Evaluation Panel: HEALTH SCIENCES - Biomedicine and Molecular Biology

Panel Members

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R&D Units

Centro de Inovação em Biomedicina e Biotecnologia (CIBB)	Universidade de Coimbra (UC)
Centro de Investigação em Biociências e Tecnologias da Saúde (CBIOS)	COFAC, Cooperativa de Formação e Animação Cultural, CRL (COFAC)
Centro de Investigação em Biomedicina (CBMR)	Universidade do Algarve (UAlg)
Centro de Investigação em Ciências da Saúde (CICS-UBI)	Universidade da Beira Interior (UBI)
Instituto de Biomedicina – Aveiro (iBiMED)	Universidade de Aveiro (UA)
Instituto de Biosistemas & Ciências Integrativas (BioISI)	FCiências.ID - Associação para a Investigação e Desenvolvimento de Ciências (Fciências.ID)
Instituto de Investigação do Medicamento (iMed.ULisboa)	Faculdade de Farmácia da Universidade de Lisboa (FF/ULisboa)
Instituto de Investigação e Formação Avançada em Ciências e Tecnologias da Saúde (IINFACTS)	Cooperativa de Ensino Superior Politécnico e Universitário, CRL (CESPU)
Instituto de Investigação e Inovação em Saúde (i3S)	Universidade do Porto (UP)
Instituto de Medicina Molecular (iMM)	Instituto de Medicina Molecular (IMM/FM/ULisboa)
Instituto Gulbenkian de Ciência (IGC)	Fundação Calouste Gulbenkian (FCG)
Laboratório Associado, Instituto de Ciências da Vida e da Saúde / Grupo de Investigação em Biomateriais, Biodegradaveis e Biomiméticos (ICVS/3Bs – LA)	Universidade do Minho (UM)
Programa Champalimaud de Investigação (CR)	Fundação D. Anna de Sommer Champalimaud e Dr. Carlos Montez Champalimaud (FC)

Evaluation Panel: HEALTH SCIENCES - Biomedicine and Molecular Biology

R&D Unit: Centro de Inovação em Biomedicina e Biotecnologia (CIBB)
Coordinator: Luis Fernando Morgado Pereira Almeida
Integrated PhD Researchers: 305

Overall Quality Grade: VERY GOOD
Evaluation Criteria Ratings
(A) Quality, merit, relevance and internationalization of the R&D activities of the Integrated Researchers in the R&D Unit Application: 4
(B) Merit of the team of Integrated Researchers: 4
(C) Appropriateness of objectives, strategy, plan of activities and organization: 4

Base Funding for (2020-2023): 3977 K€
Recommended Programmatic Support
PhD Fellowships: 10
Programmatic Funding: 1415 K€, including for 4 (Auxiliar) New PhD Researchers Contracts.

Justification, Comments and Recommendations
The Centre for Innovative Biomedicine and Biotechnology (CIBB) is a relatively young and integrated institution that stemmed out of the CNC.IBILI and includes the Centre for Neuroscience and Cell Biology and the Coimbra Institute for Clinical and Biomedical Research (iCBR former IBILI) established in 2015. The establishment of the CIBB was encouraged by the EAB Dec 2016 report. The director/coordinator L. Pereira took this up and the different institutions have taken steps to achieve a well-integrated Unit starting with a single name. Although there have been plans to integrate CIBB elements into a single building, it was not clear how complete this was, or whether there are on-going plans to complete them. Therefore the CIBB is still located in three sites - the University of Coimbra, the Heath Science Site and the CNC/UC-Biotech building in the Biotech-Park Biocant - and is connected with the CHUC University Hospitals forming the Coimbra Academic Clinical Centre (CACC). Biocant hosts 1/3 of all the biotech companies in Portugal promoting the interface with academia and the creation of spin off companies; this certainly adds significant value to CIBB, which needs to be enhanced further in the future. Biocant could become a hub, potentially for the whole Portugal for future training of new generation of scientists and clinical scientists with a focus on translation and commercialization of products.

CIBB is a large Unit now and focuses on two research areas, Biomedicine and Biotechnology with three major themes which are (i) Neuroscience and Disease (9 RGs), (ii) Metabolism, Aging and Diseases (10 RGs) and (iii) Innovative Therapies (11 RGs). The centre hosts over 580 members, including 305 PhD holders and 220 early stage researchers with 60 technicians. A total of 161 PhD students and young researchers have been recruited; three of them with prestigious Marie–Curie Fellowships. The Panel appreciates that new tenure positions are established now with 80% dedicated to research activities and not only with teaching activity. This will help to increase scientific productivity. A major still on-going integrative effort is directed towards the involvement of clinicians in CIBB activities to enhance the translational impact of the centre's basic research and achieve excellence in this area. Indeed, compared to the previous evaluation the number of clinicians (90) has doubled and comprises 40 with PhD.

CIBB hosts 6 PhD programmes, four of which are coordinated by CIBB, one of those being clinical. Some of the studentships were obtained in the context of International Networks like the ENC–Network or FP7-ITNs. It was apparent from the documentation that there was a lack of consistency in requirements and support to PhD students, across different groups. However, from the discussions of the Panel with PhD students it became clear that there was an improvement of mentoring and supervision over the last few years. PhD students have now weekly interactions with their supervisors and are included in annual meetings. Guidance is provided for career development in academia and beyond. Also, the discussions with researchers and post-docs revealed a generally positive stance towards working at the CIBB. They particularly underlined the good communication with their leaders.

In terms of research, CIBB is interested primarily in a relevant theme that is “Active and Healthy Aging”. In addition to common neurodegenerative diseases, like Alzheimer’s and Parkinson’s, and rare ones that are relevant to Portugal [e.g., Spino-cerebellar ataxia type 3 (SCA3), also known as Machado-Joseph disease (MJD)], they are also interested in stroke and epilepsy, looking at basic cellular mechanisms/pathways and searching for biomarkers. Research on autophagy has

led the team to achieve high impact factor publications in relevant scientific journals such as PNAS, Nature Communications, Brain and others. The team of Innovative Therapies has also produced research relevant to their field, published in Nature Communications, PNAS, Annals of Neurology and Brain. In addition, scientists have carried out research in the field of metabolic diseases such as diabetes, non-alcoholic fatty liver and age-related ophthalmological conditions.

The Panel commends the choice to host young dynamic team leaders with new ideas and innovative research. However, the theme leaders are facing a large number of PIs with diverse research directions. This makes integration challenging, results in fragmentation of research, lack of critical mass and resources per project, and ultimately results in publications of low or mediocre impact. While there has been an increase of publications in the reporting period, there are still only a few high impact publications. Compared to previous evaluation period the publications in the top 5% and 10% have doubled, which is very positively noted by the Panel, but there is no improvement concerning papers ranking among the top 1% in their fields. During the visit, it was noted that PhD students need to have 2 to 3 papers at the end of their studentship, which could also be a driver for lower quality papers. The Panel fully supports the initiative to change these rules in favour of only one, ideally high-level first author publication being sufficient for the PhD students to have the PhD awarded.

Unlike several other institutes of similar size, CIBB has not put in place formal instruments to assess research performance. The Panel believes that stronger leadership is required. There is a clear need for CIBB to put in place (i) a scientific performance monitoring systems with external reviewers selected by the external scientific advisory board (EAB) and (ii) an annual appraisal system for academic and non-academic staff similarly as in other international institutions for monitoring success and integration.

The centre has international links with major international Institutions. This is demonstrated by the steady increase of publications featuring international collaborators (50% in the evaluation period from 2013-2017 compared to 34% in the preceding one). The researchers are continuing to participate in International EU calls as Co-applicant in the majority of them (JPND, ERA-Nets, E-RARE and others). 51% of the funding remains from FCT and only 20% are not competitive. While this is commendable, the Panel did wonder about whether future research might become somewhat dependent upon international partners, especially if the centre does not act as coordinator.

Between 2013-2017 30 PCT protected inventions, including 4 in B-stage and 10 licencing agreements, were obtained. During the same period CIBB-based research has created 10 spin offs that are located in the Biocant.

The Clinical Translational theme has been added to the CIBB research portfolio relatively recently. The now tight interface with CHUC has produced several publications. Form the presentation during the site visit, the Panel learned that CHUC have produced 1408 peer-reviewed publications in the last couple of years but in journals of low or mediocre impact factors. As the process of integration is still on-going, the research output coming from the clinical translation team is still not generating sufficiently high impact to achieve excellence in this area.

While the main aims are clear, it seems that the strategies to achieve clinical translational excellence are still unfocused. There is a need to have a restructured plan with a very careful identification of themes in this area and clinical scientists with strong leadership qualities also in the hospital. For example, an appealing idea is the creation of a Clinical Experimental Centre that can host first-in-man trials could facilitate international visibility and attract Pharmaceutical Companies, as well as international academic partners, thus facilitating funding and high impact factor publications.

As mentioned above, CIBB have a very high number of PIs in the three scientific areas with a large range of diverse research interests. The Panel suggests focusing on areas where CIBB is strong and has clear goals of high ambition, reinforcing these areas to generate the necessary critical mass and concentrate resources. It is also crucial to promote more active integration among different areas.

It was noticed that CIBB has only one ERC grant. To achieve its ambitions, the Panel suggest to establish an internal advisory structure, for example a committee with 4-5 people with different expertise that will take care of internal peer review of the application and conduct mock interviews, in order to achieve a better outcome of EC/International grant applications.

Good PhD student mentoring and supervision is now in place compared to the previous evaluation. However, there are still issues in combining clinical and basic research training during the PhD. In order to improve this, it is essential to exercise a stronger influence on the Hospitals to reduce face-to-face clinical responsibilities (up to 50%) which are time

consuming, especially if these involve transfer between institutions. In addition, an effort should be done in maintaining technician time. More PhD student projects should include research in BioCant to learn about applied biotechnology.

Overall, the Panel concluded that the “excellence” status of this centre cannot be maintained compared to other centres that have been assessed at this level. Therefore, the Panel scored the overall quality grade of the CIBB Very Good. However, the Panel has recognised the available potential and decided to support the CIBB to achieve again the “excellence” status.

From the positive feedback we have received from the PhD students, the Panel recommends to attribute 10 PhD student fellowships to CIBB. They should be allocated to the different programmes according to the CIBB scientific priorities. The Panel recognised the strengths of the CIBB in some areas and would like to support the Centre by awarding 4 Auxiliar Researcher positions to attract high calibre scientists/clinical scientists, especially if a consistent start package will be added.

The awarded Programmat Funding is in part to promote integration between groups especially for the clinical translation groups integrating more basic research, including activities at the Biocant Park.

Evaluation Panel: HEALTH SCIENCES - Biomedicine and Molecular Biology

R&D Unit: Centro de Investigação em Biociências e Tecnologias da Saúde (CBIOS)
Coordinator: Luis António Monteiro Rodrigues
Integrated PhD Researchers: 15

Overall Quality Grade: GOOD
Evaluation Criteria Ratings
(A) Quality, merit, relevance and internationalization of the R&D activities of the Integrated Researchers in the R&D Unit Application: 3
(B) Merit of the team of Integrated Researchers: 3
(C) Appropriateness of objectives, strategy, plan of activities and organization: 3

Base Funding for (2020-2023): 180 K€
Recommended Programmatic Support
PhD Fellowships: 4
Programmatic Funding: 485 K€, including for 1 (Auxiliar) New PhD Researcher Contract.

Justification, Comments and Recommendations
The CBIOS was created in 2011 in partnership with the University Lusófona to further advance research training in the health sciences and to promote translational research in pharmacology, phytochemistry/food sciences and drug delivery systems. The Panel recognized the contribution of CBIOS' R&D activity, which targets the exploitation of local and natural products (mainly for use in the cosmetic and food industry), as well as the identification and research of potential therapeutic agents in the treatment of cancer. These include projects based on a Portuguese West coast cherry, the Lamiacese plant, milk (as well as other dairy products) and a common jellyfish.

CBIOS is now publishing approximately 30 papers a year, and citations for these have increased to about 200 per year. However, in the Panel's view, some of the publications that were reported should probably not have been profiled as highly as they were in the submitted report. This is specifically the case for papers that arose outside of the Unit. Nevertheless, the site visit revealed that the CBIOS Unit is quite productive given its limited size and financial resources, including the current lack of FCT Base Funding. Furthermore, some of the high-profile papers that were reported (e.g. Saraiva et al., Journal of Cell Biology, vol. 202; 2013) were published by postdoctoral fellows that had moved to CBIOS within the last years in order to establish a research and teaching activity at CBIOS. This ability to recruit back international talent was well received by the Panel and underscores the dynamism and potential strength of the majority of the Principal Investigators at CBIOS. Overall, the site visit impressed the Panel in terms of the energy and cohesiveness shown by the PI, especially in light of limited resources and size of the CBIOS center.

A joint PhD program has been established with the Spanish University of Alcala de Henares. The 15 CBIOS scientists currently supervise 17 PhD students, which come from these two universities, but includes also international students from Brazil and EU countries, among others, indicating a good level of internationalization in the advanced training programs. Further, members of CBIOS participate in several EU COST programs, helping to promote international collaborations and networking. In addition, short visits to Uppsala, Pavia, São Paulo and Thailand have been organized for the PhD students and several research courses have been organized. The training program is focused on multidisciplinary and translational aspects, in tune with the research orientation of CBIOS.

