I-THE ICVS/3B'S ASSOCIATE LABORATORY

The External Advisory Committee of the ICVS/3B's visited this Associate Laboratory on January 20-21 2014. On that occasion the Committee visited the facilities in Campus de Gualtar, Braga (ICVS) and AvePark, Caldas das Taipas (3B's), attended presentations by the Research Domain Coordinators and met with the Direction and research staff. In this report we summarize our judgment about their accomplishments and offer some suggestions for the future.

In our opinion the site visits, the analysis of the latest scientific reports, as well as the staff presentations, confirmed the strong progression of this Associate Laboratory (AL). This AL continues to perform exceptionally well, according to the highest international standards.

Of note, we would like to stress the following achievements of the ICVS/3B's, already appreciated by this committee and that have been consolidated over the last year:

- The exceptional scientific production, reflected by the number and quality of articles published in international peer-reviewed journals.
- The significant patent portfolio and the strong links with industry, demonstrating the ability to generate value from knowledge.
- The entrepreneurial capacity, as revealed by the number of spin-off launched, some already able to attract relevant private investments.
- The outstanding involvement of the ICVS/3B's in graduate and post-graduate activities. It deserves particular mention the quality of the MSc and PhD programs, in collaboration with international partners of leading universities, such as Columbia and Thomas Jefferson Medical Schools and the MIT in the USA, as well as partners of the European Institute of Excellence on Tissue Engineering and Regenerative Medicine.
- The strong commitment to internationally recognized advanced training in health sciences/technologies, with more than 300 foreign participants in courses/workshops of the International Post-graduation Program over the last five years.
- The organization of major conferences, workshops and advanced courses (e.g. Gordon Research Conference-like meetings), as well as the leadership in National and major International Scientific Societies by ICVS/3B´s members.
- The global level of internationalization of the ICVS/3B's, as shown by the diversity of nationalities of its researchers (from more than 30 countries), by the high percentage of publications resulting from international collaborations and, importantly, by the capacity to attract competitive funding (including large projects) from international agencies, for example the FP7 of the UE, including the most prestigious European Research Council (ERC) Advanced Grant.

- The high quality of the research infrastructures, with state-of-the-art equipment, as well as the recent availability of a fully operational Clinical Academic Center, to perform clinical research, as well as the hosting of the headquarters of the European Institute of Excellence on Tissue Engineering and Regenerative Medicine.

RECOMMENDATIONS

We acknowledge the suitability of the model of scientific organization and governance adopted by the ICVS/3B's, based on two Institutions, the ICVS and the 3B's. This organization facilitates a high critical mass within a multidisciplinary networking environment. As previously addressed by this committee, we recommend that this structure, which is at the basis of the excellent outputs of the R&D unit, should be maintained.

The ICVS and the 3B's have a strong degree of complementarity and both pursue highly competitive research programs in the general area of health sciences. The biological and clinical expertise at the ICVS and the expertise in material sciences at the 3B's provide a unique interface to bring about significant progress in the diagnosis and treatment of human diseases. We encourage both Institutes to permanently nurture even closer interactions between their research groups. Two particularly important ways to achieve this aim would be:

a) The recruitment of PhD students co-supervised by scientists at both Institutions
b) The funding of collaborative research projects associating scientists at both Institutions

Future opportunities and synergies.

There are many areas of research strength and synergy already in place among 3B's and ICVB. These existing interactions provide strong synergy for the current efforts and also a template upon which to grow and expand efforts. For example:

Information Exchange

Current seminar exchanges among the two Centers is active and productive, generating new insight and opportunities for research. This type of exchange should be continued and even expanded in the renewal plans. One option is to initiate ideas with clinical input to guide new opportunities, as this will expand on the current mode of learning about ongoing research efforts at each location upon which to build. A suggestion is to establish a set of very informal round table meetings, led by physicians at the medical school. Perhaps a 4-6 researchers from 3B's and ICVB would attend to each table to listen to the needs from the physicians. The goal would be for the

physician to discuss her/his specific problems or needs regarding medical devices, biological complications or related needs. The participants can ask questions and ultimately identify new joint target research opportunities. The seed funding planned for the program could be used to get some of these projects underway, projects that would lead in new directions for the teams and build upon synergy in expertise between biology, engineering and medicine.

