HCERES

High Council for the Evaluation of Research and Higher Education

Research units

HCERES report on research unit:

Cancer Research Centre of Lyon

CRCL

Under the supervision of the following institutions and research bodies:

Université Claude Bernard Lyon1 - UCB

Centre National de la Recherche Scientifique - CNRS

Institut National de la Santé et de la Recherche Médicale - INSERM

Centre Léon Bérard

Evaluation Campaign 2014-2015 (Group A)

HCERES

High Council for the Evaluation of Research and Higher Education

Research units

In the name of HCERES,[1]

Didier HOUSSIN, president

In the name of the experts committee,[2]

Margaret FRAME, chairwoman of the committee

Under the decree N°2014-1365 dated 14 november 2014,

[1] The president of HCERES "countersigns the evaluation reports set up by the experts committees and signed by their chairman." (Article 8, paragraph 5)

[2] The evaluation reports "are signed by the chairman of the expert committee". (Article 11, paragraph 2)

Evaluation report

This report is the result of the evaluation by the experts committee, the composition of which is specified below.

The assessments contained herein are the expression of an independent and collegial deliberation of the committee.

Unit name:	Cancer Research Center of Lyon
Unit acronym:	CRCL
Label requested:	UMR_S, UMR
Present no.:	UMR INSERM 1052 – CNRS 5286
Name of Director (2014-2015):	Mr Alain PUISIEUX
Name of Project Leader (2016-2020):	Mr Alain PUISIEUX

Expert committee members

Chair:	Ms Margaret FRAME, Edinburgh Cancer Research Centre, UK
Experts:	Ms Armelle BLONDEL, Cochin Institute, Paris
	Ms Susan CHAN, IGBMC, Strasbourg
	Mr Bruno CLEMENT, University of Rennes
	Mr Brian HUNTLY, Cambridge Institute for Medical Research, UK
	Mr Gareth J. INMAN, University of Dundee, UK
	Ms Clare M. ISACKE, Institute of Cancer Research, London, UK
	Mr Jos JONKERS, Netherlands Cancer Institute, Amsterdam, The Netherlands
	Ms Fatima MECHTA-GRIGORIOU, INSERM, Curie Institute, Paris
	Mr Tony NG, Kings College London, UK
	Mr Owen SANSOM, Beatson Institute, Glasgow, UK
	Mr François VALLETTE, INSERM, Nantes
	Ms Ellen VAN OBBERGEN-SCHILLING, Institute of Biology Valrose, Nice

Scientific delegate representing the HCERES:

Mr Jean ROSENBAUM

Representatives of the unit's supervising institutions and bodies:

Mr Alain EYCHENE, CNRS

Mr François-Noël GILLY, Université Claude Bernard Lyon 1

Ms Marie-Josèphe LEROY-ZAHMIA, INSERM

Ms Françoise MONEGER (representative of Doctoral School BMIC n°340)

Ms Marina ROUSSEAU-TSANGARIS, Centre Léon Bérard

1 • Introduction

History and geographical location of the unit

The Cancer Research Centre of Lyon (CRCL, UMR INSERM 1052 CNRS 5286 - Centre Léon Bérard, director Pr Alain PUISIEUX) was initiated in January 2011 in order to create a centre of excellence in tumour biology and participate in education and training in oncology in Lyon. The CRCL relies on strong links established with clinical departments from the Léon Bérard Centre and the Hospices Civils de Lyon, fostering translational research aiming to improve the lives of patients. The CRCL is composed of around 20 teams, organized into three scientific departments, with a total of around 400 researchers, including 118 permanent researchers. The CRCL has made good progress since its inception in 2011, for example with the hosting of four new teams (two ATIP-AVENIR laureates and two laureates of the international and emergences calls in 2013). The CRCL teams benefit from direct access to rapidly developing state-of-the-art core facilities (cell sorting and cytometry platform, imaging facilities, drug discovery laboratory, animal services, and others).