A significant part of the CBIOS R&D activity is taken up by the organisation of advanced training courses and conferences and producing guidelines, which generates some revenue (that feeds back into the R&D activities). There is a bi-annual CBIOS science symposium and a platform for technology transfer (The Knowledge Transfer Center) has been started by CBIOS members in an effort to improve contacts with Portuguese and international businesses. However, some of these activities appeared to be in their infancy and will likely benefit from further growth and a more formal organization. Clearly, several connections to businesses were discussed, and these engagements generate revenue for the benefit of the CBIOS R&D program. However, there appeared to be no formal, long-term R&D contracts, rather a service-for-fee arrangement. It was therefore difficult to judge to what extent these industry contacts amounted to an academic research activity or were more purely based on a service-model. Going forward, some formal R&D contracts with industry where the research and training aspect are in the foreground, would likely be very beneficial for the continuing

evolution of the CBIOS program. It would serve CBIOS well to spell out what are the unique expertise/services that CBIOS can offer to industrial partners.

The CBIOS is organised into 3 main groups of 5 Integrated Researchers and their students. These groups work on either: (i) the extraction and testing of bioactive compounds, mainly from plants (PFS group), (ii) the development of in vitro models for skin and oncobiology research and animal models to test these products (PT) and (iii) the development of delivery systems for both drugs and non-drug products (eg food supplement and cosmetic products) using nanotechnology (DDS group).

The majority of independent investigators publish actively (4-9 publications per year). Considering the limited available financial resources, this is considered to be a good publication output.

The director of the CBIOS publishes a significant number of papers in The Biomedical and Biopharmaceutical Journal (BBR), which in principle is a good platform for CBIOS science. The journal provides visibility and internationalization, although online access rights to the articles published in the journal appeared to be unclear, and downloads of publications either not possible or only available for certain years. Nonetheless, as an Editor-in-Chief of this journal, the CBIOS Director helps to provide a platform for publications in English/Portuguese, which certainly is of value. What was less clear was whether and how this activity impacted the researchers negatively in terms of their ability to pursue other priorities. Editing a research publication is a time-consuming responsibility and there is a risk that it would dilute efforts to promote a joint research strategy, increase EU funding streams, and thus allow CBIOS to depend less on funding from its host organization.

As the CBIOS grows further and matures into a competitive research and education program, it would appear wise to further evolve a robust strategy for the development of CBIOS, including the establishment of a mechanism that will – over time – identify the next generation of scientists capable and willing to drive CBIOS' success to the next phase. In light of this recommendation, the FCT Panel of experts would also recommend CBIOS to establish a truly international, strong and present External Advisory Board capable of chaperoning, guiding and evaluating the CBIOS Director for the important next stage of the center's existence. The Panel found the institute's Self-Assessment to be useful. However, this was felt not to be an adequate replacement for a strong and guiding EAB. Hand-in-hand with the funding support that the FCT Panel will recommend, the Panel advises that some of these new resources be used to implement a yearly EAB meeting and review process.

A current limitation is that most integrated researchers appear to spend a majority of their working time on teaching and are therefore not able to dedicate significant effort to R&D activities. Since the group is rated to be productive and well-integrated as an overall team and as funding streams improve, a more balanced effort should allow the investigators of CBIOS to expand their R&D activities. Considering these limitations, the FCT Panel identified a clear potential for future growth.

The FCT Panel recommends that an increased effort should be made to try and link to some of the activities and facilities, in particular to those of other Portuguese or Lisbon centers of excellence, since excellence in science will require access to more sophisticated expertise and methodology that cannot be easily replicated at CBIOS for the foreseeable future due to the lack of critical mass, as well as the high costs of establishing and maintaining such resources.

The FCT Panel was impressed by the environment created by the current investigators and detected enthusiasm among the postdoctoral fellows. The same positive feedback also emerged in the Panel's discussion with the PhD students. The researchers are offered practical guidance and engendered a culture that appears to have established a young and dynamic group of people. Together with the energy of the laboratory heads, this bodes well for the CBIOS going forward.

In the objectives and strategy of the R&D Unit, emphasis is placed on further developing the institutional science culture, the promotion of training and dissemination activities, while the scientific activities are largely articulated along the existing organizational lines represented by the 3 main groupings present at the CBIOS. Going forward, the development of a clear, joint vision for CBIOS is encouraged, as at the moment, it is not clear where the emphasis of the R&D of these groups will be placed in terms of biological questions, biotechnological applications or medical/commercial relevance. Ideally, CBIOS should be identified with a clear scientific mission statement, which currently has not been sufficiently elaborated.

Given that one of the major goals of the CBIOS is translational research, a fully convincing strategy for how additional, robust and long-term links to industry could be established should be provided in the future.

In summary, the FCT Panel was impressed by the productivity and spirit within CBIOS and was convinced that the center now has reached the maturity to be run as an official center.

The focus of the CBIOS on teaching via research will continue in the coming years. A total of 6 PhD fellowships have been requested, with 3 PhD students starting in 2019 and 3 more in 2021. In addition, 2 contracts for staff with PhD at the Auxiliar level were requested. The subjects that the PhD students will be working on have not been defined. Similarly, for the post-doctoral contracts, these will reinforce the competence of existing groups. However, it is unclear which group these young scientists would join if awarded. Considering the relatively modest number of positions that were sought and that can be accommodated at the relatively small CBIOS center, such information may be useful for planning purposes and to help identify and discuss the institute's strategy in the future.

In light of the significant improvements at the CBIOS center and the available resources, it is recommended to fund a total of 4 PhD fellowships and 1 Auxiliar Researcher contract at this emerging center.

The Programmatic Funding awarded should in part by applied to strengthen the indicated training and course participation efforts, as well as for the purchase of new equipment. The FCT Panel clearly felt that investments made through this scheme would very much benefit CBIOS in terms of helping it to markedly improve its equipment range and thus allowing the researchers to gain access to a broader and relevant range of methodological expertise.

Evaluation Panel: HEALTH SCIENCES - Biomedicine and Molecular Biology

R&D Unit: Centro de Investigação em Biomedicina (CBMR)
Coordinator: Karl Magnus Petersson
Integrated PhD Researchers: 40

Overall Quality Grade: WEAK
Evaluation Criteria Ratings

(A) Quality, merit, relevance and internationalization of the R&D activities of the Integrated Researchers in the R&D Unit Application: 2
(B) Merit of the team of Integrated Researchers: 2
(C) Appropriateness of objectives, strategy, plan of activities and organization: 2

Justification, Comments and Recommendations

The CBMR Unit at the University of Algarve in Faro was founded in 2003 and currently receives core funding by the FCT. It is managed by Professor Karl Magnus Petersson, an expert on human cognition and language processing.

In terms of research questions, CBMR's research activities are structured along four major themes, ranging from cardiovascular biology, oncobiology, biomolecular research and developmental/degenerative CNS disorders.

CBMR's cardiovascular theme has the objective to identify novel factors that contribute to congenital malformations or other heart pathologies by taking advantage of gene-variation within patient cohorts, coupled with the determination of the role of these genetic variations using animal- and cell models. More recently, this theme has been expanded by taking into account the role of gut microbiota in congenital heart, cardiovascular and metabolic disease.

The oncobiology theme includes classical approaches to studying the role of oncogenes in tumor formation and maintenance, with an aim toward establishing novel diagnostic markers and therapeutic targets. One area of focus has been the study of the role of the PI3K/AKT/FOXO cascade and ROS-dependent signaling.

A third theme is more methodological than driven by an overarching biological theme, namely the biomolecular research theme. This is focused on biomedically relevant molecules, including the determination of their biophysical properties and function. Efforts are under way to solidify a protein analysis platform for the in vitro study of new target molecules and to develop novel instrumentation, including bio-layer interferometry to measure binding events.

CBMR's brain theme focuses on the broad neurobiology and behavior themes of learning & memory, language processing and reading skill development, mechanisms that underpin the development of neurological diseases, including neuromuscular changes related to aging and neurodegenerative diseases such as dementia and Parkinson's disease, which the Unit seeks to address also by developing advanced gene-based and cellular strategies to delay neurodegenerative disease.

At the structural level, the CBMR is an R&D Unit of the Algarve Biomedical Research and Training Center, of the Department of Biomedical Sciences and the Department of Medicine of the Algarve Hospital and Algarve Regional Administration. It houses core facilities in microscopy, cell culture, cell sorting, gene expression, animal house, brain and biomechanics within the context of a new research building.

CMBR seeks to develop biomedical research and translation, as well as training, and to leverage these efforts in order to establish valuable new partnerships. It has been key in developing a unique link to a major Portuguese Biobank facility, which could be extremely valuable to the researchers on-site. In addition, it enjoys links to a Medical Simulation Center, a Clinical Research Incubator Center, an Eye-Tracking and Biomechanics Platform and is involved in the expansion of the Animal Facility. The stated goal of the CMBR is to take advantage of this local context to innovate research and develop several clinically-oriented research programs toward the development of new partnerships and in order to attract more extramural funding. These activities have allowed CMBR, for example, to establish collaborations with a network of cardiologists involving 10 Portuguese Hospital Centers that collect biological samples and patient data on specific cardiomyopathies. Together with the establishment of the Biobank, this achievement certainly represents a potential strength of the Unit, local university and regional context. Moreover, the CMBR has participated in four COST Actions, organizes public outreach activities and several conferences and workshops.

In reviewing the quality, merit, relevance and internationalization of the four presented research themes, the site-visit confirmed that the four themes co-exist together without sufficient integration into an overarching research theme, Unit strategy or Unit culture.

Moreover, while some areas are of reasonable strength and originality and have potential impact, such as the oncobiology, going forward the strength of these areas is in serious jeopardy. This is because several key investigators have either left CMBR recently or are about to move to other institutions. A strong institution would generally welcome the turnover of key talent as a sign of research excellence, career development and as an opportunity for local, institutional and strategic renewal. However, this Unit is short of strong teams and neither were these departures appropriately discussed in the general presentation of the Unit nor was any strategic vision presented for the possible evolution of the Unit. Clearly, the action of the Unit's direction is inadequate to both this apparent threat of losing key personnel and to the overall evolution of the Unit. Typically, in such a situation the direction should seek advice from a strong and unbiased external Scientific Advisory Board (SAB). The SAB should be also instrumental in the assessment of potential candidates to join the Unit and give advice on the research plans of the teams.

Within the four themes, the brain topic (coordinated by K.M. Petersson) publishes quite well and is reasonably well-funded, albeit it was not clear which fraction of the non-Portuguese grants are available for research at the CBMR, as several grants mention as affiliation the Max Planck Institute for Psycholinguistics (MPI) in Nijmegen (Netherlands), but not the CBMR. The specific research questions addressed in this theme were judged to be of value. However, the research on dyslexia fits less well into an otherwise predominantly molecular/signaling-driven R&D Unit. A concern of this committee was the apparent double affiliation of the CBMR coordinator as a MPI researcher. A high number of research papers of this group have double affiliation and the PI spent a significant amount of time (40% according to the Coordinator) in the Netherlands. While, in principle, such transnational affiliations and contacts are highly welcomed by the Panel, as they can help promote internationalization, the serious scientific and organizational problems of the CBMR clearly require full-time leadership. The current arrangement did not convince the Panel as being beneficial to the development and management of a robust research institute in Faro. As pointed out later, the benefits of the link to the Max Planck Society do not appear to spread across the entire Unit, but rather appear to perpetuate some of the observed weaknesses within the Unit. These weaknesses include, but are not limited to an insufficient focus, lack of transparency relating to management decisions and an insufficient drive toward the establishment and maintenance of a R&D Unit that takes advantage of and complements the specific strengths of the local and regional research environment.

The cardiovascular research theme (coordinated by J. Bragança) has a good number of publications across the reporting period, takes advantage of the biobank and cardiovascular clinic collaborations in order to gain access to patient cohorts and is planning to expand to timely research questions, such as the study of the microbiome. However, what is unclear is how this latter aspect is going to be integrated into the overall research plan, as this is considered challenging and likely difficult to reproduce easily using model organisms. In addition, international competition is fierce in this field of research and the Panel is not convinced that the CBMR team is competitive at this level.

The Biomolecules Research (BR) theme (coordinated by E. Pinho Melo) is dedicated to small molecules, protein biochemistry and the biophysical characterization of proteins involved in disease mechanisms. While this type of research would be worthwhile and capable of providing methodological expertise across the CBMR, it was inadequately integrated into the Unit's vision. Indeed, the discussion with the coordinator who returned from a sabbatical in the UK revealed the complete lack of concept. While recognizing that much of these assets are still underdeveloped and that the University would stand to profit from this biomolecular expertise, this section's strength and expertise was far from being mature. The acquisition of novel biophysical instruments, such as a hybrid QCM/HCC instrument, may be useful but needs a convincing rationale. What remained unclear is how the expertise developed at the CBMR in this area would stand to benefit the Unit, university, region and Portugal as a whole. In addition, considering the Unit's goal to develop biomedical research and translation, the current number of patents is very low compared to other Portuguese institutions.

The strongest theme relates to cancer and cell signaling with a very good publication record, international visibility, a compelling leadership and an ability to clearly articulate its scientific approach and cohesion among the teams. Unfortunately, it emerged during the site visit that W. Link, the coordinator of the oncobiology theme, will shortly be taking on a distinct appointment outside of Portugal. He informed the Panel that this decision was motivated exclusively by private reasons. While it reflects well on the CBMR that one of its Principal Investigators is able to secure a competitive group leader position abroad, this loss of expertise and the apparent absence of new talent being recruited, represents a serious threat to the Unit.

The departure of the Oncobiology coordinator W. Link and the departure of another successful scientist (R.G. Martinho), who moved to the University of Aveiro, significantly weaken the oncobiology and cell signaling themes and the CBMR as a whole.

It is especially within this context of staff turnover and recruitment that strong management and leadership, coupled with a clear vision for the future development of the CBMR would be required. In the assessment of this review Panel, this is the strongest limitation to this Unit, which benefits – in principle – from specific local strengths, such as the new biobank and the potential to develop a strong bioinformatics expertise. This concern extends to the training level as the Unit contributes to a computational biology module within its Master degree and can recruit from a good pool of undergraduates in this research area.

