverse reaction. This can be done through various methods, such as spontaneous reporting systems, electronic health records (EHRs), and pharmacoepidemiology studies. The design of a study that aims the characterization of signal detection in Europe is ongoing. The database with the studied signals has been updated to include the most recent data, ensuring a comprehensive analysis as the study progresses.

REPRESENTATIVE PUBLICATIONS

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Translational Vision Research Program

Coordinators: António Francisco Ambrósio

Research Team: Ana Raquel Santiago, Celso Henrique Alves, Hélène Léger, José Cunha-Vaz, Raquel Boia, Rosa Fernandes

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AIBILI and the Faculty of Medicine - University of Coimbra (FMUC) have a long-term collaborative research partnership, particularly with the Coimbra Institute for Clinical and Biomedical Research (iCBR, former IBILI). This represents an excellent and strategic opportunity for the facilitation of Translational Research and innovation based on knowledge gathered from fundamental research on vision science.

The Translational Vision Research Program results from the collaboration between AIBILI and the Retinal Dysfunction and Neuroinflammation Lab, a research Group from iCBR-FMUC, headed by the coordinator of this Program, Francisco Ambrósio.

MAIN GOALS

To promote innovative translational vision research, with two main focuses:

- translating important findings gathered in basic research into new therapies of retinal degenerative diseases;
- establishing novel biomarkers of disease, disease progression and response to therapy.

ONGOING PROJECTS

Novel therapeutic strategies: Dissecting the mechanisms of action of sitagliptin - potential drug repurposing

The therapies available for retinal degenerative diseases are scarce and are mainly targeted for the later stages of disease. Moreover, they are not effective in a high percentage of patients and can cause some adverse effects. Therefore, novel therapies are needed, particularly for the early stages of disease, which could delay their progression for sight threatening retinopathies. To tackle this, we have two main goals:

- testing the efficacy of molecular entities that have been identified based on our studies dissecting disease mechanisms;
- testing the efficacy of drugs that are already in the market, which can exhibit pleiotropic effects beneficial for the retina.

We previously reported that sitagliptin, a drug used in the treatment of type 2 diabetes, has significant protective effects in the retina of diabetic animal models, including an animal model of type 1 diabetes. In this model, the glycemic levels are very high, despite the sitagliptin treatment, indicating that the protective effects of sitagliptin can be independent of the glycemic control. Moreover, sitagliptin has potent anti-inflammatory effects in the retina of diabetic animals. (Neuro)inflammation has been regarded as an important player in neural and vascular dysfunction and degeneration in diabetic retinas. Microglia, the immune cells of the central nervous system, including the retina, have a key role in mediating neuroinflammation. Our preliminary data also indicate that sitagliptin is able to inhibit retinal microglia reactivity and the effects of sitagliptin can be exerted directly on microglia. Taking this into account, we are dissecting the mechanisms underlying the anti-inflammatory effects of sitagliptin on microglial cells. We are investigating whether those effects are exclusively mediated by the inhibition of the enzyme DPP-IV, the pharmacological target of sitagliptin, which is expressed in microglia, or if the inhibition of microglia reactivity can be also due to pleiotropic effects of sitagliptin.

The results of this project might open new avenues for drug repurposing of sitagliptin, which could potentially be used in the treatment of retinal and brain pathologies characterized by neuroinflammation-mediated neural and endothelial cell dysfunction and death.

hiPSCs derived endothelial cells to identify novel mechanisms of disease and drug targets in diabetic retinopathy (Project C2C)

We have collected skin biopsies from patients with proliferative diabetic retinopathy and from age and sex-matched non-diabetic individuals (3 samples from each group). With the collaboration of Center for Neuroscience and Cell Biology (CNC), we have obtained fibroblasts and iPSCs samples from the skin samples of those patients and controls (approximately 200 aliquotes). We have already implemented the protocol for the differentiation of hiPSCs into RPE cells. Currently, we are working on protocols to differentiate hiPSCs into endothelial cells, photoreceptors, and retinal organoids. These cells will be used to investigate diabetic retinopathy disease mechanisms and to identify potential novel therapeutic targets.

