AIBILI

ANNUAL REPORT

2023

AIBILI association for innovation and biomedical research on light and image

ANNUAL REPORT

2023

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Message from the President

AIBILI is a renowned institution focused on translational research and technology transfer in the health area. In 2022, it was again recognized by the Portuguese Ministry of Economy as a Centre for Technology and Innovation (CTI). This recognition reinforced the importance and relevant role that AIBILI plays in the development of innovative technologies and in the promotion of health in Portugal, demonstrating the institution's continued commitment to research and the transfer of knowledge and technology to society.

Over more than 30 years, AIBILI has grown and responded to emerging scientific questions adapting to market needs. The Clinical Trial Centre (CEC), which in recent years has registered a decrease in its activity in line with the national scenery, has once again been chosen as a clinical site in several trials and studies given the recognition of the appropriate conditions that are crucial for carrying out clinical research. The Reading Centre (CORC) has been increasingly sought after and selected over others worldwide due to the continuous recognition of the excellent performance and high quality of the services provided.

The Coimbra Coordinating Centre for Clinical Research (4C) kept its crucial role in supporting the development and coordination of clinical research studies initiated by researchers or sponsored by industry, and as Coordinating Centre of EVICR.net – European Vision Institute Clinical Research Network. This network, presently with 95 Clinical Site Members in 16 European countries involving more than 800 investigators, constitutes an important resource due to growing recognition in strengthening the European Union's capacity to carry out multinational clinical research in ophthalmology, with the highest standards of quality. The Coimbra Pharmacovigilance Unit (UFC), as a Regional Unit of the National Pharmacovigilance System, supported by the National Authority for Medicines and Health Products (INFARMED, IP) since 2008, has also proven to be of great importance in the national network.

The Centre for New Technologies in Medicine (CNTM), through innovative research projects, some in partnership with international companies, remains particularly dedicated to the development of new methodologies, currently also using artificial intelligence to identify new biomarkers, remarkably relevant for early diagnosis.

The Data Centre (DC), a key unit of the institution, is increasingly focused on improving AIBILI's information security, cybersecurity, and privacy protection, ensuring the safety and integrity of data collected for clinical research.

Over the last year, with the help of a dedicated and determined team, it was possible to overcome the main objectives proposed, in this very challenging area of research and innovation in the health sector. The scientific activity developed, and represented in the different lines of research, well expressed in our Strategic Scientific Research Program, shows our ability to answer current scientific questions, whenever possible, in collaboration with other national and international investigators/institutions, contributing to increasing knowledge with the ultimate aim of improving patients' quality of life.

Conceição Lobo
President


AIBILI
associação para
investigação biomédica e
inovação em luz e imagem

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Introduction

AIBILI – Association for Innovation and Biomedical Research on Light and Image is a Research Technology Organisation in the health area dedicated to the development and clinical research of new products for medical therapy and diagnostic imaging.

AIBILI is a private not-for-profit organisation, founded in 1989, established to support technology transfer and translational research in the health area. It is a Centre for Technology and Innovation (CTI) in the health area of the National Network of the Economy Ministry.

AIBILI main areas of activity are:

- Performance of Clinical Studies
- Planning, Coordination, Monitoring of Clinical Research Studies
- Health Technology Assessment
- 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.

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.

Regarding human resources it has a permanent staff of 57 people including medical doctors, researchers, engineers, pharmacologists, technicians, project managers, statisticians, data managers, quality managers, study coordinators and administrative personnel. Another 49 professionals collaborate regularly in research activities.

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 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: by increasing 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.

The main goals of AIBILI are translational research and innovation in order to improve human health and wellbeing.

2023 HIGHLIGHTS:

- Participation of Dr Daniel Figueiredo and Dr Joana Abrantes in **World Logic Day**, in Aveiro, on 17/01/2023, as part of a UNESCO initiative, where the work Probabilistic Models for Health Technology Assessment was presented;

- Participation of Dr Cecília Martinho and Dr Joana Tavares in the First CUF Clinical Research Days, in Lisbon, on 20/01/2023;

- Dr Pier Basile was certified as a Certified Clinical Data Manager by SCDM – Society for Clinical Data Management;

- Member Participation of the **Economy and Health Working Group**, organised by the Ministry of Economy and the Sea, Ministry of Health, and the Ministry of Science, Technology and Higher Education (Despacho nº 461/2023). This working group has the mission to present measures to boost Industrial Health Policy, AIBILI specifically in clinical research;

- 4C was recognised in February 2023 as an EATRIS Expert Centre for Regulatory Support and HTA capabilities;

- Representation by Eng. Torcato Santos and Dr. Daniel Fernandes at **TECH4INNOV** in Santa Maria da Feira, 29/03/2023, organised by ANI – National Innovation Agency and with demonstration of technologies/innovations. An interview for RTP was made by Eng. Torcato Santos in which he explained the relevance of the OCT-Leakage patent and its importance for identifying and quantifying abnormal fluid accumulation in the retina. This technology is particularly relevant for diagnosing changes in the blood-retinal barrier and for monitoring changes and therapeutic efficacy;

- Participation of Dr Joana Tavares and Dr Luis Mendes in the Meetings with **Health Innovation in Lisbon**, 29/03/2023, organised by HCP – Health Cluster Portugal in partnership with the Global Coalition for Value in Healthcare of the World Economic Forum (WEF) and on the theme Advancing High-Value Health Outcomes;

- Dr Patrícia Barreto's speaker in the "**À Mesa com Saúde"** event held in Coimbra on 05/05/2023. This is a health literacy initiative organised by FMUC and ICBR, in partnership with the Coimbra School of Hospitality and Tourism and the Coimbra university Hospital, which consists of organising dinners with commentary by chefs, researchers and clinicians, aimed at addressing diseases and their prevention through food;

- Participation in the **2nd National Meeting on Clinical Research & Biomedical Innovation**, held in Coimbra on 23/05/2023;

- AIBILI's organisation of the **3rd AIBILI Research Groups Meeting**, which took place on 24/05/2023 and where ongoing activities in AIBILI's various lines of research were presented;

- The integration of the new AIBILI Associate, in May 2023, of the **Escola Superior de Saúde do Politécnico do Porto** with the prospect of starting collaborative projects;

- Signature of a Collaboration Protocol with IPN – **Instituto Pedro Nunes** in May 2023 with a view to boosting research technology innovation in health;

- Participation in the meeting **Pharmacovigilance: Involving the citizen** organised by INFARMED on 30/05/2023 in Porto, where the UFC was represented by Dr Lisete Lemos, Dr Joana Abrantes, Dr Inês Tavares, Dr Ana Rita Gaspar and Dr Inês Jordão;

- The organisation of the **33rd EAsDEC – European Association for Diabetic Eye Complications Annual Meeting**, which took place in Coimbra on 1-3/06/2023. AIBILI was the organiser of this European congress, which brought together more than 100 participants;

- **Dr Cláudia Farinha took her PhD exams** on 06/07/2023 with the thesis: Age-Related Macular Degeneration in Portugal Prevalence, Incidence and Risk Factors in the era of Multimodal Imaging. The exams were unanimously approved with praise and distinction;

- The announcement that **Prof Cunha-Vaz will be awarded the prestigious Helen Keller Prize for Vision Research** in partnership with the BrightFocus Foundation. The prize is awarded in recognition of the excellence in research demonstrated by a significant number of contributions to vision science throughout his career. The award ceremony will take place at ARVO 2024 in Seattle, USA;