Techniques/Training Modules

One suggestion to build upon current efforts and to further engage the students at both programs would be to organize a set of short training modules. These modules would focus on 'techniques' and not specific research projects. For example, 3B's could organize modules to cover materials analysis, bioreactor design, stem cell characterization, and related themes. These might be one week lab type classes, taught by the 3B students and staff and attended by students from ICVS and possibly other students outside of the programs. This would provide opportunities for discussions about research needs while the students learn the new techniques. These modules could be run any time and students could sign up for one or more modules to learn topics of interest. These modules can serve as nuclei for new ideas and enhance project activities.

Student Exchanges

There are solid interactions already underway between the two programs. Suggestions would be to enhance these exchanges by housing students from each of the locations in the other labs for an extended period of time, to learn techniques, build joint projects and continue to enhance interactions. The plans for a joint PhD program would provide an excellent opportunity to address this need, as well as the possible establishment of some joint lab space at each location. This joint research space would be temporary for the users and available to the other group to come and work to get the new projects started or to optimize synergy in the short term.

Research Excellence

It is clear by the metrics provided and the scientific review that was provided, that both groups are at a high level of scientific excellence. This is a terrific starting point to build synergy and the points above (joint lab spaces, joint PhD programs, new projects originating from physicians) will provide additional traction and growth for these efforts in the five years ahead.

Government Funding

From all the data available that was analyzed by the EAC, including the official information provided by the FCT on their web-site, we conclude that the ICVS/3B's plays a leading role in the national effort to attract funds from international agencies and companies. The outputs of the

ICVS/3B´s are also quite impressive on all the parameters evaluated by FCT on their recent bibliometric study.

This Committee notes however that, in contrast, the national basic and strategic funding provided by the FCT has been very limited and disproportionately lower than the average funds provided to the universe of portuguese R&D units with comparable outputs. This is particularly striking when comparing the ICVS/3B´s to the other Associate Laboratories in Portugal. Taking into account the number of scientists holding a PhD and, above all, their scientific productivity (international publications, patents, citations and the spin-off companies created) this is a very inequitable situation.

We think that an increase in the basic and strategic funding provided to the ICVS/3B's by the national funding agencies would be justified, in order to redress this unfairness. This would be instrumental to guarantee the sustainability of this AL. A regular and reliable source of national funds would fill the financial gaps between competitive calls, including hiring and maintaining human resources (research staff and highly specialized technicians) and the maintenance of the ICVS/3B's technological platform.

In addition, this Committee considers that relevant public funding should also be attributed to match the international efforts of the ICVS/3B's in the consolidation and update of its highly competitive scientific platform at the forefront of technological advances, namely in the context of the Portuguese Strategies for Smart Specialization.

II- ICVS – SUMMARY – REVIEW

The Panel heard presentations by the Director (**Jorge Pedrosa**) and by the Coordinators of the three research Domains at the ICVS (**Fernando Rodrigues** - *Microbiology and Infection*; **Nuno Sousa** – *Neurosciences*; and **Jorge Correia-Pinto** - *Surgical Sciences*) and discussed their past activities and future plans.

The ICVS is a world-class research Unit on biomedical and clinical sciences integrated, since 2003, in the Portuguese R&D network. In spite of being a fairly young Unit, it has already established a very effective organizational structure characterized simultaneously by its dynamism and flexibility, which has allowed scientific outputs marked by excellence. Indeed, a clear policy was established implementing integrated management of the Institute; shared high-tech core laboratories organized by function; shared technical/financial resources; as well as structured and

efficient mechanisms to foster scientific productivity (such as for example: the provision seed money for scientific projects; the co-funding of basic reagents; the internal awards for the best publications; etc.). Overall, this collegial and integrative policy has been crucial to unite the ICVS members around the strategic goals of the Institute.

It has been very rewarding to follow the impressive progress of the scientific indicators of the ICVS over the last ten years, with a substantial increase in the number of publications (more than 150 only in 2013) and quality (their Impact Factor has steadily improved, including publications in leading journals such as Nature and Science), the impact and high level of internationalization of its post-graduation programs (where an impressive number of participants, from both scientific and medical backgrounds – more than 700 in 2013 – is to be noted), the creation of three spin-off companies in the last five years, and the strong interaction with other technological research units from the University of Minho, particularly the 3B's Group.