The Panel noted the shift of a member of the BR theme (M. Futschik) to the University of Plymouth, his new primary base of scientific activity. He was instrumental in developing a systems biology initiative at the University of Algarve (since 2008). Considering the on-going rapid pace of changes within life science and medicine, this was considered an important development. Furthermore, it fitted well with the local training environment, providing a fertile ground for training and career development for young people in this less privileged region of Europe. While M. Futschik was present at the review and clearly maintains links to the CBMR, the site visit did not help the committee obtain a convincing understanding of how the Unit plans to address this current and future opportunity in human health. The planning for a strong systems and computational biology was judged to be underdeveloped and thus not aligned with the potential that this Unit and the University could stand to gain (e.g. biobank, patient cohorts, genomics, very good access to local student talent pool). This was also raised as a concern by the Scientific Advisory Board, which concluded that the Unit would be well served to recruit strong PIs from the outside. At the time of the site visit, no convincing plans to compensate for this loss of expertise were presented.

Particularly disheartening to this committee was the fact that most of the PhD students appear to be highly motivated and happy to work within the CBMR, but suffering from the inability to conduct science at a top level due to administrative issues. Considering that the investigators judged that recruitment to Faro was easy, the vicinity to medical students, and the running of an innovative Masters program, these administrative shortcomings are a major hurdle that needs to be addressed.

Further, the University was tasked with showing its commitment to the importance of scientific research in order to maintain a visible systems biology profile. Unfortunately, the site visit did not make it sufficiently visible or clear how the University intends to address the serious loss of expertise within the CBMR and how it intends to support scientific research in this field. This includes specifically systems biology and health medicine, for which CBMR appears to be ideal to develop a local hub or expertise.

Laboratories have insufficient technical help and central administration offices appear to “shut down” for several months a year for internal accounting. While this appears to be a problem across Portugal, the length (extent of time) that this occurs at the University of Algarve appears to be unprecedented. This Panel feels that the University needs to strongly re-evaluate its procedures or risk its stated commitment to research.

A current limitation is that most integrated researchers appear to spend a majority of their working time on teaching and are therefore not able to dedicate significant effort to R&D activities. The University should identify a mechanism to allow researchers within the FCT Unit to expand their R&D activities, for all integrated researchers that are judged externally to be scientifically productive.

The site visit revealed a Unit currently defined by a high amount of scientific dispersion and a strategic management of the Unit that is insufficiently proactive about managing turnover, performance and implementing a robust plan. This is a concern, since a focused, integrated approach would benefit the training of PhD students and postdocs, and promote the visibility of the Unit.

This Panel recommends CBMR maintains and strengthens the impact of its SAB. Indeed, it is essential that the leadership of CBMR works with the SAB to ensure the steady development of the Unit. At the present time, there seems to be insufficient motivation within the Unit leadership and the University to follow the SAB’s advice: the review committee noted the on-going shortage of staff within the platforms; there are too few technicians, many on only 1 year contracts and few perspectives; the animal house is understaffed; the SAB recommended that PIs should meet for chalk talks, discuss priorities and set them in agreement with the scientific leadership of the institute. Such an exercise is deemed essential, but appears to be underdeveloped across the Unit. While at least one of the themes organizes

retreats and others review each other's grants, there is insufficient cross-fertilization of activities within the four themes and leadership. The Unit would also profit from implementing an external review of the performance of its PIs.

The FCT Panel also recommends that an increased effort should be made to link the CBMR to activities and facilities of other Portuguese centers of excellence. This is particularly true for advanced expertise and methodology that cannot be replicated at CBMR for the foreseeable future. Due to the lack of critical mass and the high costs of such resources, the CBMR should seek out, establish and maintain such strategic alliances.

Some of the limitations within the Unit do not appear to be the result of an insufficient number of capable scientists, but rather appear to result from insufficient communication. Concerns were raised about the lack of transparency with management decisions, relating for example to the (few) council meetings. Concerns were also raised internally about the Unit leadership. However, it was not clear whether these issues could be resolved by acknowledging the concerns and changing course. This Panel received local input seeking for new Unit leadership. Overall, the Panel feels that the Unit did not do a sufficiently good job at preparing itself for the review. Ultimately, the Unit director will be well served to analyze how the current situation, particularly at the level of communication and teamwork arose, and to take the necessary steps to permanently steer the Unit in a new, positive direction.

The shortcomings were in display when discussing plans to recruit new PIs, considering the departures of the strong PIs Futschik, Link and Martinho. There appeared to be no strategy in place to manage the situation and the opportunities that this turnover represents. At the level of scientific coherence, there appeared to be no strong vision for the CBMR coming from the leadership of the Unit, other than that coherence comes from the structure, internal procedures and processes within the Unit. This Panel was expecting to hear a strong vision for the Unit that takes robust advantage of the local environment and that factored in the strengths of this region of Portugal. Moreover, several PIs have appointments elsewhere in Europe. This could be used to strengthen the Unit and to add value. Yet, this aspect is underdeveloped and not integrated into the Unit's vision. Moreover, several young PIs had good ideas about big data, genomics, epigenomics and medicine, the clinic and graduate education. Less clear was how these ideas could be implemented or whether and how they formed part of the vision of the Unit. Overall, this Panel was seriously concerned about the lack of strategy, vision and plan, which are the responsibility of the Unit's leader.

There are also structural problems at the University that became apparent. In addition to the long administrative "closure" periods mentioned earlier, there is no functioning grants office. A support system for handling external grants is necessary, considering the complex financial and legal requirements for many external grants. It would be useful if the Unit or University organized grant writing workshops and other transferrable skills training to become competitive as an organization for inclusion in EC grants. This Panel encourages the University to use some of its resources toward establishing a modest, but clearly visible and robust set of activities and resources that will facilitate the further integration of the CBMR in a European context.

Considering the criticisms raised above, this FCT Panel cannot recommend funding to the CBMR R&D Unit, nor a contribution to the salary costs of new PhD researchers. The FCT Panel recognizes the individual strength of individual investigators, and recognizes the activities present within several of the themes in the R&D Unit. However, overall and on balance with other Portuguese institutions, this Panel deems the overall strength of the Unit not to be sufficiently clear at the present time. With adequate changes, this Panel is convinced that there is the local potential at the University of Algarve to build on the current strengths through appropriate new hires and – importantly – several major administrative changes, re-organization and new resources, including a stronger and permanent leadership with broad competence and management skills, more technical support for facilities and animal house, grants office, faster admin financial procedures and the provision of courses typical of EU-funded institutions. With these changes in place, a reorganized CBMR will deliver a robust vision for the Unit.

Evaluation Panel: HEALTH SCIENCES - Biomedicine and Molecular Biology

R&D Unit: Centro de Investigação em Ciências da Saúde (CICS-UBI)
Coordinator: Ana Paula Coelho Duarte
Integrated PhD Researchers: 67

Overall Quality Grade: GOOD
Evaluation Criteria Ratings
(A) Quality, merit, relevance and internationalization of the R&D activities of the Integrated Researchers in the R&D Unit Application: 3
(B) Merit of the team of Integrated Researchers: 3
(C) Appropriateness of objectives, strategy, plan of activities and organization: 3

Base Funding for (2020-2023): 719 K€
Recommended Programmatic Support
PhD Fellowships: 5
Programmatic Funding: 445 K€, including for 1 (Auxiliar) New PhD Researcher Contract.

Justification, Comments and Recommendations
CICS-UBI is a relatively young health and science research centre implanted in the University of Beira Interior. It is currently composed of 67 scientists working on research and development, often of regional products for clinical and pharmaceutical applications, or involved in more fundamental research focused on neurological and endocrine-related disorders.

During the evaluation period, CICS-UBI has made a number of contributions both technologically and in understanding molecular mechanisms underlying diseases with high social impact (prostate cancer, endocrine disorders, Parkinson's disease, Alzheimer's disease, Candida infections, delivery of anticancer and anti-epileptic drugs). The Unit published 573 papers in the last 5 years giving an average of 2 publications per year per PhD, with an impact factor of 3 to 4. In the Panel's view the overall scientific productivity and output quality of the Unit was deemed to be good but not yet at sufficient level to compete effectively internationally; this is largely due to the great number of different on-going research projects. Indeed, this point was raised by the EAC and led to a recent restructuring of the centre in order to consolidate areas of interest between CICS-UBI scientists. Nevertheless, quite a high degree of dispersion in the research topics presented by each group remained obvious during the site visit and efforts should be continued to focus on the niche strengths of each of the teams.

The centre is currently organised into 4 research groups comprising 14 to 21 PhD scientists. The Biomedicinal Chemistry and Drug research group work on drug discovery based on bioactive compounds in natural regional products. Their work has led to 3 international patents and a spin-off that interacts closely with the Unit. However, they are targeting a wide variety of domains ranging from gynaecology, dermatology, gastrointestinal and respiratory disorders and it is not clear how all the pipelines to screen these products are defined. The Panel felt that a more focused approach and collaborations in specific areas with other national units that have developed high throughput screening techniques would improve the visibility of this dynamic group.

Work of the Biopharmaceuticals and Biomaterials group has led to the development of effective and economically affordable biotechnology approaches for drug delivery and biomaterials for tissue repair as well as the development of fast and simple purification processes. For this the group has established close collaborations with national and international companies as well as a CNRS laboratory in France.

On the fundamental research side, studies of the Hormones and Metabolism group are focused on endocrine disorders and hormone-dependent cancers and have led to the identification of new susceptibility genes, biomarkers and molecular pathways. The PI is the Coordinator of National multi-centre research projects to identify and genetically characterise patients with endocrine diseases.

Finally, the major focus of the Neurologic and Neurovascular Disorders group has been the choroid plexus. They have more recently been investigating a variety of brain disorders, including Alzheimer's disease, Parkinson's disease, multiple sclerosis, stroke and brain tumours. Notably, their studies have led to the identification of active compounds in

pre-clinical models of Parkinson's disease and stroke and to the development of nano and micro-formulations capable of crossing the blood-brain barrier that are effective in promoting neuroprotection and brain regeneration/repair. This work has led to higher-level publications and one of the PIs obtaining the L'Oréal Medal of Honour for Women in Science.

CICS-UBI scientists have been involved in EU Training Networks and COST Action programs in the last few years, which has helped increase the international visibility of the Unit and led to higher impact factor publications. This effort should be continued to try to obtain competitive international funding in the future. A current limitation is that the majority of integrated researchers with PhDs have teaching or clinical positions and devote less than 50% of their time to research. The centre would benefit from the input of an increased number of young full-time researchers.

Moreover, the CICS-UBI has an active graduate program with 150 masters and PhD students. They organise a cycle of seminars for PhD students with invited speakers from other national and international institutions. They are also active in outreach activities and use social media for the dissemination of scientific educational material, as well as organising initiatives to interest undergraduate students and school children in scientific research. Within the CICS-UBI, a number of "structural programs" have been developed to improve communication and image of the centre, search for funds, monitor scientific output, promote international collaborations as well as collaborations within CICS-UBI.

All this contributes to creating a positive and dynamic working environment within the CICS-UBI, which is further supported by the good relationship that exists between the University of Beira Interior and the centre. This, together with the increase in international collaborations and original findings of individual researchers in their field was perceived by the Panel as clearly positive factors, which should contribute to further progression of the centre in the coming years. Nevertheless, the scope of research interests within the CICS-UBI is undoubtedly too vast for a centre of this size. Important efforts should be pursued in order to focus both applied and scientific research into a more limited number of areas of investigation to obtain greater visibility, higher impact factor publications and competitive international funding in the future. The Panel feels that it will be difficult for the CICS-UBI management team to achieve this alone. Therefore, the Panel strongly advises the Unit to form an enlarged, both critical and constructive EAC comprising competent international experts in each of the areas of research within CICS-UBI in order to help the Unit to build on their existing niche positions and strengths.

Given the good level of training at the CICS-UBI, the Panel recommends that the Unit be attributed 5 out of the 6 PhD fellowships requested. The distribution of the fellowships to the centre's PhD programs should be decided by the Unit based on their future scientific strategy. In addition, the Panel recommends that CICS-UBI be attributed 1 Auxiliar Researcher position and strongly supports the Unit's wish to use this position to strengthen a more collaborative and integrated research within the centre. The Panel recommends Programmatic Funding to be used in part to support integrative, transversal lines of research building on the niche positions and strengths of the Unit.

Evaluation Panel: HEALTH SCIENCES - Biomedicine and Molecular Biology

R&D Unit: Instituto de Biomedicina – Aveiro (iBiMED)
Coordinator: Manuel António da Silva Santos
Integrated PhD Researchers: 46

Overall Quality Grade: VERY GOOD
Evaluation Criteria Ratings
(A) Quality, merit, relevance and internationalization of the R&D activities of the Integrated Researchers in the R&D Unit Application: 4
(B) Merit of the team of Integrated Researchers: 3
(C) Appropriateness of objectives, strategy, plan of activities and organization: 4

Base Funding for (2020-2023): 554 K€
Recommended Programmatic Support
PhD Fellowships: 8
Programmatic Support: 770 K€, including for 2 (Auxiliar) New PhD Researchers Contracts.

Justification, Comments and Recommendations
The Aveiro Institute of Medicine iBiMED was created in 2014 and its first FCT funding arrived in May 2015 with groups starting to be hosted together in early 2016. Whereas iBiMED could have expected a mid-term evaluation as they were only recently formed, under the FCT auspices we submitted them to a full evaluation in late 2018, which should allow them to keep their impressive momentum.