A new therapeutic approach to leverage vision restoration in glaucoma

Although anti-glaucoma eye drops effectively lower intraocular pressure, glaucoma may continue to progress and threaten vision in many patients. Thus, there is an urgent need to rethink the therapeutic paradigm of glaucoma to halt disease progression. A drug able to target retinal ganglion cells could be an important glaucoma management tool.

Retinal ganglion cell loss and degeneration that leads to permanent vision loss is attributed to an initial injury to optic nerve, resulting in a permanent loss of axonal connections with specific brain targets. Thus, the goal of this project is to protect sight by preserving the function of retinal ganglion cells (neuroprotection), while enabling these cells to re-extend axons and re-establish connections in appropriate target areas of the brain (neuroregeneration).

The failure of axonal regeneration in the mature central nervous system has been attributed both to an insufficient intrinsic growth capacity of its neurons and an inhibitory extrinsic environment. Thus, grounded in our previous work that A3R agonist protects retinal ganglion cell from glaucomatous, this project is evaluating the A3R activation in the promotion of long-distance regeneration of retinal ganglion cell axons and correct reintegration in retino-recipient brain targets, aiming vision restoration.

REPRESENTATIVE PUBLICATIONS

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4

International Networking

EVICR.NET - EUROPEAN VISION INSTITUTE CLINICAL RESEARCH NETWORK

The EVICR.net is a network of European Ophthalmological Clinical Research Centres, dedicated to performing multinational clinical research in ophthalmology, following the European and International Directives for Clinical Research.

At present, EVICR.net has 95 Clinical Ophthalmological Research Centres members from 16 European countries. EVICR.net strengthens the capacity of the European Union to explore the determinants of ophthalmic diseases and to develop and optimise the use of diagnostic, prevention and treatment strategies in ophthalmology, by performing multinational clinical research.

It is a platform for ophthalmology multinational clinical research in Europe and a structure to support multinational Investigator-Initiated Research (IIR). EVICR.net is also a resource for Industry in the development of new drugs and medical devices in ophthalmology.

Scientifically it is organised by ophthalmology subspecialty Expert Committees namely: Age-Related Macular Degeneration; Retinal Dystrophies; Diabetic Retinopathy and Vascular Diseases; Glaucoma; Anterior Segment; and Ocular Surface, Inflammation, Dry-Eye & Allergies. It also has Transversal Sections in Rare Diseases and Reading Centres.

The present Chairman of EVICR.net is Prof. Francesco Bandello from Department of Ophthalmology, University Vita Salute – Scientific Institute of San Raffael, Milan, Italy, Clinical Site n° 67.

AIBILI is the Coordinating Centre of EVICR.net, and is responsible for the management of the Network, coordination of multinational clinical research studies, as well as for developing training activities in ophthalmology clinical research.

Becoming a Member

In order to become a member of EVICR.net, each Clinical Research Centre must apply to the Network and fulfil basic requirements, such as dedicated space to perform clinical studies, qualified and experienced personnel, experience of multinational clinical research and agree to implement organisational SOPs according to ICH – GCP Guidelines.

Once a member, the Clinical Site can adopt/harmonise EVICR.net SOPs with the help of the Coordinating Centre in order to become a EVICR.net certified Clinical Site of Excellence. This certification is valid for 4 years period which can be renewed.

Clinical Studies and Registries

AIBILI, as EVICR.net Coordinating Centre, assumes the coordination and management of Investigator-Initiated Research (IIR) in ophthalmology across Europe through the Network. EVICR.net Members have the opportunity to participate in IIR, as well as to submit abstracts for IIR to the Coordinating Centre in order to be evaluated by a specific Expert Committee. When approved, they will have access to support in coordinating and implementing the IIR. All information is available at www.evicr.net.

EVICR.net Investigator Initiated Research (IIR) has been growing in the last years, giving the opportunity for investigators to perform multinational clinical research of high quality in compliance with ICH-GCP Guidelines, assuring that the rights, safety and wellbeing of the trial subjects are protected, and that the clinical data are credible.