- The participation of Dr Cecília Martinho and Dr Joana Tavares in the **ERA4Health Workshop** – Analysis of bottlenecks and challenges in designing and conducting investigator-initiated multinational clinical studies, which took place in Paris, France, on 15-16/09/2023. The challenges in designing and conducting investigator-initiated multinational clinical studies were discussed;

- Dr Daniel Fernandes' participation in the **EATRIS-PT** meeting on 4 October 2023, which brought together the members of this network in Portugal with the aim of consolidating potential collaborations and participation in projects that result in better solutions in Personalised Medicine;

- Representation by Dr Luis Mendes at the **Digital Transformation Summit 2023** – EVOLVE, where the EVICR.net Eye Platform was presented;

- Signature of a **Collaboration Protocol with MIA-Portugal** in November 2023 with the aim of developing collaborative activities and accelerate the development of technologies and the generation of innovative products, processes and services for the health market in the field of ageing;

- During 2023, AIBILI members participated actively through presentations and posters in the following **international congresses**: 46th Macula Society Meeting, Miami, Florida, USA; 7th San Raffaele OCT & Retina Forum, Milan, Italy; COPHY 2023, Lisbon, Portugal; ARVO 2023, New Orleans, USA; Ophthalmic Artificial Intelligence Summit (OAIS) 2023 (virtual); 33rd EAsDEC Meeting, Coimbra, Portugal; 23rd EURETINA Congress 2023, Amsterdam, Netherlands; 18th EVICR.net Meeting, Milan, Italy; AAO 2023, San Francisco, USA; E3 Meeting 2023, Nijmegen, Netherlands; and FLORetina 2023, Rome, Italy.

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Centre for Technology and Innovation (CTI) in the Health Sector

AIBILI is a Centre for Technology and Innovation (CTI) in the Health Sector of the National Technology Network of the Economy Ministry. This recognition identifies AIBILI as the facilitating partner between scientific institutions, enterprises and industry in order to bring novel solutions to the health market.

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

- To maintain a critical position in clinical and translational research allowing the creation of new knowledge in collaboration with other reference institutions and participation in international consortia;
- To increase research in the areas of diabetes, neurology and cardiology, taking advantage of the articulation with primary health care units and the established capacities to study the retina-brain relationship;
- To develop new imaging biomarkers to support the diagnosis and identification of disease stages and facilitate the analysis for risk of development and progression of disease;
- To increase AIBILI's technological strength through the qualification of human resources, the use of state-of-the-art equipment and research collaborations.

With these priorities and 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 that will benefit the society through the contribution of improvements in clinical practice.

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

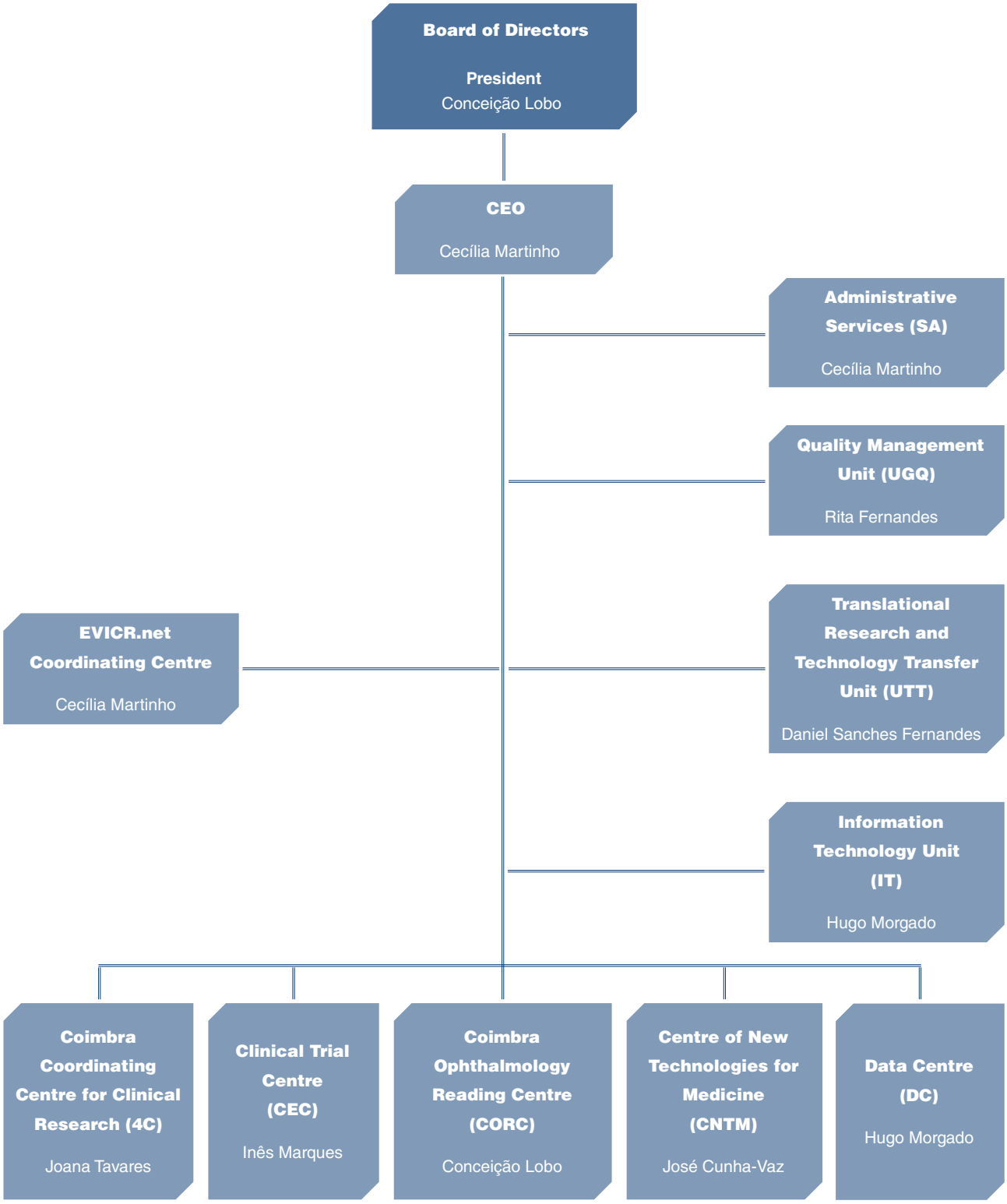
Other Associates

- 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
EVICR.net Coordinating Centre
Cecília Martinho
Translational Research and Technology Transfer Unit (UTT)
Daniel Sanches Fernandes
Information Technology Unit (IT)
Hugo Morgado
Coimbra Coordinating Centre for Clinical Research (4C)
Joana Tavares
Clinical Trial Centre (CEC)
Inês Marques
Coimbra Ophthalmology Reading Centre (CORC)
Conceição Lobo
Centre of New Technologies for Medicine (CNTM)
José Cunha-Vaz
Data Centre (DC)
Hugo Morgado

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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 by Ministry of Economy

Fulltime Staff	57
N° of PhD	19
N° of Consultants	49
N° of Ongoing studies, services, projects, contracts	135
N° Patents	3 (USA) + 1 (Europe)
N° of European Union funded projects (ongoing)	3
N° of Publications (2022-2023)	41
N° of Publications/PhD (2022-2023)	2