Within the review period (January 2011 – August 2014), the CRCL productivity was excellent, including large numbers of publications, with 126 of these articles in journals with Impact Factors >10. CRCL researchers also filed 45 patents, of which 6 have been licensed to industry. CRCL scientists have contributed to the local environment in Lyon, including via participation in the DEVweCAN LabEx (Laboratoire d'Excellence, director: Mr Patrick MEHLEN) and the LYRIC (LYon integrated Research Institute in Cancer, director: Mr Jean-Yves BLAY, deputies: Mr Alain PUISIEUX, Mr Charles DUMONTET).

To increase its international recognition, the 1st CRCL symposium in February 2013 centred on the fundamental aspects of the biology of cancer, while linking basic, clinical and translational research. The CRCL aspires to enhance its international reputation further in the coming years. In addition, the CRCL launched a new Master in oncology. Together with international student exchange programmes, this provides clear evidence of significant contribution to training of the future generation of cancer researchers.

The CRCL is located on a unique site in Lyon which benefits from all the necessary facilities required to develop interactions between basic cancer researchers, clinical practice, education and training. Indeed, it is co-located with, or in close proximity to, the Centre Léon Bérard hospital, the Édouard Herriot hospital (HCL), the Faculties of Medicine and Pharmacology and the International Agency for Research on Cancer (IARC, a WHO organization). The 20 CRCL teams are all located within a relatively small area in Lyon, with 16 of the teams based within the Cheney A and D buildings on the Centre Léon Bérard site, 2 teams located in the Inserm building Cours Albert Thomas and two teams located at the Rockefeller and Laennec medical schools. Moreover, a new research building is under construction within the CLB site (expected delivery date mid 2014). This new building will host additional research teams from basic research in the CRCL and translational/applied clinical research.

Management team

The CRCL has been Directed by Mr Alain PUISIEUX since 2011. Mr Alain PUISIEUX is assisted by two deputy directors, Mr Patrick MEHLEN and Mr Charles DUMONTET. All three are excellent and experienced internationally renowned researchers in their own right and direct teams within the CRCL in addition to their management duties.

HCERES nomenclature

SVE1_LS3 Biologie cellulaire, biologie du développement animal

SVE1_LS6 Immunologie, microbiologie, virologie, parasitologie

SVE1_LS1 Biologie moléculaire et structurale, biochimie

SVE1_LS4 Physiologie, physiopathologie, biologie systémique médicale

Unit workforce

Unit workforce	Number as at 30/06/2014	Number as at 01/01/2016
N1: Permanent professors and similar positions **(staff with half-time research activities)**	53	62
N2: Permanent researchers from Institutions and similar positions	55	65
N3: Other permanent staff (without research duties) **+ CRCL staff members affiliated to common services and technological platforms**	61	73
N4: Other professors (Emeritus Professor, on-contract Professor, etc.) **including PH with part-time research activities**	21	33
N5: Other researchers (Emeritus Research Director, Postdoctoral students, visitors, etc.)	38	38
N6: Other contractual staff (without research duties) **including CRCL staff members affiliated to common services and technological platforms**	27	33
TOTAL N1 to N6	**255**	**304**

Unit workforce	Number as at 30/06/2014	Number as at 01/01/2016
Doctoral students	65	
Theses defended (in the 2009-2014 period)	112	
Postdoctoral students having spent at least 12 months in the unit (in the 2009-2014 period)	52	
Number of Research Supervisor Qualifications (HDR) taken (in the 2009-2014 period)	11	
Qualified research supervisors (with an HDR) or similar positions	77	90