Despite its young age and relatively small size iBiMED is starting to implement a management infrastructure on par with that of more established and bigger units. Firstly, it has invested in setting up a structure that helps in writing and preparing project proposals. This structure was immediately fruitful. It incentivized researchers in submitting proposals and those were more successful than the national average. For example, 56% of Aveiro's projects were funded by FCT in 2018 compared to a national average of 38%. Secondly, iBiMED wants to increase the management skills of its PIs and career development of its members by financing, respectively, their participation to EMBO leadership courses, which are highly recognized in the field and courses organized by the Portuguese start up Ciencia Clara. Of note two young PIs already attended the EMBO laboratory management course. Thirdly, upon its creation it has established an international Scientific Advisory Board (SAB) to provide guidance on scientific and organizational matters.

Following, the SAB recommendations written after its October 2016 visit, iBiMED has continued to embrace its responsibility in training the new generation of scientists through (i) a two supervisors scheme, (ii) establishing student's joint meetings and (iii) requesting funding to organize a scientific retreat. The iBiMED graduate students and postdocs were appreciative of these training possibilities and enthusiastic in working in a young and motivated environment. To foster interaction between researchers at all levels equipment is shared and laboratories are organized either as Open Space or in specialized research facilities.

Since its implementation, i.e. between 2015 and 2017, iBiMED has produced a total of 236 papers listed in ISI Web of science. Not only iBiMED's productivity looks to be on an upward trend, but also the quality of the published reports is increasing with the number of top 10 percentile publications growing yearly and the median impact factor on the rise. Both the senior and young PIs publish regularly, with each having a fair amount of reports being published in top 10 percentile of publications.

Although the Panel recognized the substantial efforts in attracting senior established foreign scientist and in recruiting young high profile national researchers (see below) a specific effort should be dedicated to increase the level of contributions from the local scientists. This might require reorganizing the existing laboratories and PIs into more productive structures. Revealing is the fact that only one of the three publications with highest impact that were highlighted in the report is emanating from iBiMed while the other two arise from collaborative work not led by scientists in the Institute. Indeed, the prestigious 2013 New England Journal of Medicine and 2014 Nature Genetics publications do not specify iBiMED as the address of the Portuguese co-authors and thus, cannot be considered bona fide achievements of this institute.

Worryingly for the Panel, two of the most successful PIs (publication wise) are heading laboratories in multiple countries and thus are only part time in Aveiro. These international recruits are funded through rolling contracts renewed yearly and funded by the private Ilídio Pinho Foundation (IPF) or via part time teaching contracts of the Department of Medical Sciences of the University of Aveiro. While the above situation benefits iBiMED in the short term as these researchers bring noteworthy skills to Portugal, it is unclear how this could be sustained on the long run. The iBiMED directorship and Scientific Council are well aware of this threat and are committed to try to find perennial solutions. The Panel lauds their willingness to attract the best scientists using the tools and funds that are available even with the inherent risk. Importantly, the greater visibility that the international appointments provided to iBiMED allowed the Unit to successfully recruit three young and one established PI in Bruno Jesus, Bruno Neves, Ramiro Almeida and Rui Martinho. The Directorship has identified two other top-level young researchers at the University of Göttingen, who are potentially keen to join in the future.

Whereas iBiMED research is driven by PIs curiosity, collaboration is further nurtured via a Transversal Research Program (TRP). The ongoing TRP aims at understanding i) the role of age related protein aggregation on cognitive decline and in the etiology and development of chronic diseases and ii) clarify how down regulation of protein synthesis during aging impacts musculoskeletal and other diseases. It is transversal to iBiMED PIs research topics such as dementia, diabetes, cancer, respiratory diseases, inflammation and aging. Importantly, laboratories are incentivized but not obliged to work in the TRP. The TRP is supported through multiple funding schemes (iBiMED´s own budget, FCT joint actions, regional government projects and IPF). About 80% of iBiMED PIs are currently participating to the TRP. Promising but preliminary results obtained by the TRP were presented to the Panel during the site visit. The TRP identified at which developmental stage and in which tissue aggregation was prominent and which proteins were involved.

Now that the TRP is well underway, iBiMED wants to widen its scope to systems biomedicine with the goal of detecting early physiological signs. Towards this goal it will create together with other local entities the conditions to carry out translational and clinical research in the Aveiro region. This initiative plans to “expand the local hospital as well as create an academic clinical center to transform the existing clinical assistance in a teaching and research hospital”. Would this be successful, it will allow building bridges between iBiMED basic research and local clinical entities. Successfully integrating basic research and clinical infrastructure is always a tour-de-force; however, it comes with economical and organizational challenges, often exacerbated by conflicting goals of scientific and clinical endeavors.

In summary, the FCT Panel was impressed by how fast iBiMED was able to create a collaborative and productive research team. We commend its directorship and scientific council for fostering a highly dynamic and excellent work environment.

The iBiMED graduate students are enrolled in three different PhD programs of the University of Aveiro, i.e. Biomedicine (PDBM), Health Sciences (PDCS) and Biotechnology. A total of 64 PhD fellowships and three new researchers at the Auxiliar level have been requested, which is, however, entirely unrealistic in view the number of fellowships to be awarded through this FCT Program.

In light of the scientific achievements of iBiMED in spite of its young age, the Panel recommends that a total of 8 PhD fellowships and 2 Auxiliar Researcher contracts be awarded to this emerging center.

The Programmatic Funding awarded should in part be used to strengthen the indicated training and course participation efforts, as well as primarily for the purchase of new equipment. The FCT Panel clearly felt that investments made through this scheme would benefit both iBiMED and the Genome-Portugal initiative.

Evaluation Panel: HEALTH SCIENCES - Biomedicine and Molecular Biology

R&D Unit: Instituto de Biosistemas & Ciências Integrativas (BioISI)
Coordinator: Margarida Sofia Pereira Duarte Amaral
Integrated PhD Researchers: 131

Overall Quality Grade: GOOD
Evaluation Criteria Ratings
(A) Quality, merit, relevance and internationalization of the R&D activities of the Integrated Researchers in the R&D Unit Application: 3
(B) Merit of the team of Integrated Researchers: 4
(C) Appropriateness of objectives, strategy, plan of activities and organization: 3

Base Funding for (2020-2023): 1567 K€
Recommended Programmatic Support
PhD Fellowships: 8
Programmatic Funding: 435 K€, including for 1 (Junior) New PhD Researcher Contract.

Justification, Comments and Recommendations
The BioSystems and Integrative Sciences Institute (BioISI) was created in 2015 with the aim of using integrative systems approaches in biomedical, physics and computational sciences. It hosts 8 research groups (with more than 130 integrated PhD researchers), each with a single group leader and several principal investigators. Research groups are integrated in thematic lines headed by a coordinator. The Scientific Committee is composed of the group leaders chaired by the director. Most of the groups contribute to all the 5 thematic lines (Biomedicine, Biotechnology, Biological Chemistry, Bioinformatics, Biological Physics). This is a very especial organization that is probably due to the fact that these lines are defined using a technical rather than scientific perspective. Interestingly every group contributes to the three flagship research projects: Grapevine and wine optimization; cystic fibrosis and neurodegeneration; and enabling biotechnologies (AFM-based technologies and innovative computational approaches). Overall, the structure seems to be quite focused to these research areas and the Panel is fully supportive of a clear strategy to make strong research outputs based on collaborative efforts and new technologies. The special focus of the Unit and the relevance of biosystems and technological approaches combining physics and biocomputation makes this young Unit quite attractive with an added value as collaborator for many other institutions in Portugal and abroad.

BioISI governance is established by three major bodies: Director and Executive board (including coordinators of the thematic lines), Scientific Committee (with all group leaders) and the Scientific Advisory Board composed of 6 European/USA scientists. Additional administration offices include communication and outreach, industry liaison, etc. The Panel appreciates the effort dedicated in the last few years to make this recent merging a successful operation and recommends to reinforce the use of the External Advisory Board for the strategic decisions in the future. In particular, the scientific and technical focus as well as the strategy for the recruitment of new young investigators are major topics for discussion as indicated below.

The Unit has been only active since 2015 and it is difficult to evaluate whether the current structure has been critical for the productivity reported so far. In any case, the Panel feels that the groups are quite cohesive and the technological focus will be critical for the strategy in the upcoming years. The BioISI shows a strong interest in providing excellent technical services (AFM, EM, 4D, Genomics, Proteomics, Computing, etc.) not only to BioISI investigators but also to other labs in the University of Lisbon or other institutions. The Panel is fully supportive of promoting technological development in BioSystems whitin BioISI as a major flagship for further development in the future.

Scientific focus in the different thematic lines is much more disperse than expected from the three flagship projects. Each thematic line hosts multiple unrelated research projects that are not aligned with the central goals of the Unit (e.g. research projects on Braf and colon cancer, mTOR in the cell cycle, miRNAs in stem cells, etc.). Whereas many of these areas are of general interest, the Panel is worried about the dispersion in many topics in which the BioISI teams are not competitive at the international level. The Panel is also concerned about the relatively low level of interaction between different thematic lines. For instance, research activities in the BioPhysics thematic line would be really useful in many projects in the Biomedicine or Biotechnology TLs but this integration does not seem to occur at the moment. The Panel

strongly recommends to work out a more real integrative model among the different teams to consolidate scientific and technical excellence in a few research topics.

The record of publications is good with papers in top journals, a large number of papers published, and a good percentage of moderate-high quality papers among them. It is a bit surprising that the total number of publications and the publications within Q1 have been decreasing since the creation of the Unit in 2015. A possible explanation is the tendency to increase the average impact factor of top publications suggesting a strategy to increase international visibility. The Unit indicates 872 publications (174 per year) since 2013 although it was officially created in 2015. It is not easy to discriminate which publications are actually a result from the structure of the Unit itself. For instance, the work reported in some relevant papers was performed before 2015 (Almaca et al., Cell 2013; Alves et al. Hum. Mol. Genet 2014; Hadley et al., Nat Commun 2014; a patent in 2013, etc.). Overall, the Panel agrees on the need to increasing the scientific and technical quality of the publications in favor of stronger publications that may contribute to the attraction of young scientists and international funding in the future.

Current international funding is limited (less than 10% total budget) and additional strategies to improve this situation need to be implemented in the future. The Panel agrees with the current efforts in the institution to increase international applications, participation in international networks, etc.

Several PhD programmes at the University of Lisbon host BioISI students. However, the Panel considers especially relevant the PhD programme focused on Systems Biology, in line with the overall strategy in the Unit to focus on BioSystems research. This programme hosts about 11 fellowships per edition including a significant ratio (1:2) of international students. Whereas students are motivated and appreciate the technical focus of training at the BioISI, some of them miss a more real integration with BioISI research lines, especially those who do not belong to the BioSystems programme. Further effort in consolidating a training office and improving communication with students seem also needed. The Unit has also dedicated a special effort to develop an advanced training postdoctoral programme to carry out multidisciplinary cross-group projects on major BioISI thematic lines. This initiative is very well evaluated by the Panel and further efforts to focus on the strengths of the Unit will be quite useful to consolidate the Unit.

The strategies for the next years show a clear interest (more apparent on the paper than when reviewing the actual projects in the Unit) in the three general research lines of interest and strong commitment to promote internationalization, partnerships, high level training, new technologies, etc. Within the plan for the next years, the Unit proposes to hire 6 new PIs to reinforce the same three main projects, and 4 new PIs to reinforce technology development (AFM, FFM, nano-methods, etc.). The plan includes a 25k€-installation grant for these PIs. Whereas the Panel appreciates this effort, it seems that a rapid, unfocused growth in the number of group leaders may produce more dispersion than cohesive growing. The Panel strongly recommends to dedicate additional efforts to recruit a few, but very promising scientists in very special areas required for further consolidating the BioSystems focus in the Unit. These new PIs would benefit from bigger start-up budgets so they may become competitive at the international level in these specific areas.

Two new core facilities (flow cytometry and protein services) are proposed. The Panel agrees with the need to increase the power in protein technologies as a major area of growth for the future in BioSystems. Other activities are planned for expanding dissemination activities, collaborations, networkings, industrial partnertships, etc.

Overall, the plan is appropriate for a young institution with ambitious plans and clear ideas for the future. However, how these ideas are being implemented at the moment is not as clear. The Panel recommends to make a strong commitment to focus in BioSystems (scientifically, technically and in training) with a minimal dispersion, and to invest in a few, but highly promising young scientists that may increase the quality of scientific papers, international visibility, and secure international funding.

The Panel fully supports the plan for hiring new researchers. The Panel recommends to start hiring a young but promising researcher with chances to obtain international funding and a clear focus on Systems Biology complementary to other research lines in the institution.

The proposal for 2019-2022 actions to reinforce research includes hiring new researchers at different levels, and increasing the technical power by investing in the core facilities.

Given the scientific and technical focus of BioISI in BioSystems, the Panel feels that the opportunities for collaborative international efforts are of great interest.

The proposal also indicates the interest in hiring 10 new PIs in the next years. Whereas this is in line with the general goal of growing in the next years, the Panel recommends to evaluate very carefully the new incorporations at the PI level to select candidates that may really promote the international visibility and the opportunities to secure international funding at the BioISI. Assigning an appropriate installation grant to the new PI may also favor its rapid international competitiveness. The Panel also supports the investment in a protein core facility given the relevance of protein technologies in Systems Biology.

Evaluation Panel: HEALTH SCIENCES - Biomedicine and Molecular Biology

R&D Unit: Instituto de Investigação do Medicamento (iMed.ULisboa)
Coordinator: Cecília Maria Pereira Rodrigues
Integrated PhD Researchers: 115

Overall Quality Grade: GOOD
Evaluation Criteria Ratings
(A) Quality, merit, relevance and internationalization of the R&D activities of the Integrated Researchers in the R&D Unit Application: 3
(B) Merit of the team of Integrated Researchers: 3
(C) Appropriateness of objectives, strategy, plan of activities and organization: 3

Base Funding for (2020-2023): 1407 K€
Recommended Programmatic Support
PhD Fellowships: 4
Programmatic Funding: 445 K€, including for 1 (Auxiliar) New PhD Researcher Contract.