EVICR.net has contributed to the improvement of diagnostic, prevention and treatment strategies in ophthalmology. In 2024 there were six ongoing multinational clinical research studies, of which two are European Union funded.

ONGOING CLINICAL STUDIES AND ACTIVITIES

Age-Related Macular Degeneration

MACUSTAR - Intermediate AMD: Development of novel clinical endpoints for clinical trials in patients with a regulatory and patient access intention
ClinicalTrials.gov ID: NCT03349801
Financial Support: European Union and EFPIA - Innovative Medicines Initiative 2 Joint Undertaking - Grant Agreement n° 116076

INTERCEPT-AMD - A collaborative resource of Heidelberg multimodal imaging of Intermediate AMD with and without early atrophy to study prediction of disease progression
ClinicalTrials.gov ID: NCT05698316
Financial Support: Boehringer Ingelheim

MONDEGO - A phase IV, multicenter, open-label, single-arm study to investigate the efficacy and safety of faricimab (RO6867461) in caucasian patients with polypoidal choroidal vasculopathy
ClinicalTrials.gov ID: NCT06709339
Financial Support: IIR Grant from Roche

Diabetic Retinopathy

RECOGNISED - Retinal and Cognitive Dysfunction in Type 2 Diabetes: Unraveling the Common Pathways and Identification of Patients at Risk of Dementia
ClinicalTrials.gov ID: NCT04281186
Financial Support: European Union – H2020-SC1-BHC-01-2019-847749

CHART - Characterization of Retinal disease progression ineyes with NPDR in diabetes Type 2 using non-invasive procedures
ClinicalTrials.gov ID: NCT04636307
Financial Support: IIR Grant from Bayer

PROTOCOL AR - Observational, Longitudinal Natural History Study of Retinal Function in Eyes of Patients with Diabetes
Funding: Mary Tyler Moore Foundation

ORGANISATION OF MEETINGS

The 19th Members Meeting took place on November 7-8, 2024, in Milan, Italy. The meeting gathered more than 70 participants that discussed ongoing and new study ideas, as well as funding opportunities. Industry Advisory Board members were present: Bayer, Boehringer Ingelheim, Novartis, Théa, Viatris and SIFI (observer). Keynote lecture on “Central Serous Chorioretinopathy: Evidence for treatment through IITs” was given by Prof. Camiel Boon. Two sessions were organized dedicated to Eye Platform and Secondary Use of Data and to Gene Therapy in Ophthalmology.

The 20th Members Meeting in 2025 will take place in Belfast, UK, on November 13-14, 2025.

EVICR.net has organised the Symposium "EVICR.net – European Multinational Clinical Research in Retina” on September 22, 2024, during EURETINA 2024 in Barcelona, Spain. This symposium was an opportunity to present updates on the MACUSTAR, CHART, RECOGNISED and INTERCEPT-AMD studies. The collaboration with the DRCR Retina Network from USA was also shared and will proceed with the participation of EVICR.net Members in the Protocol AR. The Eye Platform: European-wide high quality ophthalmic imaging database for large data analysis and clinical research was also presented.

EVICR.net EYE PLATFORM

The EVICR.net Eye Platform is a long-term initiative designed to collect in a common platform high-quality ophthalmology data (namely imaging data) generated in Europe and allow secondary use of data and foster clinical research in all ophthalmology subspecialties.

The analysis of imaging data enhances the understanding of disease progression, contributing to the improvement of patient care in ophthalmology.

Ophthalmology relies on imaging data, which is objective and can be automatically verified and analyzed for consistency, accuracy, completeness, auditability, validity, uniqueness, and timeliness. This makes imaging data highly suitable for efficient and secure collection.

INTERCEPT-AMD Study - A collaborative resource of Heidelberg multimodal imaging of Intermediate AMD with and without early atrophy to study prediction of disease progression.

EVICR.net Eye Platform first study was a collaborative project organised by the AMD Expert Committee.