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

2019

2021

Data Centre Recertification

2022

Recognition by Ministry of Economy

2023

Recognition of 4C as an EATRIS Expert Centre

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AIBILI Research Centres and Organisational Units

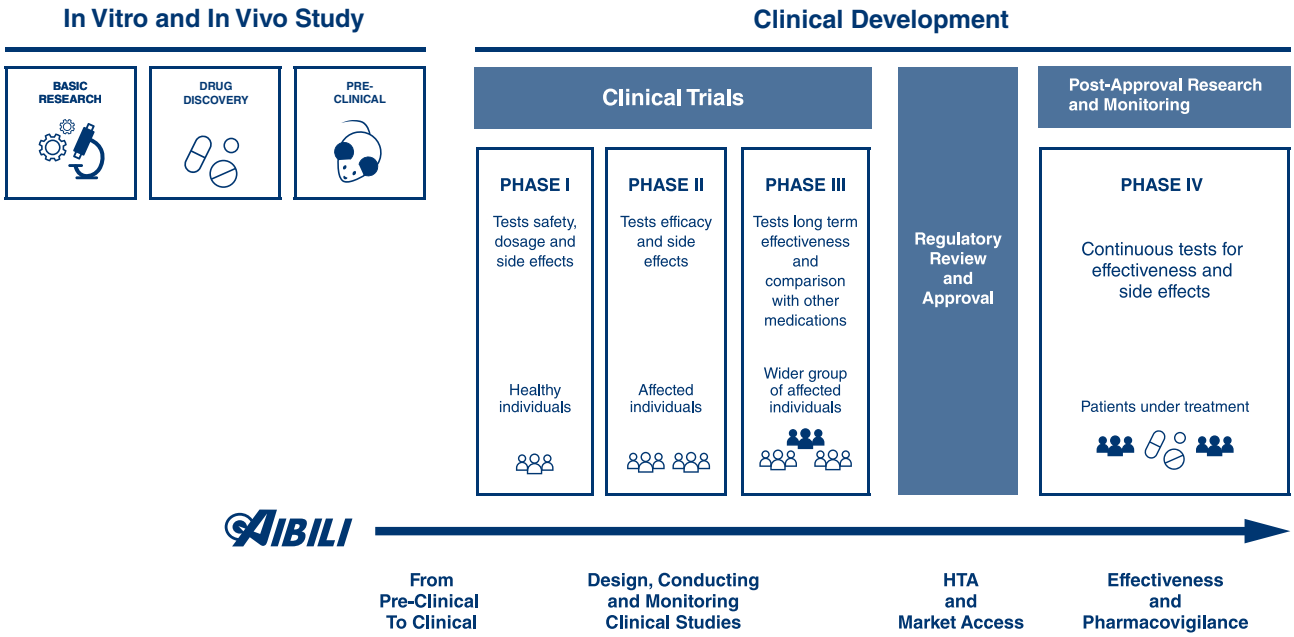
AIBILI is organised in Research Centres and Organizational Units.

The Research Centres are:

- 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 are:

- 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: Cândida Dias, Cecília Martinho, Conceição Lobo, Daniel Fernandes, Daniel Figueiredo, Débora Ferreira, Fábio Mesquita, Inês Aires, Inês Tavares, Joana Abrantes, José Cunha-Vaz, Laura Seco, Liliana Carvalho, Liseta Lemos, Pier Basile, Raquel Branco, Rita Coimbra, Rita Fernandes, Rita Ribeiro, Sónia Simões

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:

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PRE-STUDY	IN-STUDY	POST-STUDY
• Study Design	• Study Coordination	• Data Base Lock*
• Statistical Plan	• IMP/MD Management*	• Data Transfer*
• Protocol and Informed Consent development	• eCRF Management and Support*	• Biostatistics
• Clinical Centre selection	• Data Management	• Final Report
• eCRF development*	• Monitoring	• Medical Writing
• Data validations and implementation*	• Pharmacovigilance and Risk Management	• Publication
• MF and Site File development		• Archiving
• SOPs development		
• Regulatory Affairs		
• Contracts and Insurance		
• Monitoring Plan		

* Services provided by the AIBILI Data Centre

4C uses a Clinical Management System (CMS) developed in house, used for an effective planning, management and monitoring of clinical studies.

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 with national legislation.

4C is a useful resource to work closely with Pharmaceutical Industry in all the different phases of drug development. 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 (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).

The 4C also supports industry on evaluation of medicines and other medicinal products for market access purposes by providing the following services:

MARKET ACCESS	PRIMARY RESEARCH	SECONDARY RESEARCH
• Early advice to develop a value strategy for market access • Supporting strategic value enhancements through expert panels and advisory boards • Core value dossier elaboration • HTA, pricing and reimbursement submissions	• Patient-reported outcomes (PROs) • Real world effectiveness studies	• Literature searching and evaluation • Systematic reviews • Indirect/mixed treatment comparisons according to methodological guidelines • Comparative effectiveness studies • Expert reports

Nº OF CLINICAL STUDIES / PROJECTS AT 4C (2021-2023)

Year	Coordination of Clinical Studies (N°)		Drug Safety	Market Access	Other	Total
	Investigator Initiated	Industry Sponsored				
2021	15	3	9	15	5	47
2022	18	2	8	8	4	40
2023	**16**	**3**	**10**	**2**	**7**	**38**

REPRESENTATIVE PUBLICATIONS

Barreto P, et al. **Association of genetics and the adherence to the Mediterranean diet: the risk for agerelated macular degeneration. Coimbra Eye Study Report 8.** Eye Vis (Lond). 2023;10(1):38. doi:10.1186/s40662-023-00355-0.

Donato A, et al. **The impact of a reimbursement rate reduction on the utilization of antiulcer, antidepressants and antidiabetics in Portugal: A time series analysis.** Int J Healthc Manag. Published online March 29, 2023. doi:10.1080/20479700.2023.2193008.

Figueiredo D, et al. **Performance of Aptima-HPV in the cervical cancer screening program of Portugal: a cost-analysis.** BMC Womens Health. 2023; 23(1):96. doi:10.1186/s12905-023-02219-0.

Hernández C, et al. **Serum glial fbrillary acidic protein and neuroflament light chain as biomarkers of retinal neurodysfunction in early diabetic retinopathy: results of the EUROCONDOR study.** Acta Diabetologica. 2023;60(6):837-844. doi:10.1007/s00592-023-02076-1.

Reste-Ferreira D, et al. **Retinal neurodegeneration in eyes with NPDR risk phenotypes: a two-year longitudinal study.** Acta Ophthalmologica. Published online October 5, 2023. doi:10.1111/aos.15787.

Saßmannshausen M, et al. **Characteristics and Spatial Distribution of Structural Features in Age-Related Macular Degeneration: A MACUSTAR Study Report.** Ophthalmol Retina. 2023;7(5):420-430. doi:10.1016/j.oret.2022.12.007.

CEC – Clinical Trial Centre

Director: Inês Marques, MD, PhD | **Assistant Director:** Patrícia Barreto, MSc

Staff: Aida Vitorino, Ana Almeida, Ana Francisca Almeida, Ana Rita Santos, Ana Rocha, Beatriz Maia, Catarina Eloy, Céu Simões, Cláudia Farinha, Conceição Lobo, Cristina Fonseca, Cristina Januário, Denise Domingues, Filipe Martins, Inês Pinto, Isabel Pires, Joana Abrantes, 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

The Clinical Trial 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 and 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 structured and quicky access to patient's data for clinical research.

