

SCIENTIFIC REPORT 2014

JOSEP CARRERAS LEUKEMIA RESEARCH INSTITUTE (IJC)

It has been four years since the IJC was created in November 2010. With regard to the work that has been carried out, on 5 September 2014 the University of Barcelona Hospital Clínic Campus was opened, the cost of the investment made by the Josep Carreras International Foundation (FIJC) for the construction of the laboratories, the acquisition of equipment and a donation to the University of Barcelona Faculty of Medicine comes to a total of more than 3 million euros. At the present time work is taking place on a collaboration agreement between the FIJC and the Hospital Clínic in Barcelona (HCB) for the enlargement of the HCB Clinical Trials Unit. The FIJC's contribution to the building of this unit is one million euros.

At the Catalan Institute for Oncology/Germans Trias i Pujol Campus (ICO/GTiP) Phase 0 of the building work was completed in December 2014 (earth moving, car park, and the building's general structure) at a cost of €2,362,000. In January 2015 building work commenced on Phase 1 of the building (ground floor and 50% of the laboratories on the 1st, 2nd and 3rd floors). The invitation to tender was made for a total cost of €8,094,281 and was awarded for a total cost of €6,306,563. The building work will be performed by the company Construcciones ACR (€3,245,424.80) and the facilities will be the responsibility of the company UTE AGEFRED-ADISGRUO (€3,061,138.50).

Building work started on a new research building at the St. Pau Campus in January 2015. Work is due to be completed by December 2016. The IJC will occupy an area of approximately 300 m² of this new building. Furthermore, the Functional Plan for the St. Pau Campus is being drafted for the period 2016-2020 for which possible means of financing are being sought.

Various items of equipment have been acquired: a) a small animal irradiator costing €450,000, of which €225,000 were provided by the FEDER (MINECO) fund, and €225,000 by the FIJC; b) a Fluidigm, a

piece of equipment that enables the cell-by-cell study of genes, costing €336,698, of which €168,349 were provided by the FEDER fund (Generalitat de Catalunya) and €168,349 by the FIJC; c) a metaphase scanner costing €138,000 paid for by the FIJC and d) two cytometers (Attune-Life Technologies and CUBEB-Sysmex Partec) costing €500,000 provided for Dr. Jordi Petriz, who has recently joined our Institute.

The IJC currently has 60 members of staff, 23 at the University of Barcelona Hospital Clínic Campus, 14 at the ICO/GTiP Campus, 4 at the St. Pau Campus, and 19 more from the Institute for Predictive and Personalized Cancer Medicine (IMPPC) SUMA Project, as well as an additional 8 administrative staff.

Furthermore, the staff at the Hematology services at the three campuses must also be borne in mind (15 at the University of Barcelona Hospital Clínic Campus, 30 at the Catalan Institute for Oncology/Germans Trias i Pujol Campus (ICO/GTiP) and 33 at the St. Pau Campus). These members of staff are progressively becoming functionally ascribed to IJC research. The four group leaders who are incorporated into the IJC, together with their respective groups from the IMPPC, are Drs. Marcus Buschbeck (Chromatin and Cell fate), Mayka Sánchez (Iron and Cancer), Fumiichiro Yamamoto (ABO Histo-blood groups and Cancer) and Tania Vavouri (Regulatory Genomics). These groups are progressively channeling their activities towards research in the field of malignant blood diseases.

With regard to scientific production during 2014, IJC researchers published 75 scientific works with an average IF of 6,8671 and with 62,67% of articles published in scientific publications in the first quartile.

It should be stressed that the IJC has started to appear as a Research Institute in the world's most important scientific publications such as the New Engl. J. Med., Cell, Lancet Oncology, Cancer Cell, J. Clin. Oncol., J. Exp. Med., Genome Res, and so forth.

The first patent has also been registered with the title: "Treatment against hematological tumors (Acute Myeloblastic Leukemia) with serotonin receptor antagonist APOMORPHINE" (ITALFARMACO-BRITANNIA PHARMACEUTICAL, Ltd.). The inventors are Drs. Ruth Muñoz Risueño, Meritxell

Nomdedeu, María Carmen Lara Castillo, Marta Pratcorona and Jordi Esteve, and the Titular Institution is the IJC. During the month of May a meeting will take place between representatives of the IJC and Britannia Pharmaceuticals, Ltd. to discuss clinical trials to study the therapeutic effect of Apomorphine in patients with acute myeloblastic leukemia that is resistant to treatment.

With regard to scientific activities, the IJC's Second Scientific Meeting was held at the University of Barcelona Hospital Clínic Campus on 16 January 2015. It was extremely well attended and the scientific projects of the three campuses were presented.

The IJC, together with the Centre for Genomic Regulation (CRG), is organizing an International Congress for 24-26 November of this year on "RNA and disease", the organizers being Drs. Juan Valcárcel (CRG) and Mayka Sánchez (IJC). The Congress will be held at the PRB and will bring together more than 300 scientists from around the world. A great deal of attention is being given to the affiliations, signatures and acknowledgements which must appear on scientific works relating to all the organizations that collaborate with the IJC such as the Instituto de Salud Carlos III (ISCIII), La Obra Social "la Caixa", pharmaceutical laboratories, hospitals and their corresponding Hematology Services, universities and various foundations.

