NCBIO
ERA CHAIR

D4.2
Report on the Bi-annual Capacity Building and Knowledge Transfer Plans 2

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Abbreviations and Acronyms

Abbreviation Acronym	Definition
D	Deliverable
IBMC	Institute for Molecular and Cell Biology
M	Month
WP	Work Package
SBG	Synapse Biology Group
PN&ND	Neurobiology and Neurologic Disorders integrative program

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Executive summary

The Synapse Biology Group (SBG) is now complete and fully integrated at the IBMC/i3S. The lab members have already undergone the settling-in program (internal training courses on safety issues, use of facilities, etc.) and quickly initiated Dr. Holt's research program. There has been a continuous, natural knowledge spillover through scientific activities within the SBG and with other research groups of the IBMC/i3S. Within SBG, natural knowledge spillover has taken the form of lab meetings and one-to-one sessions with Dr. Holt. Under his supervision, gaps in knowledge and competences were identified and mechanisms were put into place to address those gaps for every lab member (e.g. participation in training courses).

The IBMC/i3S continues to benefit from the presence and network of Dr. Holt. Concretely, Dr. Holt has already given a presentation internally to the i3S community in the "Group Leaders Seminar" series (September 2022). He has also identified topics of interest and knowledge needs of the IMBC/i3S within the Neurobiology and Neurologic Diseases integrative program (PN&ND) and has continued to invite high-profile scientists (including a two-time ERC Advanced awardee and the science director of the Paris Institut du Cerveau) to NCBio-sponsored seminars.

To the date of writing this report, Dr. Holt has competed—as coordinator of a consortium—to funding from laCaixa (Health call 2024) and from the Portuguese Foundation for Science and Technology (FCT). He has also submitted an application to the European Innovation Council (EIC) Transition Grant as part of his spin-off biotech company, Aila Biotech.

Finally, following Dr. Holt's suggestion to implement faculty meetings (deliverable D4.1), the first faculty meeting will be held in September (M45) to discuss the Neuro Day (which is brings together the entire PN&ND thematic program once a year).

1. Improving the scientific capacity of IBMC/i3S

Natural knowledge spillover

The ERA Chair Team/SBG has currently a total of 11 lab members. The core members of the team (i.e. funded by this grant) include the ERA Chair Holder (Dr. Holt); one Project Manager (Dr. Olga Sin); one Senior Lab Technician (Dr. Simone Bessa); two Junior Post-doctoral Researchers (Dr. Maria Pinto and Dr. Ana Eufrásio) and two Ph.D. candidates (Mr. João Guimarães and Ms. Rafaela Seixas). The team is additionally joined one external Ph.D. candidate (Mr. Domenico Natale) and three M.Sc. students (Ms. Luísa Florido; Mr. Carlos Pinto; Mr. Ahmed Obaid).

To accelerate the molecular identification of the inhibitory tripartite synapse, the lab was organized in two teams: team "membrane", focused on the identification of the transmembrane proteins mediating astrocyte-neuron contacts, and team "secretome", focused on the identification of secreted synaptogenic proteins from astrocytes. A natural knowledge spillover has been taking place between the senior and junior lab members within each team and between both "membrane" and "secretome" teams in bi-weekly lab meetings.

A natural knowledge spillover has also taken place in collaboration with research groups of the IBMC/i3S. The lab of Dr. Paulo Aguiar (Group Leader, Neuroengineering and Computational Neuroscience Group) shared knowledge in the use of advanced cell culture systems. Concretely, his lab taught our senior technicians how to isolate and purify astrocyte primary cell cultures from rat brain. Once they became proficient at this protocol, our senior technicians adapted the protocol for mouse brains, since this is the main model organism used in the lab. Currently, the ERA Chair Team is able to obtain astrocyte primary cell cultures from mouse brain that are 81-98% pure. Dr. Boris Safronov (Group Leader, Neuronal Networks Group) has also become a close collaborator by making his lab available to the ERA Chair Team to process mouse brain slices for biotinylation experiments and for performing electrophysiology experiments.

Finally, the institute's Animal Facility has been giving continuous support to the ERA Chair Team with animal handling as well as training on specific surgery procedures necessary to execute the project.