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Clinical Research

- Diabetic Retinopathy
- Age-Related Macular Degeneration
- Glaucoma
- Neurology
- Diabetes

Nº OF CLINICAL STUDIES ONGOING AT CEC (2021-2023)

Year	Clinical Studies (N°)		Total
	Investigator Initiated	Industry Sponsored	
2021	8	10	18
2022	11	8	19
2023	**12**	**10**	**22**

INVESTIGATOR INITIATED CLINICAL STUDIES

Diabetic Retinopathy

1. RECOGNISED – Retinal and Cognitive Dysfunction in Type 2 Diabetes: Unraveling the Common Pathways and Identification of Patients at Risk of Dementia
ClinicalTrials.gov nº: NCT04281186
Financial support: European Union – H2020-SC1- BHC-01-2019-847749

2. PROGRESS 10 – Progression of Diabetic Retinopathy. Identification of Signs and Surrogate outcomes – 10-year follow-up
ClinicalTrials.gov nº: NCT04650165
Financial support: AIBILI

3. CHART – Characterization of Retinal disease progression in eyes with NPDR in diabetes Type 2 using non-invasive procedures
ClinicalTrials.gov nº: NCT04636307
Financial support: IIR Grant from Bayer

4. RICHARD – Retinal Ischemia characterization in diabetes
ClinicalTrials.gov nº: NCT05112445
Financial support: IIR Grant from Boehringer Ingelheim

5. Exploratory project – Diabetic Retinopathy: from clinical to cellular phenotyping
Financial support: AIBILI

6. PREDICTION – Prediction of Retinal Ischemia in Diabetes
ClinicalTrials.gov nº: NCT05581225
Financial support: AIBILI

7. CLARUS DR – Diabetic Retinopathy Classification: ETDRS 7-fields vs Widefield Imaging
ClinicalTrials.gov nº: NCT05746975
Financial support: IIR Grant from Zeiss

Age-Related Macular Degeneration

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

9. AMDMetab – Metabolomics: An Integrative Tool for Investigating the Pathogenesis of Age-related Macular Degeneration Partner: Massachusetts Eye and Ear Infirmary (MEEI) and the Harvard Medical School, Boston, USA
ClinicalTrials.gov nº: NCT04241536
Financial Support: EURETINA Clinical Research Award

10. AMD_LifeGene – Diet, medication, and lifestyle in Age-related Macular Degeneration: can the genetic expression be modulated?
ClinicalTrials.gov nº: NCT05735730
Financial Support: EURETINA Clinical Research Award

Retinal Degenerative Diseases

11. STAR – Development of a Model for Advanced Screening for Timely Treatment of Age-Related Eye Diseases
Financial support: AIBILI

12. EYEMARKER – Characterization of potential biomarkers of Eye Disease and Vision Loss
ClinicalTrials.gov nº: NCT02500862
Financial support: AIBILI

INDUSTRY SPONSORED CLINICAL TRIALS

Diabetic Macular Edema

1. A Multicenter, Open-Label Extension Study To Evaluate The Long-Term Safety And Tolerability Of Faricimab In Patients With Diabetic Macular Edema (Rhone-X)
EudraCT nº: 2020-000402-29

2. 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 (NEON)
EudraCT nº: 2020-002333-15

Age-Related Macular Degeneration

3. A 52-week multicenter, randomized, double-masked, 2-arm parallel study to compare efficacy, safety and immunogenicity of SOK583A1 to Eylea®, administered intravitreally, in patients with neovascular age-related macular degeneration (MYLIGHT)
EudraCT nº: 2019-004838-41

Uveitic Macular Edema

4. 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 (MEERKAT)
EudraCT n.º 2022-501793-19-00

Macular Edema Secondary to Retinal Vein Occlusion

5. 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 (QUASAR)
EudraCT n.º 2022-502174-16-00

Glaucoma

6. Long-Term Surveillance Study of Latanoprost to Monitor Hyperpigmentation changes in the eye in Pediatric Populations (A6111144)

Neurological Disorders

7. A multicenter, randomized, double-blind, parallel-group, placebo-controlled variable treatment duration study evaluating the efficacy

and safety of Siponimod (BAF312) in patients with secondary progressive multiple sclerosis (EXPAND)
EudraCT nº: 2012-003056-36

8. **Multicenter, non-comparative extension to study AC-058B301, to investigate the long-term safety, tolerability, andcontrol of disease of ponesimod 20 mg in subjects with relapsing multiple sclerosis (OPTIMUM)**
EudraCT nº: 2016-004719-10

9. **A Multicenter Longitudinal Study to Evaluate the Correlation between Oculometric Measures and Clinical Assessment in Patients with Idiopathic Parkinson's Disease (PALOMA)**
ClinicalTrials.gov nº: NCT05862649

Oncology

10. **A Phase 3 Multicenter, Open-Label, Randomized, Controlled Study of Oral Infigratinib Versus Gemcitabine With Cisplatin in Subjects With Advanced/Metastatic or Inoperable Cholangiocarcinoma With FGFR2 Gene Fusions/ Translocations: the PROOF Trial (PROOF)**
EudraCT nº: 2018-004004-19

REPRESENTATIVE PUBLICATIONS

Barreto P, et al. **Interaction between genetics and the adherence to the Mediterranean diet: the risk for age-related macular degeneration.** Coimbra Eye Study Report 8. Eye Vis (Lond). 2023 Aug 14;10(1):38. doi:10.1186/s40662-023-00355-0.

Marques IP, et al. **Different Risk Profiles for Progression of Nonproliferative Diabetic Retinopathy: A 2-Year Study.** Ophthalmol Ther. 2023 Feb;12(1):485-500. doi:10.1007/s40123-022-00623-7.

Mauschitz MM, et al. **Association of lipid-lowering drugs and antidiabetic drugs with age-related macular degeneration: a meta-analysis in Europeans.** Br J Ophthalmol. 2023;107(12):1880-1886. doi:10.1136/bjo-2022-321985.

Reste-Ferreira D, et al. **Retinal neurodegeneration in eyes with NPDR risk phenotypes: A two-year longitudinal study.** Acta Ophthalmol. Published online October 5, 2023. doi:10.1111/aos.15787.

Santos AR, et al. **Central and Peripheral Involvement of the Retina in the Initial Stages of Diabetic Retinopathy.** Published online December 8, 2023. doi:10.1097/IAE.0000000000004021.

Santos T, et al. **Retinal Capillary Nonperfusion in Preclinical Diabetic Retinopathy.** Ophthalmic Res. 2023;66(1):1327-1334. doi:10.1159/000534553.

Vergroesen JE, et al. **Association of Systemic Medication Use with Glaucoma and Intraocular Pressure: The European Eye Epidemiology Consortium.** Ophthalmology. 2023;130(9):893-906. doi:10.1016/j.ophtha.2023.05.001.