The Coordinating Investigator is Prof. Sobha Sivaprasad, NIHR Moorfields Clinical Research Facility, Moorfields Eye Hospital, NHS Foundation Trust, London, United Kingdom (EVICR.net CS nº 10), together with Prof. Francesco Bandello, Department of Ophthalmology, University Vita Salute – Scientific Institute of San Raffaele, Milan, Italy (EVICR.net CS nº 67) as Coordinator of the AMD Expert Committee.

Investigators from 26 EVICR.net Sites participated in the study, contributing with anonymised datasets from 1.000/819 patients, on multimodal imaging of intermediate and early atrophic AMD to develop a resource for secondary analysis and co-author publications.

The first publication “Visual acuity in various phenotypes of intermediate AMD in a multicentre cohort study in Europe- INTERCEPT-AMD Report 1” was submitted in November 2024 and the second publication “Baseline factors that are associated with change in visual acuity in intermediate AMD over two years in a multicentre cohort study in Europe- INTERCEPT-AMD Report 2” is being finalised.

The Eye Platform and the INTERCEPT-AMD study are funded by Boehringer Ingelheim.

EDUCATIONAL PROGRAMME

EVICR.net has developed a comprehensive program of continuous training and educational contents, with webinars on ophthalmology clinical research, which are available to the entire community at www.evicr.net/webinars/webinars/.

REPRESENTATIVE PUBLICATIONS

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C-TRACER - CHAMPALIMAUD TRANSLATIONAL CENTRE FOR EYE RESEARCH

Champalimaud Foundation

AIBILI is recognized as a C-TRACER - Champalimaud Translational Centre for Eye Research by the Champalimaud Foundation for its activities in translational eye research.

This Network is of great relevance because it brings together, under the Champalimaud Foundation, three major eye research institutions in the world and creates links between three major continents: Asia, Europe and South America.

The C-TRACERs Network brings together the LV Prasad Eye Institute in Hyderabad, India; AIBILI in Coimbra, Portugal and the Institute for Vision at the Federal University of S. Paulo in S. Paulo, Brazil.

ECRIN - EUROPEAN CLINICAL RESEARCH INFRASTRUCTURES NETWORK

ecrin

ECRIN-ERIC is a network dedicated to improving the health of patients and citizens across the world through clinical research. ECRIN-ERIC supports multinational collaboration in clinical research, acting through correspondents hosted in national clinical research hubs and networks. ECRIN is based on the connection of coordinating centres for national networks of clinical research centres and clinical trials units, able to provide support and services to multinational clinical research.

AIBILI as Coordinating Centre of EVICR.net, a disease-oriented network clinical research in ophthalmology, is an Affiliate Partner of ECRIN-ERIC. Thus, EVICR.net serves as a resource to ECRIN-ERIC in the area of vision and ophthalmology multinational clinical research, particularly by providing scientific and medical expertise, access to patients and research capacity, whereas ECRIN provides support in the submission and coordination at national level. The MACUSTAR clinical study is as example of this collaboration where the overall clinical study coordination is performed by EVICR.net under the leadership of Prof. Frank Holz, University Hospital Bonn, Germany (Sponsor), and the submission and monitoring activities are performed by ECRIN.

More information
https://www.ecrin.org/

EATRIS - EUROPEAN INFRASTRUCTURE FOR TRANSLATIONAL MEDICINE

eatris
European infrastructure
for translational medicine

EATRIS is a client driven, non-profit organization comprising European academic centres of excellence in translational research. EATRIS partner institutes support in bringing innovative ideas for novel preventive, diagnostic or therapeutic products towards first in human application and on to clinical proof of concept. EATRIS partner institutes provide services and expertise in the following areas: Advanced Therapy Medicinal Products; Biomarkers; Imaging & Tracing; Small Molecules; and Vaccines, Inflammation and Immune Monitoring.

AIBILI is a member of EATRIS and has capacities in the Biomarkers and Imaging and Tracing platforms.

More information

https://eatris.eu/

ERN-EYE - EUROPEAN REFERENCE NETWORK ON RARE EYE DISEASES

European Reference Networks

The European Reference Network on Rare Eye Diseases (ERN-EYE) is led by Prof. Hélène Dollfus (Strasbourg, France) and is composed of 52 full members and 8 affiliated partners in 24 EU countries. ERN-EYE is organised in thematic groups: Retinal, Neuro-ophthalmology, Paediatric Ophthalmology and Anterior Segment.