2 • Overall assessment of the unit

Global assessment of the unit

The cancer research centre of Lyon (CRCL) was formed in 2011 with the remit of bringing together scientists, teachers and administrators to create a centre of excellence in tumour biology, form close functional links with the local cancer treatment (hospital) centres, primarily the Léon Bérard Centre and the Hospices Civils de Lyon, so promoting clinical translation of CRCL research. The CRCL participates in teaching in both research and clinical disciplines. It is the view of the review panel that a huge amount of progress has been made on the journey to creating a comprehensive cancer centre in Lyon, and the director and his senior colleagues should be congratulated on progress to date. The environment is dynamic, with some 400 researchers, which includes 108 permanent researchers and 20 physicians, also with introduction of new groups and some excellent early career researchers during the review period. These researchers benefit from state-of-the-art facilities which are being developed rapidly in the CRCL, together with excellent scientific equipment and administrative services that create an environment persimissive for science at the very top level. Overall, the director (Mr Alain PUISIEUX) and his deputy directors (Mr Patrick MEHLEN and Mr Charles DUMONTET) should be congratulated for their vision and progress. There are some outstanding scientific groups in the CRCL; as always with review of organisations like the CRCL, there are also some groups that are less strong and require monitoring and mentoring by the director and his senior colleagues.

There are three main scientific themes in the CRCL organised into departments, in the review period these were: 1) Tumoral escape, 2) Information flow in the cancer cell, and 3) Immunity, micro-environment, virus. The high impact research outputs of each department in terms of publications and patents were considered to be excellent, and the panel noted a very large volume of papers to which CRCL researchers had contributed. Going forward, some reorganisation and team reassignment is proposed – giving rise now to three departments for the next contract period: 1) Tumour escape signalling (7 teams), 2) Cancer cell plasticity (7 teams) and 3) Immunity, virus and inflammation (9 teams). These themes are extremely relevant and important in modern cancer research, and the panel considered the proposed new organisation to be appropriate. It was noted, and considered important, that there was significant collaboration and exchange between teams within departments and between departments, and future joint publications were expected to reflect excellent team science that provided added value in the future. It was welcomed that the departments were provided with some resources to promote meetings, seminar series and facilitate inter-team interactions. The CRCL management team, committees, working groups and dedicated heads of core facilities all generate a professional environment for optimising science and the smooth running of the CRCL.

The panel commends: 1) the contribution of CRCL scientists to the award and success of the LabEx (DEVweCAN; dir: Mr Patrick MEHLEN) programme, which is to study developmental processes in oncogenesis and which involves several CRCL teams, and 2) the contribution of senior members of CRCL staff to the formation of LYRIC (dir: Mr Jean-Yves BLAY) which brings together lab- and hospital-based researchers from around Lyon so as to integrate basic science with clinical/translational opportunities. The panel considers that both of these 'structures' are very important to the ambition of creating a comprehensive cancer centre that will ultimately integrate cancer research and treatment in Lyon. The CRCL involvement in both the LabEx programme and LYRIC appear to be successful. Due consideration needs to be given to how the funding associated with these, in particular DEVweCAN, may provide sustainable long-term value to the overall comprehensive cancer centre ambition once the particular tranche of funding ends.

The ambition to be world class requires that the international reputation and visibility of the CRCL teams is consolidated, and enhanced in the longer term. Multiple approaches to ensure this are wise, and the Director and deputy directors are aware of these. More EU, ERC, H2020 etc. funding applications should be encouraged, and endeavour and funding dedicated to travel to increase invited speaker invitations at key international meetings should be considered a high priority. However, the panel did note that several international scientists had been recruited during the review period. Those who had been recruited via rigorous external assessments were generally considered to be excellent, especially the early career researchers. However, the panel urged that such rigorous Principal Investigator (PI) appointment criteria and assessment was carried out for **all** appointments, including internal promotions to PI/team leader, to ensure that the future research leaders within the CRCL will all be of the highest quality. The panel was very positive about the Scientific Advisory Board (SAB) and urged the director to ensure that they were fully engaged in providing crucial advice, particularly in making new appointments and internal PI promotions.