CORC – Coimbra Ophthalmology Reading Centre

Director: Conceição Lobo, MD, PhD | **Sub-Director:** Ana Rita Santos, PhD

Staff: Alda Baltar, Ana Catarina Almeida, Ana Cláudia Rocha, Ana Francisca Almeida, Ana Paula Pascoal, Ana Raquel Branco, Ana Sousa, Beatriz Lopes Maia, Carla Castro, Carla Sofia Gomes, Carla Sofia Maia, Catarina Neves, Christian Schwartz, Cláudia Farinha, Cláudio Ferreira, Daniel Figueiredo, Emmanuel Neves, Diana Ramos, Gil Calvão-Santos, Inês Marques, Inês Pais, Inês Pinto, Isa Sobral, Isabel Pires, João Bernardes, João Gil, João Pedro Marques, José Cunha-Vaz, José Filipe Costa, Judite Ribeiro, Keissy Sousa, Márcia Ferreira, Maria Filipa Ponces, Maria Inês Figueiredo, Maria da Luz Cachulo, Marta Lopes, Miguel Raimundo, Nuno Gouveia, Telma Machado, Rui Pita

The Coimbra Ophthalmology Reading Centre (CORC) is a central reading centre for multinational and multicentric clinical studies, as well as for the Diabetic Retinopathy Screening Programmes of the Central and South Regions of Portugal. It is a qualified provider for central grading of ophthalmology exams contributing to high quality data/results.

CORC focus its activities on grading of ophthalmic exams for characterization and quantification of ophthalmic diseases.

Contacts
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CORC AREAS OF EXPERTISE:

Posterior segment / Retinal Diseases	• Diabetic Retinopathy (DR) • Age-Related Macular Degeneration (AMD) • Retinitis Pigmentosa (RP) • Retinal Vein Occlusion (RVO)
Anterior Segment Diseases	• Neurotrophic Keratitis

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

- 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 Protocols development
- Study-specific Reading Centre Manual development
- Participation in Investigators meeting(s) under Sponsor request

Training and Certification

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

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 monitoring the quality of data, for data validation and data transfers
- Exploratory analysis under Sponsor request
- Data backup procedures and a Disaster Recovery Plan
- Secure long-term archiving of study materials, both digital and hardcopy

CORC IT SYSTEMS* FOR:

Transmission of images between Clinical Sites and CORC

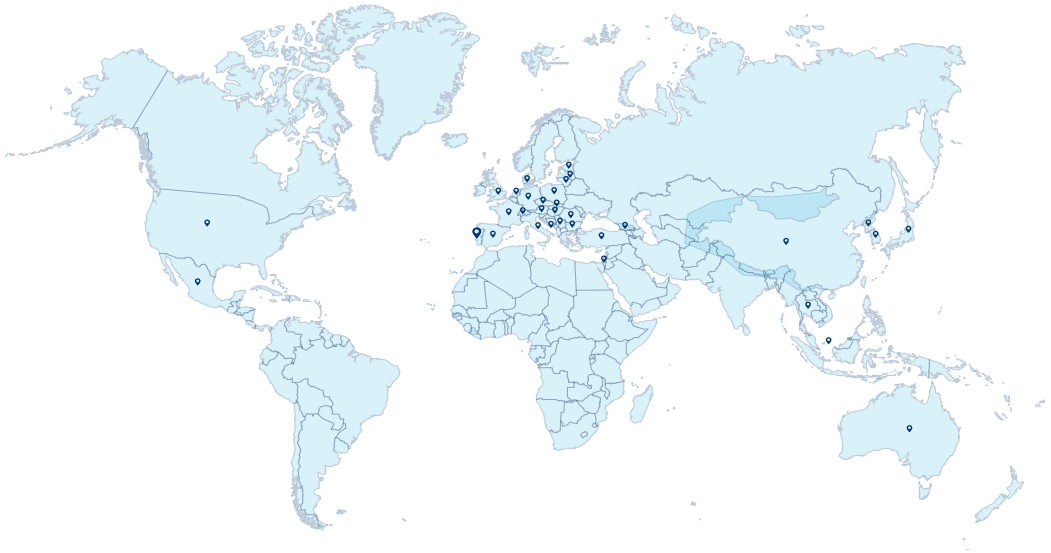
- CORC Studies Platform, a secure custom-designed web-based tool: https://studies.corc.pt/

Grading

- Digital grading forms using a secure web application: REDCap
- Licensed software from the equipment suppliers (e.g., Cirrus (Carl Zeiss Meditec), 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)

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

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
- POLAND
- PORTUGAL
- ROMANIA
- SERBIA
- SLOVAKIA
- SPAIN
- SWITZERLAND
- THAILAND
- TURKEY
- UK
- USA

Nº OF STUDIES AT CORC (2021-2023)

Year	Projects (N°)			
	Diabetic Retinophaty	AMD	Others	Total
2021	12	2	4	18
2022	11	3	6	20
2023	**12**	**3**	**8**	**23**

REPRESENTATIVE PUBLICATIONS

Farinha C, et al. **Common and rare genetic risk variants in age-related macular degeneration and genetic risk score in the Coimbra eye study.** Acta Ophthalmol. 2023;101(2):185-199. doi:10.1111/aos.15232.

Reste-Ferreira D, et al. **Retinal neurodegeneration in eyes with NPDR risk phenotypes: A two-year longitudinal study.** Acta Ophthalmol. Published online October 5, 2023. doi:10.1111/aos.15787.

Lobo C, et al. **Characterisation of progression of macular oedema in the initial stages of diabetic retinopathy: a 3-year longitudinal study.** Eye (Lond). 2023; 37(2):313-319. doi:10.1038/s41433-022-01937-3.

Farinha C, et al. **Retinal layer thicknesses and neurodegeneration in early age-related macular degeneration: insights from the Coimbra Eye Study.** Graefes Arch Clin Exp Ophthalmol. 2021;259(9):2545-2557. doi:10.1007/s00417-021-05140-0.

Silva R, et al. **Efficacy and Safety of Intravitreal Aflibercept Treat and Extend for Polypoidal Choroidal Vasculopathy in the ATLANTIC Study: A Randomized Clinical Trial.** Ophthalmologica. 2022; 245(1):80-90. doi:10.1159/000518235.

CNTM – Centre for New Technologies in Medicine

Director: José Cunha-Vaz, MD, PhD

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

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

The eye offers unique opportunities to obtain, in a noninvasive 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.

CNTM has been able to patent novel biomarkers of disease progression, such as microaneurysm turnover in diabetic retinopathy identified automatically by software developed in-house, the Retmarker®, developed in a partnership with Retmarker SA. (Meteda Group, Rome, Italy), and fluid quantification in the retinal diseases by identifying non-invasively changes in the Blood-Retinal Barrier in the retina, using a novel algorithm, the OCT-Fluid, formerly known as OCT-Leakage. 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 the Cloud's computing capabilities for gathering high-quality ophthalmology data generated in Europe to allow secondary use of data and foster clinical research.

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.

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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 using artificial intelligence
- Characterization of response to treatment in Diabetic Macular Edema

Nº OF PROJECTS AT CNTM (2021-2023)

Year	Projects (N°)		
	Imaging/ Artificial Intelligence	Diabetic Retinopathy	Total
2021	9	6	15
2022	11	6	17
2023	**12**	**8**	**20**

REPRESENTATIVE PUBLICATIONS

Marques IP, et al. **Different risk profiles for progression of nonproliferative diabetic retinopathy: a two year study. Ophthalmology and Therapy.** 2023;12(1):485-500. doi:10.1007/s40123-022-00623-7.