EVICR.net is a member of the Scientific, Medical and Ethical Advisory Board (SMEAB). EVICR.net collaborates with ERN-EYE through the Rare Diseases Transversal Section, with its long experience in Quality Systems and certification of Clinical Sites, as well as by providing overall management and logistical support needed in multinational investigator-initiated studies in rare eye diseases.

More information

https://www.ern-eye.eu/

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Partners

Partners

ARSC – Health Administration of the Centre Region of Portugal

ARSC regulates the organization and functioning of healthcare institutions and services in the Centre Region of Portugal.

The Protocol between AIBILI and ARSC is of great relevance as the area of primary healthcare is a major research interest as screening and prevention are priorities for AIBILI research particularly in imaging diagnostics.

Since 2011, AIBILI-CORC has been the Reading Centre for fundus images from the Diabetic Retinopathy Screening Program of Portugal's center region Local Health Units (ULS).

School of Health Polytechnic of Porto

The School of Health (e2s) is a well-established school with a recognised path in education and research in Technologies and Health Sciences. The TBIO - Center for Research in Translational Health and Medical Biotechnology intends to rely on AIBILI to pursue its objectives of solving problems for bioindustries and developing new diagnostic technologies and therapeutic approaches.

CHUC - Coimbra Hospital and University Centre

CHUC is the largest Hospital Center in Portugal playing a central role in the hospital structure of the Center region of Portugal. CHUC, which integrates the Local Health Unit of Coimbra, is a regional and national reference hospital center for a significant number of highly complex pathologies and has the recognition, by the competent bodies, of a large number of reference centers for complex and/or rare pathologies that require a degree of professional, technical and scientific differentiation.

AIBILI and CHUC have a Protocol in place that allows the performance of ophthalmology clinical research through clinical trials, as well as observational studies.

FMUC – Faculty of Medicine of the Coimbra University

The Faculty of Medicine of the University of Coimbra (FMUC) is one of the most important schools of medicine in Portugal due to its vast research areas.

The partnership between AIBILI and FMUC allows AIBILI to support FMUC investigators in the overall development and coordination of clinical research studies.

HCP – Health Cluster Portugal

AIBILI is member of the Health Cluster Portugal (HCP) whose main objective is the promotion and implementation of initiatives and activities leading to the consolidation of a national cluster for competitiveness, innovation and technology in the health area.

AIBILI contributes as a Research Technology Organisation dedicated to developing, coordinate and perform clinical research studies needed before launching medicines or medical devices in the market.

Hospital CUF Coimbra - José de Mello Saúde

The CUF Coimbra Hospital provides access to excellent health services, both inpatient and outpatient with a comprehensive and innovative offer in diverse medical-surgical areas.

The partnership between AIBILI and CUF Coimbra Hospital main goal is the development and coordination of clinical research activities facilitating the exchange of scientific and technical knowledge and taking advantages of the expertise and resources of each institution.

iCBR – Coimbra Institute for Clinical and Biomedical Research

Coimbra Institute for Clinical and Biomedical Research (iCBR) is a multidisciplinary research unit from the Faculty of Medicine, University of Coimbra (FMUC). Research at iCBR aims to investigate molecular and cellular mechanisms underlying the pathophysiology of chronic diseases, to identify innovative therapeutic strategies and disease biomarkers, as well as to unveil and implement new approaches to promote the quality of life and wellness.

The partnership between AIBILI and iCBR aims to establish the link between pre-clinical and clinical research, setting the ground for the development of innovative research projects, translating basic science into new therapeutic strategies, but also by using human samples to find new biomarkers of disease, disease progression and response to therapy.

i3S – Institute for Research and Innovation in Health of the University of Porto

The i3S merges three institutes and researchers from several schools of the Porto University, thus consolidating an extensive collaboration between all institutions. This wide participation of schools, research institutions and hospitals in a research institute is unique in Portugal and is a valuable asset for science and technology development, while creating an environment that feeds real breakthrough research and translation of discoveries into the clinic.