Justification, Comments and Recommendations
iMed.ULisboa is a large R&D institute with a drive towards growth and a desire to deliver impressive aims and ambition. It is apparent throughout the application and the site visit that they are an evolving and developing, transdisciplinary Institute. There has been some attempt to refocus of the research programs, centering upon “Drugs” as a core theme centered around the drug development cycle. Upon further inspection this refocusing appears more semantic rather than in practice as the Institutes research themes and subgroups are diverse, ranging from liver research, infectious disease, metabolism, neuron-glia, medicinal and development chemistry, ‘nano’ modulation, immunology, through to HIV evolution and social pharmacy.

There have been some strong successes over the last evaluation period which need to be noted, including inclusion in collaborative EU projects which helps encompass scientific platform development (EU OPENSCREEN), all based around open innovation; Precision Oncology POINT4PAC, EUCOMPETE2020, and EU H2020 IMI-RIA. Institutional recruitment has been good with 20 new recruits (FCT funded) 2007-2015 and 7 new Auxiliar professors (2016-17). A sign of an upward trajectory is that iMed.ULisboa has nearly doubled funding levels from €10.8M 2008-2012 to €20M 2013-2017.

Being integrated with U.Lisboa and the Lisbon Academic Medical Centre has started to open up improved clinical relationships, beyond Pharmacy, and stronger links to industry. Yet with such a broad research approach and diverse research portfolio this integration is not so evident and focus on bona fide strengths is encouraged for further development. This could be perceived to be at odds with their Institutional primary headline of [to] "create innovation in pharmaceutical research and apply it to the benefit of patients and society".

The overall leadership team is engaging and dynamic and the presentation of the Institute was collegial. Indeed, across the whole of iMed.ULisboa, there is evidence towards promoting collaboration, for example, internal proof of principle funding to develop new, integrated projects. This, in part, has led to EU successes via EU/H2020 funding and it is time now to push this even further – but as leaders. It was noted that approximately 70% of the Institute funding is from FCT and 23% from competitive sources - this needs be driven to increase the latter and that requires Institutional focus.

Industrial engagement is an area that is mostly good and Integrated Researchers and Fellows have had opportunities for being involved in some International research and have had published outputs. However, Industry-focused dynamism and guidance could be further developed; more so the development of the translational arms (towards the clinic, line of site to the patient) of the application could be a clear aim for 2018-2022. Indeed, the industry links presented are obvious but how they align with the absolute objectives of iMed.ULisboa lack some clarity, as they appear via the site visit to want to compete with Industry. For example, the work on developing p53 mutant/mdm2 inhibitors and also K Ras modifiers is intriguing. The competitive advantage or USP of iMed.Lisboa was not so obvious here as the larger pharmaceutical companies, and historically, a number of other academic labs, have failed in this regard. We acknowledge iMed.ULisoba’s ambition but is it pragmatic and achievable? A focus on the Institutional or methodological differentiating step(s) (competitive niche) compared to published science would be worthwhile developing.

There was a strong message and reiteration by iMed.ULisboa of their relationship with Astra Zeneca which could help develop this differentiating USP, potentially via a strategic partnership. Here, there was a discussion utilizing the AZ Mol Bio Screening platform (phenotypic screen and hit to lead project) where >250K compounds have been phenotypically screened via iMed.ULisboa assays. The Panel questioned the novelty of this as it follows the accepted AZ Open Access route; the functional novelty could well be in the Institutional assay screen which needs exploring further. However, this would need professional Technology Transfer Office coordination and exposure to clinical/hospital partners. This strengthening of clinical integration is a must and the Panel encourage this, but this must be governed and focused.

Likewise, the IP control over iMed.ULisboa's work presented with Novartis, and more national Portuguese companies (Bluepharma and Havione) must be ensured. The mention of the partnership with Bioinformativ for rapid data generation and analysis (potentially in real time) was intriguing but it was not so clear how it was a partnership rather than a service; are staff intellectually involved and importantly for all of the Industry-related projects, are the research staff (integrated researchers and fellows) involved or exposed to industry activities. Here, the coLAB/Company Vector B2B could well be an ideal springboard.

iMed.ULisboa has been rewarded by involvement in many EU funded opportunities which have attracted strong resources for R&D activities; but this is mainly as partners or collaborators. It will be useful over the next funding cycle for iMed.ULisboa to step up and lead on more and for that to extend to other funding streams such as CRO opportunities. The application mentions that industry pay for access to HTS equipment etc but how is this organized, monitored and costed was not evident and how the income (surplus/profit) is reinvested in to the Institute was also unclear. It is hoped that Industry access to iMed.ULisboa's facilities is not in direct competition to the internal research groups.

Elements of internationalization are evident – especially in the HIV/ AIDS area, other infectious diseases and some good research collaborations (UK, Germany, USA) that have been rewarded with good publication outputs (>70% of authors are from collaborating international groups). How though, beyond papers, these have developed, especially with regards to funding and job creation and knowledge creation, are unclear.

It was impressive to see that animal models for exploring a number of diseases are also being developed; and iMed.ULisboa's international partnership in EU programs is very good in developing these. The research presented on liver disease (via LITMUS) is very good and the development of diet induced liver disease(s) models(s) was exciting, especially those focusing upon NFALD, NASH etc. However, without scientific detail it was not apparent on the global competitive edge of these models and if they have been validated in human disease. It would certainly be excellent, comparative science to see how these compare to gold standard models. Again, the EU offers the favored route for this.

There were comments given during the site visit presentations concerning iPSC generation for organoids which was provided via "masters students". The Panel felt that must be carefully monitored for QA and QC purposes – especially if using in the Drug Cycle.

The research being undertaken on infectious disease, such as that Mycobacteria drug resistance and yellow fever outbreak in Angola is incredibly relevant socially and yet iMed.ULisboa were not primary lead or PI by the Institute groups but only in collaboration, the reason why being unclear.

As stated, this is a large Institute yet the outputs are asymmetric with around only 5-10% of group leaders publishing in globally acknowledged top journals; many iMed.ULisboa's researches publish in much more average journals. Understandably, and rightly so, most of the paper outputs are areas of expertise and chemistry- or pharmacology-focused journals whose impact is traditionally less; but nevertheless important. There are some seams of good science with many of the publication outputs being good in subject-specific areas, such as those from J Med Chem, J Controlled Release through to very good ones in J Hepatology and CDD.

However, the Panel urges the Institute to carefully reassess some of the papers they present as actually coming from iMed.ULisboa. There is a need for complete transparency and clarity over the Unit's involvement at the scientific inventive and leadership/ coordinating levels, not just those which are collaborative. Similarly, the type of article presented as a "highlight", the Panel would recommend to be primary research papers preferably.

The Panel appreciated the interest in a quite diverse number of topics even within a single R&D Unit: Clearly this creates a rich scientific environment but this fragmentation possibly contributes to the publication of lower-impact papers in a large variety of topics. Finding common lines of interest would potentiate the relevance of the findings, the impact of the publications and very likely will help in a higher success in obtaining funding, especially from international agencies.

Moreover, we advocate much more involvement of the integrated PhD students in these 'top' journal papers as in the selected papers offered to the Panel, demonstrated very few.

The Panel wanted to reiterate focus especially on the various EU partnerships. The IMI initiative is challenging and giving revenues as 7 different companies involved, yet its management and benefit to iMed.ULisboa was limited to being the Portuguese country leaders in the work package of animal models.

As funding has improved, estates must also and there is plan for a new building. There is a plan for equipment acquisition beyond this application and equipment access/ collaboration with IMM and BioISI yet internally, new bioimaging equipment, and updated computing power (and skills) is urgently required. Moreover, the €20M of income will have huge administration demands and the Institute must expand here.

The 14 RG presented each have a leader. Most groups have students and postdocs but it was noted some PI's do not. How is their performance evaluated and indeed, consequences of under performance needs to be acted upon.

iMed.ULisboa is prime for a more collaborative 'societal challenge' - potentially iMed.ULisboa could be driving ahead with a primary USP which could well be cohesion and shared expertise such as the use of computing and in silico approaches to their "drug cycle" pathway but the application to patients and society (beyond chemistry) is left wanting. However, this must be undertaken collaboratively and maybe more locally e.g. with IMM colleagues where areas of synergy could be developed. For example, new targets and compounds developed at iMed.ULisboa could be developed jointly via the molecular expertise evident at IMM.

PhD researchers and PhD students are clearly motivated and enthused at iMed.ULisboa. There is a good training PhD program offering some networking and soft skills development and opportunities; however, an improved PhD committee/ society should be developed as this would encourage more research skills training via interaction and peer-to-peer support and mentoring. This could, via workshops, offer alternative career options. Along these lines, PhD studentds and early-career posdoctoral investigators would benefit from a careers training office to manage and advise on all different aspects of their career development.

Based on the good levels of training at iMed.ULisboa the Panel recommends the attribution of 4 PhD fellowships. We appreciate this is very far from the requested number of fellowships (60) which is, however, completely unrealistic given the total number of fellowships to be awarded to the R&D Units of all areas through this FCT Program. The iMed.ULisboa leadership may decide the actual distribution of the fellowships.

The same is true for the hiring of researchers with a PhD. The Unit has requested 5 which is also unrealistic. The Panel recommends 1 Auxiliar Researcher contract which is – like the 4 PhD fellowships – in keeping with a 'good' rating. We believe that with the good level of research this Auxiliar Researcher could provide will help drive the research trajectory and enable the competitive acquisition of additional PhD student places, possibly via EU funding or that driven by relationships with Industry.

The Unit has requested support for additional costs, mainly related to acquiring new equipment. These costs exceed by far the amount available for a R&D Unit of this size and type through this FCT Program. Nevertheless, based on the Panel site evaluation the Panel recommends to support iMed.ULisboa through the indicated Programmatic Funding, which is again in alignment with a good ranking.

Evaluation Panel: HEALTH SCIENCES - Biomedicine and Molecular Biology

R&D Unit: Instituto de Investigação e Formação Avançada em Ciências e Tecnologias da Saúde (IINFACTS)
Coordinator: Hassan Bousbaa
Integrated PhD Researchers: 43

Overall Quality Grade: WEAK
Evaluation Criteria Ratings

(A) Quality, merit, relevance and internationalization of the R&D activities of the Integrated Researchers in the R&D Unit Application: 2
(B) Merit of the team of Integrated Researchers: 3
(C) Appropriateness of objectives, strategy, plan of activities and organization: 2

Justification, Comments and Recommendations

The Institute of Research and Advanced Training in Health Sciences and Technologies (IINFACTS) is the result of the fusion in 2012 of two previous R&D institutes under the umbrella of the CESPU (Cooperative of Polytechnic and University Higher Education). After several reorganizations, it is currently composed of a single research group (Therapeutics Research) with a general coordinator and four research lines: 1) Cancer research; 2) Oral diseases; 3) Psychosocial research and 4) Drug research. The Panel agrees that this new organization, established in 2017, may be useful in selecting major research lines of interest for the investigators of the Unit. However, this does not seem the be the case yet. The current selection of topics seems a bit arbitrary likely due to the different expertise of the groups. It is also unclear whether this structure has facilitated collaborations, which would be crucial given the small size of the institution.

The Panel feels that an integrative plan in the scientific focus seems necessary to optimize the productivity of the Unit. The Unit should evaluate their strengths and elaborate a plan to become competitive at the national and international level in the selected area. Without such integration the competitiveness of the Unit will likely remain low with only the cancer theme producing the most frequent, albeit medium impact, outputs. To the Panel, one obvious ambition would be the biopychosocial angle. In a peripheral location this could well be critical. Likewise, this embeds well with the clear want for public engagement and the admission that internally barriers need to be broken down to allow progress.

Strategic decisions as the one indicated above could benefit from a clearer interaction with the External Advisory Board. This board is composed of three members and meets annually. Although there is no doubt that suggestions from the EAB are clever and useful, this board seems to be quite friendly and major defects in term of strategy are not clearly discussed or followed. The chair of the board has published several articles using IINFACTS as one of his affiliations. The Panel feels that the Unit really needs a strong external board to monitor strategic plans and advise the Unit coordinators in an active manner.

The Unit has several administrative departments: Projects, Financial, Quality, etc. However, its dependence on the CESPU is too strong due to infrastructure constraints. This results in a reduced flexibility in many administrative areas including the management of manpower. The Panel would encourage the researchers to strive for improved interaction regionally. It was noted that by publication the Unit did interact with others nationally, such as CBMR in Faro. Additional interactions, e.g. with Porto institutions, could be of great help especially for using facilities and technology not available in house.

The summary of the major contributions in the last years reveals too many topics per research area. Given the small size of the Unit, it seems that the reported outputs represent a wish list of main areas of interest rather than research lines with solid dedication. As an example, some labs show more than 10 ongoing projects despite having only a couple of part-time PhD students together with University staff or clinical doctors working in these projects. The broad range of research foci for such few staff is unrealistic and requires strong focus for the future.

Highlighted publications are of low-moderate impact with very few publications in journals of general interest. Both productivity and quality are really low in some of the thematic lines, and some teams have no own external funding available for new projects. It would be highly convenient to strengthen the relationships between the groups so that some of the small publications could merge into higher-international impact papers. The Panel feels that this level of publications contributes to the low success of the Unit in securing funding, especially from international agencies. The

low level of EU funding is a major concern and virtually all the funding in 2013-2017 either remained relatively stable/static or declined, with no growth in the last years. This indicates that the coordination team, ideally with the help of a strong external advisory board, needs to establish a new strong, ambitious strategic plan to change the situation in the next years. Without doubt, focus upon a bona fide integrative research area is needed.