Reste-Ferreira D, et al. **Retinal neurodegeneration in eyes with NPDR risk phenotypes: a two-year longitudinal study.** Acta Ophthalmologica. Published online October 5, 2023. doi:10.1111/aos.15787.

Santos T, et al. **Retinal Capillary Nonperfusion in Preclinical Diabetic Retinopathy.** Ophthalmic Research. 2023;66(1):1327-1334. doi:10.1159/000534553.

Santos T, et al. **Swept source OCTA quantification of capillary closure predicts ETDRS severity staging of NPDR.** Br J Ophthalmol. 2022;106(5):712-718. doi:10.1136/bjophthalmol-2020-317890.

Mendes L, et al. **Comparison of Different Metrics for the Identification of Vascular Changes in Diabetic Retinopathy Using OCTA.** Front Neurosci. 2021;15:755730. doi:10.3389/fnins.2021.755730.

DC – Data Centre

Director: Hugo Morgado, MSc

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

AIBILI Data Centre was built specifically to support AIBILI's information systems as well as to store clients/partners data and information. Inside the Data Centre, the server racks are connected to two separate power circuits, protected by two redundant Uninterruptable Power Supplies (UPS). These redundant power supply units ensure that a failure of one power supply unit does not cause any problems and that power is always supplied to servers. The UPS also ensures that the 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 Data Centre cooling, AIBILI has implemented a cold air container solution with redundant air conditioning units. The air is directed to the container through the floor and flows through the racks, dissipating the heat produced by servers and providing adequate temperature and humidity for electronic equipment's. Water detection sensors on the floor and automatic fire extinguisher (based on gas-based suppression system FM200) complements the Data Centre asset-protection.

The Information Technology Unit maintains more than 70 servers, either virtual or physical, supported by different 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, such as recommended by the Project Management Institute (PMI). All changes in the production environment are preceded by testing and validation processes, according to GAMP5 V-model and methodology. This Unit is responsible for guaranteeing the safety and integrity of data and images collected in compliance with GCP Guidelines and applicable national legislation.

Contacts
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In recognition of the critical importance of information security in today's digital landscape, AIBILI has been implementing the best practices in compliance, server management and information system security, in accordance with ISO 27001 (Information Security Management). Regular internal audits and penetration tests are performed to ensure the safety and integrity of data.

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 over 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 and recertification (in version 4) was achieved in February 2021. This Data Centre is the only one certified in the Iberian Peninsula. ECRIN certification confirms AIBILI capacity to provide appropriate and effective data management services for multinational, randomised controlled trials as well as clinical studies.

AIBILI has developed two databases in keratoconus and endophthalmitis for the SPO – Portuguese Society of Ophthalmology.

Main Activities

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

Nº OF SERVICES AT DC (2021-2023)

Year	Design & Development of CDMA/ eCRF and Data Management	Development of Grading Forms	Platform development for registries	Others	Total
2021	10	9	0	8	27
2022	10	10	0	6	26
2023	**11**	**12**	**2**	**7**	**32**

Organisational Units

ADMINISTRATIVE SERVICES

CEO: Cecília Martinho, BSc

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

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.

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QUALITY MANAGEMENT UNIT (QMU)

Quality Manager: Rita Fernandes, BSc

Staff: Marta Ventura

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.

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.

AIBILI is incorporating in AIBILI´s Quality Management System the ISO 27001 — Information security management systems - Requirements and other ISO 27000 family of standards to improve its information security, cybersecurity, and privacy protection.

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. AIBILI Data Centre is certified by ECRIN Data Centre requirements (https://ecrin.org/data-centre-certification).

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The QMU performs 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.

QMU has been actively participating with EVICR.net Coordinating Centre in the development and implementation of the EVICR.net Eye Platform, namely in the 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

The Translational Research and Technology Transfer Unit facilitates the development of research activities and promotes translational activities by establishing the connection between the different stakeholders. It identifies opportunities for creating new knowledge and transferring technology, by supporting contracting with industry and searching for financing 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. It also promotes the integration of all the different research groups activities and identify opportunities for funding, dissemination and research collaborations.

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INFORMATION TECHNOLOGY UNIT (IT)

IT Manager: Hugo Morgado, MSc

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

The Information Technology Unit is responsible for the management and maintenance of AIBILI Data Centre, IT networks and information systems. The Data Centre, built in 2014 for storing AIBILI's critical information, houses all AIBILI servers/systems: the Electronic Medical Record that is daily used to collect patient clinical information at CEC; the custom-designed web based platform used to transmitting grading data and images by 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.

There are also other administrative information systems supported in AIBILI's Data Centre. AIBILI Data Centre also houses EVICR.net website (www.evicr.net) and EVICR.net Eye Platform (https://www.evicr.net/eyeplatform/) and supports other administrative/office information systems.

IT has been implementing the best practices in server management and information system security and is presently working to be certified by ISO 27001.

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Ethics Committee

AIBILI has an Independent Ethics Committee (IEC/IRB) 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) 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

Director of the Centre for Biomedical Law of the University of Coimbra and Professor at the Faculty of Law, University of Coimbra

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

Father, Director of University Institute of Justice and Peace, Coimbra

Filomena Maria Ferreira Ramos Mena, BSc

Nurse at the National Institute of Forensic Medicine, Coimbra

Maria Cecília Martinho, BSc

CEO, AIBILI

Centre for Technology and Innovation

42 Research and Innovation

43 Diabetic Retinopathy Research Program

45 Age-Related Macular Degeneration Research Program

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Drug Evaluation Research Program 49

Translational Vision Research Program 51

Research and Innovation

Throughout its more than thirty 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

Diabetic Retinopathy Research Program

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

Research Team: Ana Rita Santos, Conceição Lobo, Débora Ferreira, Inês Aires, Joana Tavares, Luís Mendes, Luísa Ribeiro, Pier Basile, Rita Coimbra, Torcato Santos

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.

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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) appears to be also a good candidate 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 Number: 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 (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 Number: NCT04281186
Sponsor: VHIR, Barcelona, Spain
Financial Support: Horizon 2020 – SC1-BHC-2019 – Project nº 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 Number: NCT04636307
Sponsor: AIBILI
Financial Support: IIR funding from Bayer

CHART is a multicentre 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 Number: NCT05112445
Sponsor: AIBILI
Financial Support: IIR funding from Boehringer Ingelheim

RICHARD will use these 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
ClinicalTrials.gov Number: 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 prospective study, using OCTA metrics as potential biomarkers of progression of NPDR to VTDR. We also expect to explore which OCTA vascular metrics are better to identify progression and predict DR complications.

REPRESENTATIVE PUBLICATIONS

Marques IP, et al. **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.

Reste-Ferreira D, et al. **Retinal neurodegeneration in eyes with NPDR risk phenotypes: A two-year longitudinal study.** Acta Ophthalmol. Published online October 5, 2023. doi:10.1111/aos.15787.

Ribeiro L, et al. **Characterization of 2-Year Progression of Different Phenotypes of Nonproliferative Diabetic Retinopathy.** Ophthalmic Res. 2023;66(1):228-237. doi:10.1159/000526370.

Ribeiro L, et al. **Characterization of One-Year Progression of Risk Phenotypes of Diabetic Retinopathy.** Ophthalmol Ther. 2022;11(1):333-345. doi:10.1007/s40123-021-00437-z.