The partnership between AIBILI and i3S increases the participation in innovation and translational projects as well as to have a more complete and robust value chain for their clients, particularly, for companies.

INFARMED - National Authority of Medicines and Health Products, I.P.

INFARMED, IP is a Government agency accountable to the Health Ministry, that evaluates, authorises, regulates and controls human medicines as well as health products, namely, medical devices and cosmetics for the protection of Public Health.

AIBILI has a protocol with INFARMED to collaborate in the framework of the national strategy for the development of clinical research in the pharmaceutical sector.

Since 2008 that AIBILI has been responsible for a Pharmacovigilance Regional Unit of the National Pharmacovigilance System contracted with INFARMED, IP.

IPN - Instituto Pedro Nunes

Created in 1991 through a University of Coimbra initiative, Instituto Pedro Nunes (IPN) is a private non-profit organisation which promotes innovation and the transfer of technology, establishing the connection between the scientific and technological environment and the production sector.

AIBILI and IPN have signed a protocol to collaborate with the Laboratory for Automatics and Systems (LAS). LAS develops R&D and technology transfer activities in partnership with companies, in the field of Embedded Systems, Collaborative Robotics, Internet of Bodies, Validation, Evaluation and Certification of medical devices. The aim is to promote research, development and innovation with a focus on creating value for companies, transferring technological assets, accelerating the development of technologies and the generation of products, innovative processes and services for the market, particularly medical devices in the healthcare sector.

INFOCUS Clinical Research

INFOCUS is an ophthalmology focused full-service contract research organization (CRO) based in the USA.

AIBILI and INFOCUS are currently providers of ophthalmology clinical research development support services, respectively, in Europe and North America and together they are able to provide a global ophthalmology clinical research support to industry.

MIA – Multidisciplinary Institute of Ageing

MIA Portugal is the first research institute in Southern Europe focused on the molecular and biological basis of ageing and works for the health and wellbeing of an ageing population.

AIBILI and MIA have signed a protocol with the aim of accelerating the development of technologies and the generation of innovative products, processes and services for the health market in the field of ageing.

PtCRIN – Portuguese Academic Clinical Research Infrastructures Network

PtCRIN is the national clinical research network aiming to facilitate and improve quality in clinical research and to increase national and international research collaboration for the benefit of patients, citizens and the healthcare system.

PtCRIN is the Portuguese member of ECRIN-ERIC.

AIBILI is a founding member of the PtCRIN and is a Clinical Trial Unit as well as a Clinical Research Centre. AIBILI has the only ECRIN Certified Data Centre in the Iberian Peninsula since 2016 and recertified in 2021 by ECRIN.

SPO – Portuguese Ophthalmology Society

SPO was founded with the aim of promoting and contributing to the development of Ophthalmology in its different aspects: community and prophylactic, care and curative, scientific, educational and research, with respect for ethics and professional deontology professional ethics; defend the interests of its members, particularly in the exercise of the profession the exercise of the profession; to contribute to the correct conception of a health policy in the Ophthalmology, ensuring standards of quality and competence in accordance with the requirements of medical science. requirements of medical science.

A Protocol between ABILI and SPO is in place allowing the mutual collaboration in clinical research activities, namely training, reinforcement of existing collaboration networks and support to investigator-initiated studies promoted by SPO associates.

SANO – Centre for Computational Personalised Medicine

Sano is a non-profit foundation advancing computational medicine to enhance global healthcare efficiency and effectiveness. This partnership with AIBILI enables collaboration on joint research and innovation (R&I) projects, as well as hosting activities such as curricular internships, professional internships, master's and doctoral theses, and capacity-building and training programs for students and professionals.

UA – Aveiro University

The UA is a public foundation under private law whose mission is to contribute to and develop graduate and postgraduate education and training, research and cooperation with society. This partnership with AIBILI allows to cooperate in clinical research activities as well as to students from the Master in Medical Statistics of UA to perform internships at AIBILI.

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