On 24 November of last year we held a meeting with the members of the Scientific Advisory Board (SAB) presided by Prof. Lucio Luzzatto. The main conclusions drawn by the members of the SAB were the following: define the main aims for IJC research for the next 20 years to include 3 or 4 very strong lines; create a tumor register for malignant blood diseases; continue strengthening clinical trials with collaboration between the three campuses making use of current audiovisual technologies; consolidate the framework accords and collaboration agreements with the hospitals and their corresponding research institutes; work towards the creation of a collection of biological samples at the three campuses; continue to strengthen quality scientific production and provide support to the group leaders and PIs in their notably effective efforts to obtain funds for the acquisition of new technology and for contracting staff; delay the call for the appointment of a Scientific Director for two years; clarify the IJC's institutional relationship with the hospital institutions at the three campuses (HCB, Hospital St. Pau and ICO/GTiP); extend Dr. Evarist Feliu's post and recognition as acting IJC Scientific Director for two more

years; specify the qualities that will be required from the Institute's future Scientific Director and rationalize the implementation of research at the three campuses so as to avoid repetition between them and optimize resources.

With regard to budgetary affairs it should be said that the raising of competitive public and private funding has been very good. In 2014 and the first quarter of 2015 €8,039,970 was raised (projects underway €4,613,916, fellowships €1,065,200, accords and agreements with the pharmaceutical industry €2,154,654 and donations €206,200).

For its part, apart from fulfilling its undertaking to provide funding for the construction of laboratories and research buildings and for the acquisition of equipment, the FJC has also contributed to the Institute's operational costs in the following manner: Start ups x 3 (€540,000), presidential grants (€60,000), start ups x 4 (€200,000), Leukemia Week Campaign (€50,000) and the German Josep Carreras Foundation's projects (€800,000). In total, €1,650,000.

A meeting was held with the Scientific Directors of the accredited Research Institutes at the three campuses to establish the IJC's position within the campuses by means of agreements with the hospitals and the Research Institutes. It was agreed to start work on establishing a Trilateral Framework Accord at the ICO/GTiP Campus, with the participation of the ICO, IGTP and the IJC, similar to the one established between the HVH-VHIR-VHIO. Once established and signed the model would be exported to the other two campuses.

A meeting was also held with representatives of the Government of Catalonia (Generalitat) responsible for research with the aim of receiving a reply to the document the IJC submitted in July 2014. It was concluded that health-care and scientific alliances should be established with the hospitals and accredited research Institutes at the three campuses. The Generalitat representatives informed the FIJC/IJC representatives that the funds requested by the IJC for 2015 (€920,000) and 2016 (€1,970,000) can not be provided, the main reason being that these funds would have to be taken from other Institutes and this would cause a very large problem. Nevertheless, alternative formulas are being sought to find a way of providing these subsidies to the IJC.

With regard to the Framework Accords and Cooperation Agreements, the following have been signed: AGAUR-CERCA-IGTP-IMPPC-IJC and IGTiP-IMPPC-IJC. The agreement between the FIJC-HCB (Clinical Research Unit) is pending signature and the following agreements are yet to be drafted: ICO-IGTiP-IJC, FIJC-IJC, HCB-IDIBAPS-IJC, UAB-IJC and HStPau-FISt.PAU-IJC.

Training activities continue. In 2014, there were three FISH courses (Fluorescence in situ hybridization) applied to the diagnosis of myelodysplastic syndromes (SMD) and other hematological neoplasms and in 2015 there will be three courses on cytogenetics FISH applied to SMD.

Services are also provided to other Research Institutes and Hematology Departments. 110 gene microarray profiles were performed in 2014 as well as 60 gene expression microarray profiles.

A Communication Committee was established between the FIJC and the IJC that meets monthly and it set up the website (31.7.2014) and the IJC intranet (1.12.2014). Additionally, it publishes a monthly newsletter.

Among new projects are the requests being prepared for the German Foundation's 2015 grants on a) Project IMPULSA: CARTs: (CD19 University of Barcelona Hospital Clínic Campus and ICO/GTiP) and (CD 30 St. Pau Campus); b) Preclinical development of nanoconjugates T22-GFP-Auristatine (St. Pau Campus) and c) Genetic and functional characterization of hematopoietic leukemic cells and CMML mesenchyme stroma cells (ICO/GTiP Campus). Moreover, progress is being made on the Accords and Collaboration Agreements for the development of research projects with the pharmaceutical industry (Celgene, Celgene Internacional, Janssen and Menarini); the PRECIPITA platform (for crowdfunding) with FECYT (MINECO), with whom a project has already been presented on "infantile acute lymphoblastic leukemia" by Dr. Pablo Menéndez (University of Barcelona Hospital Clínic Campus) and on the accords to carry out research projects with the Fundació Obra Social "la Caixa".

Work is also underway on a Fiscal Optimization Project in which the Santander Bank will help to promote the R&D&I at the IJC opening up the possibility of retrieving up to 25% of project funds. Finally, a model for the categorization of scientific and professional posts at the IJC is being designed.