The overall perception of the review panel was that outstanding science and excellent clinical/translation was being performed by more established ('senior PI') groups, and that there had been an influx of outstanding talent amongst the externally recruited 'younger' groups; however, the standard of some 'mid-career' and internally promoted PIs was not universally as high. This is something the director and his deputy directors need to focus on going forward and perhaps introduce some mentoring and review with respect to their scientific strategy, productivity and presentations of those groups.

The researchers in the CRCL are extremely commercially-aware; it was noted that very many patents had been filed across the CRCL – although these varied in quality as regards likely future commercial value. Nevertheless there were a few spin out companies and there was evidence of increasing industrial partnerships. This will help to promote clinical translation and future impact emerging from the CRCL's cancer research.

Overall, the CRCL is on the right track along its journey to become an effective comprehensive cancer centre in the future – linking excellent cancer biology with clinical translation, while training and mentoring the next generation of basic research leaders and clinician scientists. The panel commends the fact that non-clinical scientists and clinical scientists are working side by side to address some of the fundamental problems in cancer research, and importantly, are aware of opportunities to make a difference to the lives of patients where this is feasible. Moreover, the CRCL staff are actively engaged in teaching and training at all levels. The staff, when met by panel members, seemed collegiate and generally pleased with the organisation, and this is testament to the work of the Director and his senior colleagues in developing the CRCL.

Strengths and opportunities in relation to the context

A real strength is in the outstanding leadership of the CRCL, and especially in the area of the links between the basic science and the clinic. Experienced staff in both basic and clincial research are working side by side to optimise the potential for clinical translation, which is excellent. The co-localisation of laboratory science beside, or near, the two treatment hospitals is ideal, and provides superb opportunities. The LYRIC structure is a great asset if it continues to work well for the researchers in Lyon. The 'buy in' at the top of all the organisations involved was rather impressive and provides an outstanding opportunity for integration and success.

A further strength is in the experience and expertise in the biology and clinical treatment of a variety of cancer types and related cancer processes. This includes good preclinical models in many cases.

The organisation within CRCL is excellent, including an excellent management team and three complementary themed departments, together with good administration support and forums for researchers from all staff categories to have input. Communication is excellent. See recommendation 1 below.

There is an excellent cohort of new PIs via external recruitments (mainy from joint ATIP-AVENIR INSERM-CNRS programmes), which makes for a dynamic research environment and staff 'refreshment'; new blood remains vital to all research organisation and this bodes well for the future of CRCL.

The SAB is a real strength and consists of well-respected cancer researchers with abundant experience and good opinions. It may need to be expanded to ensure this as the SAB members are very busy people. See recommendation 2 below.

The first CRCL symposium was a very good start to increasing visibility on the international stage. See recommendation 3 below.

State-of-the-art facilities (eg. animal facilities, genomics, associated bioinformatics, flow cytometry and cell sorting, drug screening, etc.) have grown very rapidly, and provide excellent opportunities for top level science. These needs to be developed further, and made cost-effective and sustainable, particularly animal services and other facilities which need carefully managed. See recommendation 4 below.

Finally, the development of a drug discovery programme is bold, but it is a worthy ambition. However, the goal of taking drugs all the way to the clinic may be over-ambitious for an academic unit. See recommendation 5 below.

Weaknesses and threats related to the context

In the same vein, and as mentioned above, there needs to be turnover amongst teams to refresh, given that space is likely to be limiting either now or in the future, so as to keep recruiting and refreshing – although the panel appreciates this is complex to achieve and challenging, and is tied up with French employment law. See recommendation 6 below.

The panel felt strongly that whilst much of the research was truly outstanding or excellent (at the senior team leader level and some new recruits), there was also some groups who were not performing at the same very high standards. This will be evident from the report on individual teams. It was noted that during the review presentations some of the less strong groups changed the projects from those that were described in the paperwork, which suggested to the panel there may have been a lack of clear research vision and focus in some of these teams. See recommendation 6 below.