Internationalization is also very limited, apart from participation in meetings, international networks, submission of international grants, etc. The Unit has organized some meetings including international invited speakers but it is not clear whether these were truly international. Several teams in the Unit participate in international networks although in most cases they provide services and are not members of the network; i.e. not direct funding from these international agencies. The lack of international visibility is a major problem in the Unit and the Panel feels that the coordination team does not have a clear plan for reverting this defect.

The Unit is the principal partner of a PhD program and hosts additional postdoctoral researchers, undergraduate students, etc. A new PhD program in dental sciences is proposed. Unfortunately, most if not all PhD students are part-time students such as medical doctors in private clinics or teachers. They are very motivated and dynamic; yet their contribution to the research projects is limited. The Unit should work on an ambitious plan for generating a strong PhD program, possibly focusing on the major strength in the Unit and looking for a niche not present in other institutions in Portugal. The Panel believes that this would be a major advantage to attract young scientists and promote the research lines in the Unit.

The plan for future activities contains references to the major general questions of interest to the group (new biomarkers, targets and strategies for cancer therapy, screens for new drugs, etc.), in addition to advanced training, dissemination and valorization of research results. In general, many of the questions are interesting although more cohesion among them would be desirable. The proposal for the next years is quite conservative and maintains the interest in too many research lines with a high level of fragmentation and no clear focus. Unfruitful dispersion of researchers and research topics was discussed and mechanisms of promoting integration were discussed in detail in the evaluation. The Panel seriously believes that without such integration the competitiveness of the Unit will remain low, affecting the ability to recruit researchers and funding in the future. However, it was unclear from this discussion whether the coordinators are really aware of this problem, and this, together with the lack of external help, may be the major challenge for the Unit in the future.

The future plan presented does not properly address the major problems affecting the Unit. The proposed programmatic funding is mostly dedicated to PhD salaries, technical and secretariat staff, with some budget dedicated to missions, upgrading infrastructures and equipment. In addition, the Unit has no administrative staff and one contract for secretary was also requested. Despite the lack of postdoctoral investigators or full-time PhD students, the future plan does not include hiring new researchers. This is surprising given the size of the Unit, and the serious limitations in the areas of expertise. Specifically, the possibility of hiring new junior investigators would increase the technical expertise and collaborative areas. Some additional concerns exist regarding the lack of several core services.

The Panel is aware of the fact that these proposals could help the Unit to become more independent from the CESPU. The distribution of the requested funding is logical for maintenance of the Unit, although it does not add new expertise, technologies or equipment to the Unit so the impact in the technical and scientific capacity will be very limited.

The anticipated funding income 2018-2022 seems to decrease in all fiscal lines. How the Unit will remain sustainable is unclear. In addition, the proposal is very conservative strategically and scientifically, with no clear inputs into the major problems that affect the international visibility and productivity of the Unit.

Considering all the above, the Panel is does not recommend funding at the present time.

Evaluation Panel: HEALTH SCIENCES - Biomedicine and Molecular Biology

R&D Unit: Instituto de Investigação e Inovação em Saúde (i3S)
Coordinator: Mário Adolfo Monteiro Rocha Barbosa
Integrated PhD Researchers: 431

Overall Quality Grade: EXCELLENT
Evaluation Criteria Ratings
(A) Quality, merit, relevance and internationalization of the R&D activities of the Integrated Researchers in the R&D Unit Application: 5
(B) Merit of the team of Integrated Researchers: 5
(C) Appropriateness of objectives, strategy, plan of activities and organization: 5

Base Funding for (2020-2023): 7038 K€
Recommended Programmatic Support
PhD Fellowships: 21
Programmatic Funding: 1915 K€, including for 5 (3 Junior, 2 Auxiliar) New PhD Researchers Contracts.

Justification, Comments and Recommendations
i3S is a young research center that was created in 2015 by the fusion of three R&D Units, the Institute for Molecular and Cell Biology (IBMC), Institute for Biomedical Engineering (INEB), and Institute of Pathology and Molecular Immunology of UPorto (IPATIMUP). The Panel wishes to commend the Unit and its direction for the successful merger which has created an impressive center for basic and applied biomedical research that is fully competitive at highest international level and endowed with an outstanding mode of operation.

The scientific structure of i3S comprises three thematic lines: Cancer, Host Interaction & Response, and Neurobiology and Neurologic Disorders. These research areas are subjected to studies covering Molecular and Cellular Biology, Genetics, Immunology, Pathology and Bioengineering in order to foster our understanding of the molecular and cellular basis of living systems in normal physiology and its deviations in pathological states to pave the way to the development of novel diagnostic and therapeutic strategies. The Panel is fully supportive of this modern scientific organization which fosters multi-disciplinary and cross-border thinking and suggests a reflection about enforcing the computational biology resources and expertise, which can elegantly bridge the various activities and facilitate a more sophisticated understanding of the extremely complex cellular and organismal regulatory circuits at the basis of (patho)physiological phenomena.

Moreover, the Panel was fully convinced by the organizational structure and operation of i3S which supports the above scientific organization. It appreciates that the Center will become a legal entity in 2019 after concluding ongoing discussions with the university. Following up on the brief discussion with the Rector of UPorto the Panel wishes to emphasize that the prestige gained by Porto University and the region through the presence of such a center of excellence should translate in a significantly stronger support, including the attribution of positions to researchers.

The science at i3S is outstanding, albeit with the inevitable variation between teams. The attribution of multiple ERC grants, among other distinctions, illustrates the international top quality of science done at the i3S. The Panel was very impressed by the outstanding short presentations illustrating work done in the three thematic lines. However, the significant variation in the performance of teams warrants continuous attention. In this respect, the Panel appreciates the regular monitoring of teams (see below). Notable breakthrough discoveries at i3S comprise the functional links between cell division and genome (in)stability, mechanisms involved in neurodegeneration, and advances in the mechanistic understanding of T cell differentiation. The i3S is an international reference center for Hereditary Diffuse Gastric Cancer and develops and for genetic diagnosis. The latter activity includes the development of genetic diagnosis tools.

The Panel would like to congratulate i3S for establishing principles of operation, which are available to all members of the Unit. This is a unique feature of i3S which should be adapted by all major R&D Units in the country. These principles of operation concern particularly the scientific evaluation of all teams every 4 years by external experts chosen by the external scientific advisory board, the space allocation rules and the definition of authorship. Indeed, the Panel noted that i3S is apparently the only Unit that has established authorship guidelines in line with the recommendations of the

International Committee of Medical Journal Editors and of the Council of Science Editors. Importantly, these guidelines specify, among other points, the individual contribution and scientific responsibility of all authors and the possibility of mediation in case of conflict. The Panel fully supports the anticipated establishment of an Ethics and Responsible Conduct in Research Committee, which should go into operation as soon as possible, given the many cases of improper scientific conduct in biomedical and biological sciences throughout the world that is increasingly worrying the public. The 2018 survey of the scientific platforms is another appreciated unique operational feature of i3S. It may actually be complemented by the regular assessment of the actual need of particular platforms and the creation of new services for emerging new technologies, such as genome editing. This could be done by a Technology Assessment Committee composed of technologically/computationally experienced PIs.

The Panel also endorses the transversal activities at the i3S and the translation to the clinical diagnosis lab which was visited.

Training is excellent at i3S. This is not only supported by the contribution to three ITNs but was also evident from the discussion of Panel members with the Post-docs and PhD students who are highly enthusiastic and motivated. Indeed, they organize by themselves a variety of events, ranging from scientific seminars and meetings to fundraising activities, with the support of the direction. Notably, i3S was the only Unit that provided detailed statistics of the performance of PhD students, revealing that all of them had at least one first authorship on an original publication and that PhD students at i3S published on average 2.8 original peer-reviewed publications.

The plan of activities 2018 to 2022 was rated excellent by the Panel, albeit it was – most likely due to space restriction – rather general. However, the Panel fully supports the key elements specified in the scientific strategy, the institutional integration and development of an autonomous legally recognized i3S center, career development support for young PIs and beyond, the refinement (i.e., controlled expansion together with controlled reduction) of the technological platforms, the expansion of internationalization efforts, the continued support for training and career development, the dedication to translational research ("bench to bedside") and reinforcement of the Comprehensive Cancer Center with the Porto Oncology Hospital, open science efforts and the continued refinement of the operational tools praised further above.

Based on the excellent training at i3S and the performance of the PhD students in the past the Panel decided that this is an outstanding center for training, which provides optimal conditions to learn top level science, and recommends the attribution of 21 PhD fellowships to i3S. This is very far from the requested number of fellowships (168) which is however completely unrealistic given the total number of fellowships to be awarded in all areas through this FCT Program. The i3S leadership may decide the actual distribution of the fellowships to the various PhD programs.

The same is true for the hiring of researchers with a PhD. The Unit has requested 12 which is unrealistic. The Panel attributes 3 Junior (i.e., post-docs) and 2 Auxiliar (i.e., PI) Researcher contracts to the i3S which is – like the 21 PhD fellowships – among the highest numbers attributed to a R&D Unit by this Panel. Given the excellence of research and the need to recruit excellent young scientists both as post-docs and new PIs in view of the turn over subsequent to external evaluation, this numbers appear fully justified to the Panel.

The Unit has requested support for additional costs, related to the function and staffing of the scientific core platforms, management, informatics systems, administration, technology transfer, etc. These costs exceed by far the amount that can be awarded to a R&D Unit through this FCT Program. Nevertheless, based on the excellent structural organization of the Unit which is expensive but also at the basis of the excellent science and training, the Panel recommends a substantial support in Programmatic Funding, which is the highest sum attributed by this Panel.

Evaluation Panel: HEALTH SCIENCES - Biomedicine and Molecular Biology

R&D Unit: Instituto de Medicina Molecular João Lobo Antunes (iMM)
Coordinator: Maria Manuel Dias da Mota
Integrated PhD Researchers: 193

Overall Quality Grade: EXCELLENT
Evaluation Criteria Ratings
(A) Quality, merit, relevance and internationalization of the R&D activities of the Integrated Researchers in the R&D Unit Application: 5
(B) Merit of the team of Integrated Researchers: 5
(C) Appropriateness of objectives, strategy, plan of activities and organization: 4

Base Funding for (2020-2023): 3167 K€
Recommended Programmatic Support
PhD Fellowships: 21
Programmatic Funding: 1310 K€, including for 6 (2 Junior, 2 Auxiliar, 1 Principal, 1 Coordinator) New PhD Researchers Contracts.

Justification, Comments and Recommendations
The Institute of Molecular Medicine (IMM) is an outstanding and extremely impressive research organization that is based in Lisbon. Indeed, the Panel commends the directors and key scientists for this achievement. A number of excellent researchers work at the IMM: they are able to successfully compete for national and international grants, as evidenced by the high number of prestigious grants that have been awarded to IMM teams, and have a track record of seminal studies that were published in some of the very top journals in biomedicine. The research infrastructure is hosted in an impressive building that accommodates more than 600 scientists working in a modern and vibrant environment that includes a number of very well-organized central facilities (e.g. the animal, bioimaging, flow cytometry and biobank facilities).

Several research groups can be considered to be outstanding on both national and international levels, are characterized by an extremely high scientific output, and the majority of teams are excellent. Some research also has a clear translational value and could offer answers to specific problems of public interest. For example, data reported in Nature (2014) about the importance of vitamin A for normal development of the immune system during pregnancy are of major medical and socio-economic interest considering the high prevalence of hypovitaminosis A worldwide. Similarly, results dealing with the biology of plasmodium malariae can open new ways leading to the development of vaccines or novel therapies. The dedication to translate scientific results is also apparent from the technology transfer activities. Indeed, in the examined period, IMM research activity resulted in the filing of 21 patents, 3 of which were granted, as well as in the creation of 5 start-ups.

The overall impression of the Unit as a whole is excellent and the thematic lines are in general highly productive. However, as in all institutes of this size there are some less well-performing research groups. This issue has been addressed by IMM in a rather unique way: IMM has put in place an internal assessment system (but with external reviewers and input from the SAB) that monitors and attributes traffic light colors (green, yellow, red; evaluation period is 4 years) to each team. Particular attention is given to the "yellow" teams and help will be provided to improve performance. If there is no improvement, the team will become “red” and will have a two years period to find a new research environment outside IMM. The Panel considers this an excellent tool to identify teams at risk but (i) it was not clear how the “yellow” teams will be helped and (ii) the Panel feels that the selection of the external reviewers should be done by the SAB.

As stated above, the outstanding quality of IMM in the national and European scientific scenario is confirmed by the ability of the Unit to attract a remarkable number of highly competitive international grants. Specifically, in the examined period, 10 ERC grants, 4 BMGF, 2 HFSP, 2 HHMI and other grants have been secured. The Panel applauds IMM for having more than 40% funding coming from international grants. IMM has also made a major effort in expanding, internationalizing and enriching the critical mass of researcher and, in the 2013-2017 period, has successfully recruited highly qualified researchers. This resulted in the creation of 10 new teams, five of which were able to win ERC grants and a staff where more than 250 scientists come from 40 different nations.

IMM is endowed with an excellent PhD program. PhD candidates were overall very satisfied with the environment and the quality of the training they are receiving. The Panel appreciates specifically the 8-week orientation program and the organization of periodical retreats that are shared with PhD students working in other research institutions in Lisbon. However, the students raised a number of issues which the Panel feels should be addressed by the iIMM directorate. These concern (1) improving the connectivity between IMM, the University and the Hospital; (2) standardizing the different PhD programmes and (3) supporting the office of Human Resources (which would also need to have more staff). The students suggested the creation of an International Relations office - this makes sense in consideration of the number of students that come from outside Portugal.