Capacity building and knowledge transfer

One-to-one meetings with Dr. Holt have been taking place to assess the relative strengths and weaknesses of each lab member and to draw an individual capacity building plan to address gaps in knowledge and competences. For example, Mr. Guimarães and Ms. Florido have been attending training courses as part of the development of their young careers: they attended the Rodents Introductory Course (because they will work with mice) and the Principles of High-Throughput Proteomics Research Course (because they will perform proteomics). Dr. Bessa has since strengthened her skills in animal work, specifically in animal handling and surgical procedures. Dr. Castaldo (Senior Lab Technician from M30 to M36) participated in the institute's internal course on "Building and Leading Research Teams", which was sponsored by the NCBio ERA Chair.

Knowledge transfer has also been taking place with other institutes/universities. For instance, Dr. Luís Ribeiro is an expert in cell adhesion molecules and proteomics from the Center for Neuroscience and Cell Biology (CNC-UC, University of Coimbra) who has been providing advice on biotinylation protocols. Another example is Dr. João Oliveira, an expert in neuron-glia interactions and brain circuits from the Life and Health Sciences Research Institute (ICVS, Braga). Dr. Oliveira's lab has been exchanging reagents, protocols (e.g. astrocyte isolation protocol) and mouse lines with the ERA Chair Team.

The kick-off meeting of the NCBio Stakeholder Hub provided significant knowledge transfer by facilitating access to patient samples from the Portuguese Brain Bank or from the Center for Predictive and Preventive Genetics; to align interests with pharma companies and to seek investment opportunities with venture capital firms. As a follow-up and to further boost academic-industrial interactions, Dr. Olga Sin (Project Manager) and Dr. André Albergaria (Coordinator of Translational Research & Industry Partnerships at IBMC/i3S) have been surveying all the groups belonging to the PN&ND integrative program and matching research interests with major pharma companies in Portugal, with the ultimate goal of setting up one-to-one meetings between these stakeholders.

Dr. Holt has also been contributing to the expansion of the IBMC/i3S scientific network by bringing top researchers to give talks and engage with the IBMC/i3S community. The topics covered by the invited speakers were chosen to be predominantly in line with the scientific interests of the PN&ND and to some extent with the "Cancer" and "Infection, Immunity and Regeneration" integrative programs, to foster collaborations across disciplines.

In 2023, Dr. Holt hosted two speakers for the NCBio ERA Chair Seminar series, including Prof. Dr. Adrian Liston, an expert in neuroimmunology from the University of Cambridge, UK and Prof. Dr. Bassem Hassan, an expert in central nervous system development and specification and science director at Institut du Cerveau, France. Dr. Holt sponsored the yearly conference organized by the Ph.D. student community by bringing Prof. Dr. Benedikt Berninger, an expert in human brain neurogenesis from King's College London, UK. Dr. Holt has continued supporting the local neuro community by hosting Prof. Dr. Pierre Vanderhaegen, an expert in human brain development and two-time ERC Advanced grant awardee, as an inspirational keynote speaker at the yearly IBMC/i3S Neuro Day. In 2024, he hosted Prof. Dr. Wim Annaert, an expert in Alzheimer's disease from KU Leuven, Belgium and Prof. Dr. Keith Murai, an expert in astrocyte biology from McGill University, Canada.

To maximize capacity building in the IBMC/i3S community, all guest speakers were set up in one-to-one meetings with researchers who wished to discuss and get feedback on their individual projects. Additionally, a lunch with the guest speakers was organized exclusively for young scientists (Ph.D. candidates and post-docs) to give them the time and space to ask about career advice in an informal, relaxed setting.

The NCBio ERA Chair Seminar series are having an impact beyond the IBMC/i3S and shaping the research landscape in the center and northern region of Portugal. Concretely, Dr. Holt has taken the initiative to live stream the seminars (upon prior consent from the guest speakers) to other

Portuguese research institutes, namely the CNC-UC (University of Coimbra) and the ICVS (University of Minho). The caliber of guest speakers brought by Dr. Holt means that we frequently include researchers from other institutes/universities (CNC-UC, ICVS, Faculty of Medicine of the U. Porto) for one-to-one sessions with the guest speaker at the IBMC/i3S. In fact, talks are currently underway to expand this initiative and make these seminars bilateral, so that the IBMC/i3S can also benefit from the knowledge transfer brought in by other research institutes across Portugal (e.g. University of Aveiro, Institute of Molecular Medicine, Champalimaud Centre for the Unknown).