Santos T, et al. **Swept-source OCTA quantification of capillary closure predicts ETDRS severity staging of NPDR.** Br J Ophthalmol. 2022;106(5):712-718. doi:10.1136/bjophthalmol-2020-317890.

Cunha-Vaz J, et al. **Characterization of Risk Profiles for Diabetic Retinopathy Progression.** J Pers Med. 2021;11(8):826. doi:10.3390/jpm11080826.

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Age-Related Macular Degeneration Research Program

Coordinator: Rufino Silva

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

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 genome-wide 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.

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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 Number: NCT01298674, NCT02748824 and NCT01715870

AMD_LifeGene – Diet, medication, and lifestyle in Age-related Macular Degeneration: can the genetic expression be modulated?
ClinicalTrials.gov Number: 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 Number: 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.

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Imaging Biomarkers Research Program

Coordinators: Conceição Lobo and José Cunha-Vaz

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

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 MA turnover in DR identified automatically by software developed in-house the Retmarker®, and identify non-invasively changes in theBlood-Retinal Barrier (BRB) in the retina, using also a novel AIBILI patented algorithm, the OCT-Leakage.

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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)

Widefield CFPs have become widely used as it allow imaging of more than 80% of the retinal surface area, allowing additional visualization of the retinal periphery. OCTA has also begun to play a relevant role in DR, by providing non-invasive three-dimensional mapping of the retinal microvasculature, namely allowing the quantification of capillary closure, a characteristic that correlates with the progression of RDNP. Furthermore, information on the regional distribution of retinal capillary changes is relevant, showing that changes in the periphery may be indicative of retinopathy progression, enabling a better understanding of DR progression, as well as establishing 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.

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.

Retinal-FluidMAPPING – Development and validation of OCT-based Abnormal Retinal FluidMapping
Sponsor: AIBILI
Financial Support: FCT PeX grant – EXPL/EMD-EMD/1402/2021

The project Retinal FluidMAPPING goal was to develop a software prototype tool that mapped and quantified abnormal accumulations of

abnormal fluid to be used as a DME prognostic biomarker, facilitating a personalized ophthalmological healthcare and consequent reduction of societal and economic burden of DME treatment. During the development of this project a normalization step was developed to make the OCT-Leakage method less sensitive to variations of the acquisition quality and signal strength. The detection of microcystic regions was improved by the implementation of the volumetric and density abnormal fluid accumulation metrics.

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. 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.

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

The main goal of this project is to implement 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 first study to be included in the Eye Platform is focused on intermediate AMD with and without early atrophy, to study prediction of disease progression.

Ultra-widefield CFP vs 7-fields at 30º 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 30º ETDRS 7-fields CFP and two wide-field techniques (Clarus 500 TM and OptosTM). Our goal is to demonstrate that ETDRS severity level can be accurately evaluated using only two ClarusTM high quality images with wider amplitude,

REPRESENTATIVE PUBLICATIONS

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Drug Evaluation Research Program

Coordinator: Joana Abrantes, MSc

Research Team: Daniel Figueiredo, Inês Tavares, Joana Tavares, Liseta Lemos

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 on the complexities of reimbursement. Our research is, through several interconnected ongoing projects, aimed at real world outcomes, safety, economics and market access of drugs.

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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.

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 recently concluded MARVEL study, financed by INFARMED, I.P., was designed to assess the effectiveness of educational materials for healthcare professionals and patients/caregivers for three Ophthalmology drugs. The collaboration with INFARMED, I.P. is expected to continue in 2024 with the proposal of a new study.

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 goal of signal detection is to identify potential risks as early as possible, so we expect to better evaluate the characteristics, quality, and contribution to signal detection of spontaneous reports.

Characterisation of Spontaneous Case Reports
Sponsor: AIBILI

Spontaneous case reports offer crucial insights into drug safety by analysing and interpreting information to understand the nature, frequency, and seriousness of reported adverse events. This can involve reviewing the reports to identify common characteristics, such as the specific drug or drugs involved, the type of adverse event being reported, and the population affected. In this scope, two communications were recently presented: "Characterization of Spontaneous Reports containing Immune-Mediated and Autoimmune Disorders received by the Pharmacovigilance Unit of Coimbra" and "Characterisation of Medication Errors in Spontaneous Case Reports received by the Pharmacovigilance Unit of Coimbra". Further research is needed.

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

This project proposes to study analytical and symbolic methods for the analysis of economic models, with a special focus on Markov models. For this purpose, it will be used the software PRISM – Symbolic Probabilistic model checker. This tool allows one to specify a model and proceed with it 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 will allow the researcher to use the temporal logic language embed in the software along with other functionalities.

The use of this language will allow the analytical study of Markov models and calculate probabilities for events and propositions (or properties) directly, not depending on the implementation of specific methods for each of the scenarios studied.

REPRESENTATIVE PUBLICATIONS

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Translational Vision Research Program

Coordinator: António Francisco Ambrósio

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

AIBILI and the Faculty of Medicine of the University of Coimbra have a historical relationship, 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 of innovation based on knowledge gathered from fundamental research on vision science.

This research area at AIBILI, named 'Translational Vision Research', results from the collaboration between AIBILI and the Retinal Dysfunction and Neuroinflammation Lab, a Group from iCBR headed by the coordinator of this Program, Francisco Ambrósio.

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MAIN GOALS

To promote innovative translational vision research, not only by translating basic science into new therapeutic strategies, but also by finding new molecular and cellular biomarkers of disease, disease progression and response to therapy.

ONGOING PROJECTS

New therapeutic strategies: Dissecting the mechanisms of action of sitagliptin – potential drug repurposing

The therapies available for retinal degenerative diseases are scarce and mainly targeted for the later stages of the pathology. Moreover, they are not always effective in a high percentage of patients and are not devoid of adverse effects. These unmet needs prompted us to conceive potential novel therapies for retinal degenerative diseases. To tackle this, we will try different approaches, such as:

- testing the efficacy of molecular entities that have been selected based on our studies focused on the mechanism of disease;
- testing the efficacy of drugs that are already in the market, but that can have pleiotropic effects beneficial for the retina.

We previously reported that sitagliptin, a drug used for the treatment of type 2 diabetes, has potent protective effects in the retina of diabetic animal models, including an animal model of type 1 diabetes, in which the glycemic levels are very high despite sitagliptin treatment, indicating that the effects of sitagliptin can be independent of glycemic control. We also found that sitagliptin has potent anti-inflammatory effects in the retina of diabetic animals. (Neuro)inflammation has been regarded as a trigger for neural and vascular dysfunction and degeneration in diabetic retinas, and microglia, the immune cells of central nervous system, have a key role in mediating neuroinflammation. Our preliminary data also indicate that sitagliptin is able to inhibit retinal microglia reactivity and sitagliptin effects 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, checking whether those effects are mediated exclusively by the inhibition of DPP-IV (the enzyme inhibited by sitagliptin) expressed in microglia, or if some pleiotropic effects can contribute for the inhibition of microglia reactivity. The results obtained with this project might open new avenues for drug repurposing of sitagliptin, which could eventually be used for the treatment of patients with retinal and brain pathologies characterized by neuroinflammation-mediated neural and endothelial cell dysfunction and death.

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

Until now, we 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 now fibroblasts and iPSCs samples from those patients and controls (approximately §200 aliquotes). In the near future, we will implement protocols for the differentiation of hiPSCs into endothelial and RPE cells. These cells will then be used to investigate mechanisms of disease in diabetic retinopathy and to identify potential novel therapeutic targets.