There were limited funds to attract post docs – often the life blood of the groups – and PhD students. See recommendation 7 below.

As mentioned above, the international profile of the CRCL is not yet optimised, and should be developed further through multiple mechanisms. The international reputation and visibility of the CRCL teams should be a priority. See recommendation 8 below.

As regards the development of facilities – the panel would caution against too rapid an expansion and ensure that good decisions are made with respect to sustainability plans via internal (or occasional external) facility reviews. With regard to animal useage and the undertaking of expensive projects, it is important that researchers are not tempted to do experiments "because they can", but rather they need to be able to justify the expense on the grounds of scientific value and priority. See recommendation 9 below.

The lack of a few high-end capabilities, such as high-resolution or cellular imaging, and single cell analysis, may be a little constraining for some groups, but the panel is confident this will be put right in due course. All facilities cannot be made perfect at once, and the CRCL is doing well with setting up facilities.

Finally, as mentioned above the development of a drug discovery programme a worthy ambition for CRCL. However, go/no go decision processes need to be very carefully monitored and tightly controlled if resources are not to be wasted. See recommendation 5 below.

Recommendations

The panel recommends (with great enthusiasm) that the director and deputy directors continue on their current path of building towards an effective comprehensive cancer centre in Lyon. The facilities, opportunities and environment are excellent, especially for translational cancer research. The panel is confident the structures and organisation are now in place for the science and impact to go to the next level, and commends the Directorate for their hard work and vision in developing CRCL to this point. In the long term, the panel believes that Lyon will have a cancer centre – linking research and treatment with training and career opportunities – which will be recognised as one of the best in France and internationally. Some specific recommendations are suggested below:

In regard of the points made above two sections:

1. It is important that the good communication existing between management and staff is maintained, and perhaps increased, to ensure that all staff remain engaged and content.

2. The SAB is a real strength, comprising of respected scientists; the panel urges the Director to ensure that the SAB remains fully engaged in key decisions and appointments. It may need to be expanded to ensure this as the SAB members are very busy people. The panel notes from experience of its members, that occasionally SABs can dis-engage with time.

3. The development of further symposia, interactions, collaborations, educational programmes and dissemination of findings at international meetings is to be encouraged – helping to further build local team spirit, and national and international profile of CRCL researchers and overall CRCL attractiveness to PhD students, post-docs and new PIs.

4. State-of-the-art facilities (eg. animal facilities, genomics, associated bioinformatics, flow cytometry and cell sorting, drug screening; etc.) have grown very rapidly in CRCL, and provide excellent opportunities for top level science. These needs to be developed further, and made cost-effective and sustainable, particularly animal services and facilities which need carefully managed.

5. The drug discovery activities needs to be properly resourced and processes put in place to make go/no go decisions on projects to be pursued and prioritised. With careful development and prioritization, it could lead to valuable output; however, the panel caution that the notion of taking internally CRCL discovered chemical agents into the clinic is perhaps over-ambitious.

6. There is an excellent cohort of new PIs via external recruitments (mainy from joint ATIP-AVENIR INSERM-CNRS programmes), which made for a dynamic research environment and staff 'refreshment'; new blood remains vital to all research organisation and this bodes well for the future of CRCL. Further recruitment, and perhaps some 'team turnover', is recommended if it is possible. It is vital that similar quality standards for internal appointments match those for external appointments.

7. The panel urge that all possible strategies are considered to promote funding of increased post-doc and student numbers.

8. More EU, ERC, H2020, etc. funding applications should be encouraged pro-actively. In particular, there are some team leaders who would be appropriate for ERC applications at the various stages.

9. Regarding animal facilities in particular, Interpretation and guidance on the planning of experiments, and the handling of data acquired from these experiments, are key, and one concern from the panel was that there may not be enough support or oversight in these areas. The CRCL may wish to consider a focussed oversight committee that would internally review expensive animal experiment proposals to ensure maximum value.