Dr. Holt's strong network has been instrumental for the IBMC/i3S to build relationships with companies and get access to cutting-edge technologies that are currently not available at the institute. One such example was Dr. Nachiket Kashikar—CEO and co-founder of the European Spatial Biology Center (now renamed OMAPiX)—who introduced his expertise on end-to-end spatial omics services. Another example was Inscopix, that develops cutting-edge minicameras that record free behaving mice. Dr. Holt facilitated the contact between Inscopix and the institute's Advanced Imaging Core platform to organize a promotional talk by Inscopix followed by a demonstration of these minicameras at the institute. Finally, Dr. Delfim Duarte (Group Leader of the Hematopoiesis and Microenvironments Group) sought Dr. Holt to facilitate contact with the KU Leuven Institute for Single Cell Omics for sending samples for single-cell sequencing.

Dr. Holt's position as recurring speaker at the International Astrocyte School (IAS) has benefited lab members of the SBG as well, namely Mr. Domenico Natale (Ph.D. student). Mr. Natale's participation in the 2024 edition of the IAS not only allowed him to showcase his project to leaders in the field of astrocyte research but also to build his own network, thereby increasing his chances of pursuing an excellent career following the conclusion of his Ph.D. project.

2. Improving knowledge on research administration and management at IBMC/i3S

Natural knowledge spillover

Several synergies have been taking place since the appointment of Dr. Holt as the ERA Chair Holder. Dr. Holt brings a strong network of international and national collaborations composed of very successful scientists which have exposed the institute to best practices in the identification of funding opportunities, preparation of grant applications and network and consortium building. The Research and Innovation Unit of the IBMC/i3S (including the Grants Office and the Coordinator for Translational Research & Industry Partnerships) has been pivotal in identifying calls that match the ERA Chair Holder's research interests and giving assistance whenever necessary during the grant application process.

The first joint bid for competitive funding was to the European Innovation Council (EIC) Transition Grant, written in collaboration with Dr. James Dooley (CEO of Aila Biotech where Dr. Holt is co-founder), Dr. Lidia Yshii (group leader at KU Leuven, Belgium) and Enspire Science Ltd.

The second and third joint bids for competitive funding arose from networking and consortium building, namely between Dr. Holt, Dr. Luís Ribeiro (CNC-UC, Portugal) and Dr. Jeffrey Savas (group leader at Northwestern University, USA), an expert in brain and synaptic proteomes in health and disease. This networking resulted in a joint bid writing to the laCaixa Health Call 2024. Dr. Holt also applied to the Portuguese Foundation for Science and Technology (FCT) as coordinator of a consortium with Dr. Ribeiro; Dr. Savas and Dr. Jerôme Wahis (Research Associate at KU Leuven, Belgium), expert in electrophysiology. Both joint bids counted with the additional support of the Portuguese Association for Developmental Disorders and Autism (APPDA-Norte) as a civil society organization.

At the IBMC/i3S, Dr. Holt has been sought by the faculty to review and give advice on large EU funding schemes like the ERC Advanced grant, which was recently awarded to Dr. Hélder Maiato (Group Leader, Chromosome Instability & Dynamics Group). He is also mentor to young group leaders who recently started their own independent research groups, specifically Dr. Vanessa Coelho-Santos (University of Coimbra) and Dr. Silvia Pittolo (Max Delbrück Center, Germany).

To make all funding opportunities easily available to the SBG lab members, Dr. Sin (Project Manager) wrote an internal document listing fellowships, grants and awards for each academic career stage (Ph.D., post-doc or group leader). Since this is a living document, Dr. Sin regularly updates and adds new funding opportunities whenever applicable.

Concerning the NCBio Stakeholder Hub, talks are currently ongoing with ViraVector—a national research infrastructure specialized in manufacturing vector technologies—with the aim of exploiting synergies in the development of AAVs as drug delivery systems that have the capacity to cross the blood brain barrier (BBB). Other BBB-crossing drug delivery strategies like nanobodies and nanoparticles are also of interest and we are currently mapping research groups that use

these technologies in Portugal, with the intent of organizing a workshop in this topic in the near future.

Capacity building and knowledge transfer

Dr. Holt was recently nominated vice-coordinator of the PN&ND. This enables Dr. Holt to hold a seat in the scientific council of the IBMC/i3S, meaning that he now has a direct impact on the management of the overall scientific strategy of the institute.

Dr. Holt's initiative to implement faculty meetings (alluded in deliverable D4.1) will take place next September (M45). One such faculty meeting already took place with Dr. Tiago Dantas, a young associate researcher looking to secure his own independent group. Dr. Holt offered advice on strategies to attain an independent position by addressing grant application preparation (including identification of appropriate funding opportunities to his career stage) and also research management (including project planning, risk management and mitigation, budgets).