REPRESENTATIVE PUBLICATIONS

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Supporting the development and coordination of clinical research studies

5

International Networking

EVICR.NET – EUROPEAN VISION INSTITUTE CLINICAL RESEARCH NETWORK

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

At present, EVICR.net has 98 Clinical Ophthalmological Research Centres members from 17 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. Hendrik Scholl from University Eye Clinic, University Hospital Basel, Basel, Switzerland, Clinical Site nº 110.

AIBILI is the Coordinating Centre of EVICR.net, that is responsible for the management of the Network, coordination of multinational clinical research studies as well as 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 to 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

assuming 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 2023 there were five ongoing multinational clinical research studies of which 3 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 nº: NCT03349801
    Financial Support: European Union and EFPIA - Innovative Medicines Initiative 2 Joint Undertaking - Grant Agreement nº 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 no.: NCT05698316
    Financial Support: Boehringer Ingelheim
- **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 nº: NCT04281186
    Financial support: European Union – H2020-SC1-BHC-01-2019-847749
  - CHART – Characterization of Retinal disease progression in eyes with NPDR in diabetes Type 2 using non-invasive procedures
    ClinicalTrials.gov nº: NCT04636307
    Financial support: IIR Grant from Bayer
- **Anterior Segment**
  - ANIRIDIA-NET
    Financial support: European Union – COST Action CA18116

EVICR.net EYE PLATFORM

The EVICR.net Eye Platform is a long-term initiative 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.

Ophthalmology is based in imaging data. Imaging data is objective and possible of automatic verification and analysis (consistency, accuracy, completeness, auditability, validity, uniqueness, timeless) and therefore feasible to gather in an efficient and secure manner. EVICR.net launched the Eye Platform as the means to collect imaging data in ophthalmology.

Imaging data analysis allows to improve the understanding of disease progression and contributes to the improvement of patient care in ophthalmology. The Eye Platform is a resource to be used to foster clinical research and improve patient care in ophthalmology.

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

The first study to kick-off the EVICR.net Eye Platform is 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 Member Sites interested to participate in the study, contributed with anonymised datasets on multimodal imaging of intermediate and early atrophic AMD to develop a resource for secondary analysis and co-author publications.

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

EDUCATIONAL PROGRAMME

EVICR.net has developed a continual training and educational programme with webinars on ophthalmology clinical research. The Educational Programme is organised in modules each with three webinars of one hour.

Currently the following modules are available at www.evicr.net/webinars/webinars/ to the whole community:

REPRESENTATIVE PUBLICATIONS

Cordeiro MF, Gandolfi S, Gugleta K, Normando EM, Oddone F. **How latanoprost changed glaucoma management.** Acta Ophthalmol. 2023 Jun 23. doi:10.1111/aos.15725.

Garzone D, Terheyden JH, Morelle O, Wintergerst MWM, Saßmannshausen M, Schmitz-Valckenberg S, Pfau M, Thiele S, Poor S, Leal S, Holz FG, Finger RP; MACUSTAR Consortium. **Comparability of automated drusen volume measurements in age-related macular degeneration: a MACUSTAR study report.** Sci Rep. 2022 Dec 19;12(1):21911. doi:10.1038/s41598-022-26223-w. Erratum in: Sci Rep. 2023 Mar 7;13(1):3795.

Hernández C, Simó-Servat O, Porta M, Grauslund J, Harding SP, Frydkjaer-Olsen U, García-Arumí J, Ribeiro L, Scanlon P, Cunha-Vaz J, Simó R; European Consortium for the Early Treatment of Diabetic Retinopathy (EUROCONDOR). **Serum glial fibrillary acidic protein and neurofilament light chain as biomarkers of retinal neurodysfunction in early diabetic retinopathy: results of the EUROCONDOR study.** Acta Diabetol. 2023 Mar 23. doi:10.1007/s00592-023-02076-1.

Lorenz B, Tavares J, van den Born LI, Marques JP, Pilotto E, Stingl K, Charbel Issa P, Leroux D, Dollfus H, Scholl HPN; EVICR.net study group; ERN-EYE study group. **Current management of Inherited Retinal Degenerations (IRD) patients in Europe. Results of a 2 years follow-up multinational survey by the European Vision Institute Clinical Research Network – EVICR.net.** Ophthalmic Res. 2023 Jan 2. doi:10.1159/000528716.

Lorenz B, Tavares J, van den Born LI, Marques JP, Pilotto E, Stingl K, Charbel Issa P, Leroux D, Dollfus H, Scholl HPN. **Current management of patients with RPE65 mutation-associated Inherited Retinal Degenerations (RPE65-IRD) in Europe. Results of a 2 years follow-up multinational survey.** Ophthalmic Res. 2023 Mar 6. doi:10.1159/000529777.

C-TRACER – CHAMPALIMAUD TRANSLATIONAL CENTRE FOR EYE RESEARCH

Fundação Champalimaud

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 centers 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 and biologics, Biomarkers, Imaging and tracing, Small molecules, and Vaccines.

AIBILI, is 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

ERN-EYE

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 and 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/

Improve human health and wellbeing”

6

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 is the Reading Centre for fundus images of Centre Region of Portugal Screening Programme for Diabetic Retinopathy.

ESENFC | NURSING SCHOOL OF COIMBRA

ESEnfC is a public institution of national and international reference, dedicated to the education of nurses in health education, research and innovation.

AIBILI and ESEnfC signed a partnership agreement for the development of clinical research activities that brings together two institutions in the city of Coimbra. This partnership includes the promotion of training activities focused on clinical research, as well as strengthening the international presence through the networks in which both institutions are involved.

CHUC | COIMBRA UNIVERSITY HOSPITAL

CHUC is the largest Hospital Center in Portugal playing a central role in the hospital structure of the Center region of Portugal. The CHUC 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.

SCHOOL OF HEALTH POLYTECHNIC OF PORTO

The School of Health (ESS) is a well-established school with a recognised path in education and research in Technologies and Health Sciences.

In 2023, the School of Health Polytechnic of Porto, through TBIO - Center for Research in Translational Health and Medical Biotechnology, became an Associate of AIBILI. This Center intends to rely on AIBILI to pursue its objectives of solving problems for bioindustries and developing new diagnostic technologies and therapeutic approaches.

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 develop, 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 (UFC) of the National Pharmacovigilance System contracted with INFARMED, IP.

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.

IRGB | INSTITUTE FOR GENETIC AND BIOMEDICAL RESEARCH (IRGB)

The IRGB has a long-standing experience in elucidating genetic and epigenetic factors at the base of common diseases.

A protocol has been signed between IRGB and AIBILI through their Age-Related Macular Degeneration research groups with extensive knowledge about the pathology, risk factors, genetics and imaging.

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.

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.

P-BIO | PORTUGAL'S BIOTECHNOLOGY INDUSTRY ORGANIZATION

P-BIO is the only association that brings together the vast majority of companies linked to the biotechnology and life sciences sector. P-BIO seeks to develop an environment that is favourable to the creation and growth of start-ups, promoting their corporate development domestically and internationally.

The partnership with AIBILI allows P-BIO companies to have access to differentiated support to evaluate the economic viability of medicines, value strategy design, regulation and translation of technology, market access and effectiveness after commercialization as well as to the coordination and overall management of clinical research studies.

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.

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.

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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