The Panel, in particular, agrees with suggestions raised by the PhD students on issues that still prevent complete integration between IMM and the clinics, especially given that IMM is physically located inside the largest Medical Research Campus in Portugal, in a structure that includes the biggest medical school (FMUL) and university hospital (HSM) in the country. Data from a small phase I/II clinical trial were presented, these data were not at the expected level or rigor and indicated that extra effort should be put in place to reinforce and amplify this connection. IMM is aware of this important issue and responded to the critiques raised by the Panel prior to the site visit. Indeed, their multi-level action plan includes bi-weekly 'chalk talks', the participation of clinicians to symposia and retreats, participation of basic researchers in the clinical session in the hospital and intramural funding for collaborations between basic and clinical researchers. The Panel appreciates these activities and is looking forward to its fruition.

An issue that has been addressed by the Panel are the future plans to expand and enlarge the size of the Institute, as space limitations are clearly apparent. Even when the new building becomes available allowing for further growth clear rules should be established. The board suggested in their response limiting/reducing the number of laboratories to 25 and limit the number of staff members to maximally 8 per team. While the Panel endorses this planning in general, there has to be some flexibility – as with ERC or FET-funded teams - and it is suggested that there should be clear and transparent, but flexible, rules that define the criteria for space attribution/expansion/reduction to the various research groups; as these are sensitive issues they should be discussed with all IMM group leaders in a collegial manner.

The proposed strategy plan for the next five-years period is well organized and comprehensive, although a bit generic and somehow lacking in specificity. Some proposals stand out. Thus, amongst the developments that are proposed for the next quinquennium are the idea of creating a totally renovated Technology Transfer Office, which will be fully dedicated to the translation of IMM research. This will catalyze the increase of the translational and commercial value of IMMs research and facilitate institutional collaborations with the Pharma industry. The proposal to organize twice a year an event where IMM scientists will present their ideas with translational potential to an expert audience of entrepreneurs and investors is excellent. This will be the seed for developing translational projects aimed at either patent licensing or creation of start-ups with an innovative patent portfolio.

Other interesting ideas are the reinforcement of internationalization using the H2020-funded Twinning and ERA Chair projects; the decision to cover the publication fees of all data in an open-access regimen is also excellent. Similarly, the creation of an MSc in Biomedical Research is also commendable because this will become a source of outstanding students who join the IMM Lisbon Biomed International PhD program.

Taken altogether the Panel would like to commend all IMM members that have contributed to generating such a successful and impressive scientific endeavor.

PhD candidates were overall very satisfied with the environment and the quality of the training they are receiving. Particularly appreciated is the 8-week orientation program and the organization of periodical retreats that are shared with PhD students working in other research institutions in Lisbon.

The Panel suggests that the IMM leadership considers the following issues in the new funding period: (i) the connection between IMM and the University and the Hospital should be improved; (ii) the performance of office of Human Resources should be improved, e.g. by an increase in staff numbers. The Panel also supports the suggestion of the students to create an International Relations Office, which really makes sense considering the number of foreign students. Finally, (iii) the preparation of a "welcome" brochure (in English or bilingual) that takes care of practical aspects (e.g. housing, how to open a bank account in Portugal, etc) would be highly appreciated.

Given the excellent quality of science and training at the IMM the Panel recommends funding of 21 PhD student fellowships.

The Panel fully endorses the internationalization activities of the IMM.

Based on the requests in the documents and detailed discussions with the leaders during the site visit, it became clear to the Panel that there is a need to consolidate the leadership of IMM at the present very high level. Therefore, the Panel recommends to award contracts to IMM for hiring new researchers at all four levels: 2 Junior, 2 Auxiliar, 1 Principal and 1 Coordinator.

Finally, the arguments for creating a Technology Transfer Office have convinced the Panel. The Programmatic Funding awarded can be partially used for that purpose. In this respect the Panel would like to point out its surprise that the funding requested in field 14.4 of the application form was limited to the costs of a TTO structure.

Evaluation Panel: HEALTH SCIENCES - Biomedicine and Molecular Biology

R&D Unit: Instituto Gulbenkian de Ciência - IGC
Coordinator: Monica Bettencourt Carvalho Dias
Integrated PhD Researchers: 122

Overall Quality Grade: EXCELLENT
Evaluation Criteria Ratings
(A) Quality, merit, relevance and internationalization of the R&D activities of the Integrated Researchers in the R&D Unit Application: 5
(B) Merit of the team of Integrated Researchers: 5
(C) Appropriateness of objectives, strategy, plan of activities and organization: 5

Base Funding for (2020-2023): 2120 K€
Recommended Programmatic Support
PhD Fellowships: 22
Programmatic Funding: 1810 K€, including for 6 (2 Junior, 2 Auxiliar, 2 Principal) New PhD Researchers Contracts.

Justification, Comments and Recommendations
The IGC is one of the first research institutes created in Portugal, largely funded by the Calouste Gulbenkian Foundation (CGF), which is original in many aspects of its organization. Since it was restructured starting in 1998, the Institute has establish itself as an internationally renowned scientific center largely due to an exceptional turnover policy that ensures continuous evaluation of the young and senior groups and importantly, a complete renewal of most junior groups every 5-9 years. This policy is unique in Portuguese institutions and although it generates some sense of instability in young PIs, seen through a positive standpoint it can be considered as a fantastic incubator of outstanding experienced mid-career scientists that can further thrive in other institutions. Obviously, there is a delicate equilibrium that must be achieved between a turnover rate of young scientists and a core of high profile excellent senior permanent members. In this respect, the IGC Director in agreement with the CGF have so far offered permanent positions to 6 out of the 11 senior group leaders listed presently at IGC. However, no regular call for this type of positions is scheduled and it was not clear which were the criteria behind the choices made so far; high profile excellent science was a hallmark but why one and not the other was not evident. It is essential that the criterion to offer this type of positions is transparent to avoid disturbing the relationships within the group of PIs.

The present direction will face the challenge of recognizing the need to recruit established mid-career scientists without being able to offer a stable position that international high-profile scientists might already hold. This may well jeopardize the recruitment of mid-career scientists. On the other hand an increase in the fraction of permanent contracts might result in a decreased capacity to recruit young members. Most Portuguese scientific institutions were created or restructured within the last 20-30 years by attracting young talented post-doctoral fellows many of them educated in prestigious scientific institutions all over the world. This implies that they will age and retire at the same time, thus creating a gap that needs to be anticipated and carefully prepared.

The original concept behind the creation of the Institute was scientific excellence and the track record sustained since then in most research groups is a good example of how excellent science can be produced, if the governance is appropriate. The Panel was impressed by the scope of scientific interests, which although large has nevertheless maintained excellent performance. In the last 5 years most established research groups have made important contributions that in some cases were really exceptional and overall most research groups contributed with important publications. There were in total 1055 publications in the last 5 years, with 633 peer-reviewed publications giving an average of 5.1 publications per PhD, most of them of high impact. The level of internationalization is rather impressive considering that the country has a limited and rather recent tradition of basic biological science. These contributions concerned fields with high societal impact, including aging, diabetes, infectious diseases and the development of new concepts (eg. disease tolerance in response to infection, step-wise decline in organ function during aging), but have also formed the basis of new therapeutic strategies (vaccination program for Malaria with the Gates foundation, Phase I clinical trial for sepsis). Although most PIs are Portuguese, they have done their PhD and post-doctoral training abroad and have attracted international young scientists, post-doctoral fellows and PhD students. The research groups are kept within a manageable size (15 members or below) and the PIs have been securing external funding, a large fraction of

which from prestigious international funding agencies such as Bill and Melinda Gates Foundation, HSFP and several scientists hold ERC grants at all levels. IGC scientists also include 4 EMBO members and are members of review bodies further attesting to the high level of international recognition of this Institute.

The research groups are organized around one senior PI (there are 11 listed) that have a few (2-3) young PI in their research structure with post-doctoral fellows and PhD students. Although it is mentioned that young researchers are totally independent, it is curious to see that all are attached to a senior PI. A more in depth analysis of the scientific production of some young researchers shows some weaknesses and a few (very few) have not produced strong original science in the past 5 years. This raises the question of whether this organization was strategically appropriate and whether mentoring program for junior PI should be implemented to guarantee the “incubation” and the generation of high profile scientists. The new direction that started in 2018 is aware of this need and appears to be seriously following this recommendation. The Panel recommends that the senior PIs should advise more junior PIs on career planning and strategic decisions to ensure the best outcome for the research of the Unit as a whole.

The researchers within the Institute have access to a large array of core facilities and given the limited size of the Institute the financial viability of all these facilities is not obvious. The Panel was very impressed by the managerial skills of the heads of the core facilities and although the Panel was appreciative of the array and quality of the facilities, some areas need reinforcement. The flow cytometry core facility needs additional analytical power (more than 12-fluorochrome simultaneous analysis) and therefore there is a need to invest in new machines; also the genomic facilities are under-equipped and there is a plan to increase the capacity of the animal facility to provide special services (gnotobiotic and germ free mice). Given that in the Lisbon area there are several excellent scientific Institutes, joining forces to provide shared, complementary services could be a solution to the inevitably aging of equipment needing a level of financial investment that is incompatible with a medium-sized institute such as IGC.

The Institute relies on one Director, assisted by one managing and one deputy Director and a SAB that visits the Institute yearly and that evaluates PI and proposes new applicants. The merit of the integrated researchers is on average excellent and as previously mentioned this is likely contributed by a continuous follow up by a highly prestigious SAB with 5-year in-depth evaluations for senior and young researchers on contracts that cannot be extended for more than 9 years. The Panel was very positive about the apparent excellent leadership of the present direction that just started their function in January 2018 and hopes that they continue to implement the measures discussed during the visit (career planning at all levels, ensuring total transparency in hiring and renewing staff members, permanent positions). The direction also needs to maintain a constructive dialogue with the Board of Trustees within the Gulbenkian Foundation, essential to guarantee the viability of the Institute that depends on the foundation for 30-40% of the annual budget.

The strategic future plan attempts to integrate the vast scope of interests that are presently being studied in the Institute into two main thematic lines with quite some success. There is a clear and articulated outline of the future strategies and a clear plan of future recruitment that is in line with the past policy of a high turnover rate. As in previous years, the plan of action seems to be based principally on the recruitment of 2 new, good, young groups each year. In the coming years, the Institute plans to hire young PIs interested in the physiology of metabolism who will interact with existing groups to strengthen this area of research. This strategy is possible in large part due to significant financing of the IGC (16M per year) and gives a high degree of dynamism to the Institute. The Institute has reached a size and visibility that justifies in the future an aggressive policy of national and international fund raising that, if successful, will ensure the stability of the Institute that is essential to continue to attract international renowned scientists.

The Panel recommends supporting IGC with 22 PhD fellowships and salary costs for 6 new PhD Researchers positions (out of the 9 requested). In addition, the Panel recommends to support the internationalization efforts and the requests for equipment. This support is compatible with the overall assessment "Excellent".

Evaluation Panel: HEALTH SCIENCES - Biomedicine and Molecular Biology

R&D Unit: Laboratório Associado, Instituto de Ciências da Vida e da Saúde / Grupo de Investigação em Biomateriais, Biodegradaveis e Biomiméticos (ICVS/3Bs – LA)
Coordinator: Rui Luís Gonçalves dos Reis
Integrated PhD Researchers: 161

Overall Quality Grade: VERY GOOD
Evaluation Criteria Ratings
(A) Quality, merit, relevance and internationalization of the R&D activities of the Integrated Researchers in the R&D Unit Application: 4
(B) Merit of the team of Integrated Researchers: 4
(C) Appropriateness of objectives, strategy, plan of activities and organization: 3

Base Funding for (2020-2023): 2205 K€
Recommended Programmatic Support
PhD Fellowships: 10
Programmatic Funding: 970 K€, including for 3 (Auxiliar) New PhD Researchers Contracts.

Justification, Comments and Recommendations
The application from ICVS/3B is a highly interesting and intriguing read. There have been excellent successes: parts of the bespoke training environment for students and staff, the amount of competitive, non-FCT funding is wonderful, strong efforts towards internationalisation (joint PhD research training, exchange) and innovation (spin offs and patents), important links to clinical centres, especially Braga Hospital within the Clinical Academic Centre, 2CA, novel routes for surgical development and the use of IT/ AI in helping with the translational aspects of the Institute's research. The Panel was particularly fascinated by the longitudinal cohorts as these will undoubtedly become a fantastic resource.

What is strikingly evident, however, is that even though the ICVS/3B's was established in 2011 they are still 2 very different Research Groups (RG) and the applicants verbally expressed the wish to remain as such. Even the Thematic Lines (TL) are incredibly separated and the alternating Presidents and the little impact that this has in the life of both Units is a sign of this separation. ICVS/3B has been successful but the Panel believes this would have happened irrespective of being a joint FCT R&D Institute. Moreover, the research themes are common amongst other FCT Institutes - infectious diseases, neurology, oncology etc. Of course, the 3B's are unique but this needs to integrate and translate much more than they currently achieve. As such, the application and the ICVS/3B Institute is ranked as 'Very Good'.

The Panel detected efforts over time to encourage integration and attempts to form bridges and links, such as the spin off HydrUStent, the TL7 in population health and proof of principle "out of the box" funding, but these are relatively young and need time to deliver successes.

As to international visibility, 3B's is excellent – 5 ERC grants (2 PI's left the Institute taking 2 ERC funding streams with them and a new ERC starting grant was funded recently – but outside of this review period) and integrated European Framework Programs. In fact, 3B's hosts the European Centre of Excellence on Tissue Engineering, which is a strong accolade. However, these valuable honours are not easy to discern from the publications and patents. The Panel wanted to understand what have these networks generated (science or fiscal gains, changes in care). There may be some signs of socioeconomic wealth generation (the spin offs are on the floor above the 3B's) but what is critical here, especially for Portugal, are the health benefits; the realization of novel healthcare treatment pathways. This is not clear in the application. Moreover, it is not clear how the integrated researchers or fellows will be involved or learn from these experiences and opportunities.