One of the distinctive features of the ICVS, which contributed decisively for its achievements, is the interplay and connection with the School of Health Sciences (ECS). In fact, the ICVS is part of an innovative medical school that is guided by international standards of excellence (certified by the ASPIRE initiative). This is reflected internationally by its partnerships with leading institutions, such as the National Board of Medical Examiners and the Thomas Jefferson and Columbia Medical Schools (USA). Nationally, the performance of the MD graduates from the ECS in the national exam at the end of the medical course (the first position among the graduates from all Portuguese medical schools) also reflects the high levels of excellence reached by the medical course of the ECS. The mechanisms set in place to promote interactions between the ICVS and the ECS have proven very effective and should be pursued, since they endorse a common mission: the high quality and profile of the MD graduates, and the clinical impact of the research conducted at the ICVS. This effort, developed in partnership with the affiliated network of hospitals and health centers, has also evolved in a very positive way. In fact, one of the most relevant developments was the recent creation of the Clinical Academic Centre- Braga (CCA), in partnership with the Braga Hospital run by the José de Mello Saúde Group, a leading corporation in health care in Portugal and Europe. The results achieved during the two first years of activity of the CCA are striking (around 1/3 of all clinical trials run in Portugal and several observational and validation studies) and represent an invaluable contribution to clinical research in Portugal, an activity somewhat underdeveloped in the country that is a key priority for the national R&D network. Another distinctive feature of the ICVS that resulted in high scientific productivity and should be maintained is the organization of their research activities around creative multidisciplinary research

Domains (instead of individual research groups centered in individual PIs) with high critical mass and on relevant health topics: Neurosciences; Microbiology and Infection; and Surgical Sciences.

III- 3B'S – SUMMARY – REVIEW

The major takeaway points from the review of the four areas of research focus at 3B's was that of research excellence, committed faculty and staff and strong leadership. These are remarkable factors to see given the short lifetime of the 3B's effort and reflect on the strength in vision and approaches to grow a leading research enterprise in Portugal. The research activities, the equipment, the technical staff, the faculty, the students and the facilities are impressive at all levels. Perhaps even more impressive is how this program has evolved under the unique and visionary leadership of Prof. Rui Reis, supported by a talented group of program leaders who each gave terrific talks and summaries of the efforts of their respective teams of students. The novel approach to coordinating and tracking the research plans, outputs and productivity at 3B's is also a unique model that seems to have worked well in this environment to allow rapid growth in volume and excellence in the program. The ability to automate and track all facets of the research projects is novel and is a model that others may emulate. The trajectory of scientific output, whether measured as peer reviewed papers, impact factor, patent filings, industry interactions, numbers of students involved or international networks of interactions, have all grown with impressive numbers and quality over the past five years and can be expected to continue on this path with the next five.

This program has become a gold standard in Portugal, combining local research excellence with international recognition and interactions, all achieved within a remarkably short time frame. The leadership of Prof. Reis is also quite unique in his openness and willingness to build networks of excellence in Europe as well as around the world, and this approach has in part allowed the rapid growth in quality and impact for the program. This is further enhanced by the unique talent that Prof. Reis brings to his role as Director of 3B's, in terms of running such a large organization, finding opportunities to support equipment, buildings and student needs, and providing national and international opportunities for the staff and students to experience and expand their skills and impact. In many respects, Prof. Reis and his program have put Portugal on the research map in areas of biomaterials and tissue engineering.

The four thematic areas reviewed included: *Materials Science and Technology* (**Joao Mano**); *Tissue Engineering and Regenerative Medicine* (**Manuela Gomes**); *Nanobiomaterials and Nanobiomedicine* (**Nuno Neves**); and *Stem Cells* (**Alexandra Marques**).

There are many areas of unique leadership in science and engineering in evidence in the current program. ISO certification for all aspects of lab functions, including documentation and resource tracking is novel and important in an academic setting and can serve as a model for other institutions. The focus on marine resources for novel materials is also a signature effort that reflects a unique effort and one well-matched to Portugal for the marine-rich location. Efforts with cork as a biomaterial also fits well as a natural resource to be further studies. The availability of a full suite of imaging, materials characterization, cell sorting and related equipment provides the critical support for the various projects and includes 3D printing capabilities. Marine polysaccharides such as gellan, proteins, new scaffolds and related biomaterials efforts provide distinction and a wealth of new polymers from biological to study and exploit with new properties. Suggestions include exploration of bioadhesion and interfaces would be useful to consider as part of the expanding efforts. The programs on combinatorial materials, stimuli responsive polymers, organic and inorganic materials, injectables, self-assembly and high throughput screens are all useful components to the program that can identify and promote specific materials and technologies toward new discoveries. The new porcine animal facility that is available now at ICVS should prompt additional opportunities in biomaterials and stem cell studies to support the biomaterials and tissue engineering research ongoing at 3B's.

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(on behalf of all members of the EAC)