In terms of Industry and Innovation, there have been many patents written (nearly 40); the question remains whether these led to further income/realization of funding. The Panel felt there are issues over patent focus and what a patent may really mean. Filing is one unit of currency but have they led to PCT and real/substantial income, partnering or licensing opportunities for the Institute? There is a strong message of spin offs, patents but no description why. Also, why the desire to register 70 patents in the next funding phase as this is expensive to manage and needs a clear strategy of how this will be commercialized. In this regard, a professional 'technology transfer office' at ICVS/3B's was not

described but via association this could be undertaken with the University of Minho as it was noted that Professor Reis is the VP for Research and Innovation. There was a lack of an Exploitation Board to identify and secure the best inventions from the Institute and the Panel suggests they should consider employing an exploitation manager. IP management and its budget must be carefully planned. The Panel questioned if the proposed budget match the 2018-2022 expectations.

The paper outputs presented are also intriguing. The Panel noted that paper authorship was asymmetric. The 3B's publications are clear cut and evident. Professor Reis is last and corresponding on many (in the 100's) which implies he is the scientific lead for them all, which in itself is not typical. This then questions the research structure and governance. Who are the junior leaders, sub group leaders? Their individual outputs in terms of seniority are diluted by the Director being in a leading position on so many publications. This will then affect their career opportunities.

In the ICVS cohort (9 papers presented) who has done what and how, was unclear. The Panel could not identify some of the authors locally, either international or from other Portuguese institutions – either on the website or on PubMed. For example, in Cunha et al 2014 NEJM the senior author is affiliated to the University of Perugia, Italy with a second affiliation to 3Bs/ICVS (only mentioned in the Appendix); Hauser et al 2017 NEJM has contributions from two large Consortiums one of which with one member of the ICVS; in Veiga et al Nature Communications 2016 the first author has two affiliations (one of which is ICVS) while the senior author is at Columbia University. The Panel felt that measures should be taken by the governance structuring to improve the visibility of ICVS that comprises a large number of integrated researchers with a productivity that is very good but not excellent.

The Evaluation Panel had some difficulty in discerning the financial successes and contributions of 3B's and ICVS independently. The Panel assumes that the FCT funding is common (although most PhD fellowship suggestions offered are biased towards 3B activities) but all other financial income contributions are administered independently. This begs the question, what is the advantage of ICVS and 3B's being together and why is this combination better than the sum of both?

It is clear that there are significant strengths in both RG's yet as mentioned above trans-thematic lead/ trans disciplinary workings are needed. There are significant talents in novel biomaterials yet apart from HydrUStent it is unclear to see how truly integrated the groups are. The desire to become a reference center in clinical research is ambitious and the establishment of the 2CA is an impressive foundation, but how is this to be planned proactively? Is there a Clinical Advisory Board in the planning? The Panel wondered over cGMP facilities and provisions to expand these to improve the clinical translation of the 3B more fundamental outputs in to more patient focused clinical inputs of the ICVS.

Overall, the Panel's general impression is that 3Bs/ICVS are very different RG's, especially in terms of quality. 3B is very metric driven and performing, albeit successful. The biomaterial journals are relatively bespoke, and rightly so, they are needed and showcase incredibly good science (in fact, having European Centres such as the TERM RES-Hub is impressive). There are some papers in the public domain from ICVS/3B's that do have much better citations than their average of around 7/year on the whole. As with all subject specific papers, the publications may well be inflated and that increases impact factors.

The Panel discussed the ICVS outputs, which are generally weaker, albeit the association with the Clinical Academic Centre, 2CA, is well received and applauded. Again, over the next funding period tangible, realistic and transparent outputs from ICVS/3Bs with 2CA must be delivered. The goal here was discussed with regards to real life data, in real time; the Panel felt this was overly ambitious yet with the 2CA and key foci (infection, neuropathology) there could be some quick wins. The strategy for other partnerships needed to be clarified. The line: "Health Institutions and companies" does not list whom, if they are external to the Institutional spin offs and what is the partnering priority?

There was a discussion of increasing teaching and training programs and conferences at ICVS/3B's. One assumes these are run by junior staff; raising the question of how these feed in to the research agenda (apart from identifying upcoming students).

The Panel felt the research development plan is expansive. Some of the TLs could indeed occupy the entire center, such as the MicroInfect TL (there are whole centers of comparable size focused only on this, such as the Infectious Disease Research Institute in the United States); also NeuroS TL (where there is a vast swath of the huge field of neuroscience is contemplated). A valid question is as to the number of senior recruits that would be necessary to adequately staff these research areas. It may be necessary to develop specific research questions to be addressed in some of these areas and how they could be managed. The Panel recommends a regular evaluation of the activities and of the productivity of the integrated scientists undertaken by external and preferentially international panels (every 4 or 5 years) to help the

Directors and senior leadership reorganize the RGs. An organogram of structure, lines of responsibility, decision making and ownership would be a very useful inclusion on the Institutes website and future FCT applications.

The Panel also recommends urgently replacing the SAB (considered by the Panel as friendly) to aim for a critical assessment of the different activities, help identifying arising problems and finding appropriate solutions.

The Panel was impressed by the PhD researchers and PhD students who are clearly motivated and enthused at ICVS/3B. There are very good elements of training within the PhD program offering. However, an improved autonomy of how the students interact would be beneficial. The PhD committee/society should be developed further, this would encourage more independent researcher skills training via interaction and peer-to-peer support and mentoring. This could, via workshops, offer alternative career options. Along these lines, PhD students and early-career postdoctoral investigators would benefit from a careers training office on site to help manage and advise on all different aspects of their career development.

The ICVS/3B's leadership may decide the actual distribution of the fellowships but a push towards more clinical/ translatable strengths should be encouraged.

Evaluation Panel: HEALTH SCIENCES - Biomedicine and Molecular Biology

R&D Unit: Programa Champalimaud de Investigação (CR)
Coordinator: Zachary Frank Mainen
Integrated PhD Researchers: 93

Overall Quality Grade: EXCELLENT
Evaluation Criteria Ratings
(A) Quality, merit, relevance and internationalization of the R&D activities of the Integrated Researchers in the R&D Unit Application: 5
(B) Merit of the team of Integrated Researchers: 5
(C) Appropriateness of objectives, strategy, plan of activities and organization: 4

Base Funding for (2020-2023): 1665 K€
Recommended Programmatic Support
PhD Fellowships: 8

Justification, Comments and Recommendations
The Panel considers many of the group leaders in this Unit to have international recognition and to have produced world class, cutting-edge research. They have published original research in journals of the very highest calibre, and the work has been enabled by research facilities that are clearly outstanding. In these cases, research leadership is evidenced by a high frequency of such papers that are evidently generated by group leaders. Outreach work has been outstanding. The Deputy Director mentioned that there is a strategy in place for attracting and retaining talented PIs, including substantial start-up packages. Some of the problems identified by the Scientific Advisory Board (SAB) seem to have been resolved. It is on this basis that the Panel has graded the Unit as "Excellent".

However, the Panel has a number of concerns, some of which echo those made in the reports of the SAB that formed a part of the application. While the aforementioned research groups have performed extremely well and have contributed to this research excellence, it is the view of the Panel that others have not. Within the assessment period a different, sizeable, set of group leaders have not shown the same level of research leadership. They have not led the publication of papers with a frequency that could be deemed to meet high international standards. That is, they have not published as first, lead or corresponding authors sufficiently frequently. At the site visit, the Deputy Director of the Unit expressed the view that although such publications were produced infrequently, this was in line with the ethos of the Unit which allows researchers to focus their time on high quality research protected from external pressure to publish that other Units are typically subjected to. It is admirable that the Unit wishes to foster a supportive research culture that allows researchers to promote quality over quantity. However, the Panel takes the view that the timely dissemination of research findings is an important part of the research process, and publication rate is an indicator of research productivity. The Panel also has to judge the Unit according to national and international benchmarks. Original research papers in which group leaders appear as first, lead or corresponding authors serve to benchmark the effectiveness of their research leadership. Such papers were found to be lacking for a particular set of group leaders.

Publications are also important for the career progress of early career scientists, and the Panel is concerned that low publication rates in certain groups negatively impact their career development. After the contracts of early career researchers and PhD students in the Unit come to an end, realistically, they will be expected to thrive in an environment that places much more emphasis on publications as evidence of research competence. Under these circumstances, the Panel feels that the lack of publications diminishes the training value of investments that funding organisations make into the Unit.

Due to the absence of the Director and of several other leading CNP scientists, the Panel's questions could not be answered with sufficient clarity.

The 2017 SAB report documented expressions of concern by PIs relating to the difficulties in recruitment of high quality PhD students. During the site visit, the Deputy Director disagreed with this report, and said that these views emanated from one individual at the Unit (although this is not the impression given in the report). The Panel did have the opportunity of meeting a handful of PhD students and PIs at the Unit but, there were so few present that it was difficult

to generalise on the basis of what was discussed. Any positive or negative comments made by early career scientists are not mentioned here because the low numbers may compromise anonymity.

The Panel is concerned about the degree to which the Foundation is responsive to SAB concerns. Indeed, the SAB itself is concerned about this issue (2017 SAB Report: "We have been reassured over the years that these problems would be addressed, but many of them remain.").

When the Panel asked for clarifications around financial management (e.g. the use of overheads) neither the Deputy Director nor any member of the team present were able to provide answers. The Panel felt that the leadership in the Unit needed to be more in control (or at least aware) of financial management.

The Panel was also concerned that some of the operational problems that the SAB asked to be addressed in the 2014 SAB report had still not been resolved by the time they reported again in 2017. Understandably, the 2017 report reiterated that certain issues needed to be resolved, and this time, needed "prompt serious attention". The Panel raised these issues during the site visit, and whereas some problems (such as access to research platforms) seem to have been addressed, others were not. For example, inefficiencies in purchasing still seems to be ongoing (2017 SAB Report: "…this chronic problem greatly slows the progress of science and puts CNP scientists at a serious disadvantage"). The Panel is concerned that internal processes may be hampering productivity. During the site visit the Deputy Director suggested that the problems lay at the level of the Foundation rather than the neuroscience programme itself. Although the Foundation is apparently aware of SAB concerns, the Deputy Director and others present at the site visit seemed unable to confirm the steps taken by the Foundation to remedy the problems, which therefore remain unresolved.

The Unit has ambitions to expand work into human neuroscience and into the clinical/translational domain, as suggested by the SAB. While the Panel appreciates the rationale for this strategy, it has identified the following concerns. First, clinical research efforts appear to be fragmented, focussing on disparate, unconnected areas spanning neuropsychiatry on the one hand, and oncology on the other. The Panel recognises the potential of the Unit to build a neuropsychiatry strand upon the research strength of CR which is based on systems and behavioural neuroscience. However, this strand needs to develop and mature before it could be considered a convincing proposition. Second, while a Systems Oncology research group will certainly help to build links with the CCC oncology clinic, these efforts do not build coherently upon CR strengths which are founded upon behavioural neuroscience rather than cancer research. In neither case did the Panel see evidence of plans to set up translational pipelines (e.g. viable relationships with industry, product development, patenting, manufacture etc.). Third, the success of translating work from animal models/tissues at the bench to human patients in the clinic is dependent, in large part, upon human MRI in both in patients and in healthy human subjects (indeed, the Shemesh group plans to take such an approach). The Panel considers MRI to be an important facility for meeting the goal of making clinical impact. At the site visit it was explained that the MRI facilities were for animal rather than human MRI, and used for technical development rather than data acquisition. However, the Panel understood from other researchers that indeed human MRI facilities are available to members of the Unit and there was indeed some work ongoing with human subjects. The Panel was keen to understand more about MRI facilities and how they were used and organised (especially in view of critical comments in a previous SAB report), but a request to visit these facilities during the site visit was declined.

In general, the Unit is to be commended for research excellence which emanates from a set of high performing PIs. There are particular concerns about low productivity by some group leaders, inefficient day to day operations, and internal communication problems. There are also concerns around the degree to which the Unit leadership has control over financial management. The Panel felt that these problems are likely to limit the degree to which the Unit will benefit from financial investments by FCT. These issues need to be resolved before major investments can be justified.

Specific recommendations:

i) The Unit Directors need to set clear rules for research group leaders about their responsibility for ensuring that PhD students and postdoctoral scientists leave the Unit with publications.
ii) The Unit Directors must have a clear understanding of how funds are managed.
iii) The Foundation and the Unit need to urgently update day to day financial operations so that suppliers are paid on time, and that the Unit reputation among suppliers is restored.
iv) The Foundation and the Unit need to listen to the concerns of the SAB and act on them quickly.
v) The Unit Directors need to think about how best to build upon their existing strengths in fundamental neuroscience, and how best they can compete with other highly competitive R&D Units in Portugal that have well-established clinical research programmes.

The basis of the recommendations mentioned above includes evidence from the application, the SAB comments, and interactions with staff and students at the R&D Unit. As mentioned above, there is wide variability in research productivity, with some groups operating at high, international standards, and others whose productivity is low. Low productivity will impact upon the reputation of the Unit as a whole, so the Panel has recommended that steps be taken to remedy this. Evidence from the site visit showed that Directors were not able to address questions around of financial management even though these were broad. The Panel has therefore recommended that Directors have a greater awareness of financial management. Evidence from the site visit and the SAB reports indicated that the Directors, SAB and the Foundation need to take each others perspectives more seriously. Finally, in developing a strategy for the future, the Unit needs to think carefully about whether or not it is really building upon its strengths in systems and behavioural neuroscience. The leadership in the Unit also needs to think about developing a more realistic clinical research programme which has important impact-related end points integrated into their plans. The Panel has therefore recommended that the Unit reshapes the clinical research programme so that it can be more competitive when compared with others in Portugal.