ANTICIPE - Unité de recherche interdisciplinaire pour la prévention et le traitement des cancers

Rapport Hcéres

HCERES

High Council for the Evaluation of Research and Higher Education

Research units

HCERES report on interdisciplinary research unit:

Unité de Recherche Translationnelle sur le Cancer en Normandie

URTCN

Under the supervision of the following institutions and research bodies:

Université de Caen Basse-Normandie – UCBN

Commissariat à l'énergie atomique et aux Énergies Alternatives – CEA

Centre National de la Recherche Scientifique - CNRS

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

Evaluation Campaign 2015-2016 (Group B)

HCERES

High Council for the Evaluation of Research and Higher Education

Research units

In the name of HCERES,[1]

Michel Cosnard, president

In the name of the experts committee,[2]

Florent de Vathaire, chairman 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 sole result of evaluation by the expert committee, the composition of which is specified below.

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

Unit name:	Unité de Recherche Translationnelle sur le Cancer en Normandie
Unit acronym:	URTCN
Label requested:	Inserm
Current number:	
Name of Director (2015-2016):	Mr Guy LAUNOY
Name of Project Leader (2017-2021):	Mr Guy LAUNOY

Expert committee members

Chair: Mr Florent DE VATHAIRE, Inserm

Experts:

Ms Anne GALY (representative of the Inserm CSS)

Mr Francis GUILLEMIN (representative of the Inserm CSS)

Ms Catherine HEURTEAUX, IPMC (representative of the CNRS)

Mr Lasse JENSEN, Karolinska Institutet, Stockholm, Sweden

Mr Alan RICHARDSON, Institute for Science & Technology in Medicine, Keele University, UK

Scientific delegate representing the HCERES:

Mr Emmanuel LAGARDE

Representatives of supervising institutions and bodies:

Ms Claire GIRY, CEA

Mr Vincent GOUJON, CNRS, DR19

Ms Anne GUESDON, Université de Caen

Ms Christine GUILLARD, Inserm

Mr Frédéric MARIE, CHU Caen

Mr Khaled MEFLAH, Centre Antoine Baclesse, Caen

Ms Florence NOBLE, CNRS

Mr Samir OULD ALI, Inserm

Mr Frédéric SCHMIDT, CNRS

Mr Pierre SINEUX, Université de Caen

Heads of Doctoral Schools:

Mr Patrick LEROUGE, Doctoral School n°497, EdN BISE, "École Doctorale Normande de Biologie Intégrative, Santé et Environnement"

Mr Jacques ROUDEN, Doctoral School n°508, "École Doctorale Normande de Chimie (EDNC)"

1 • Introduction

The "Unité de Recherche Translationnelle sur le Cancer en Normandie" is a multi-team project that is proposing to regroup several existing units around a new project. The project is truly multi-disciplinary with epidemiology and biostatistics, imaging, animal models, preclinical biology, chemistry and radiochemistry. Efforts will be centered on 2 main axes: cognitive function in the context of cancer treatment and advanced ovarian cancer treatment.

History and geographical location of the unit

The future center comprises four teams: two are affiliated with University of Caen and Inserm and are located in the Cancer Center François Baclesse (UMR1086 headed by Mr Guy LAUNOY, and the more recent UMR1199 "Bioticla" headed by Mr Laurent POULAIN); two originated from UMR6301, headed by Ms Myriam BERNAUDIN, affiliated with CEA, CNRS and University of Caen and located about 1km apart in the Cyceron environment.

Management team

The center will be headed by Mr Guy LAUNOY and the deputy director is Ms Myriam BERNAUDIN.

HCERES nomenclature

Principal: SVE1_LS7

Secondary: SVE_LS4 SVE_LS5 ST4

Scientific domains

The project includes epidemiology and biostatistics, imaging, animal models, preclinical biology, chemistry and radiochemistry.

Unit workforce

Unit workforce	Number on 30/06/2015	Number on 01/01/2017
N1: Permanent professors and similar positions	19 (7,36)	17 (6,7)
N2: Permanent researchers from Institutions and similar positions	20 (14,3)	19 (14)
N3: Other permanent staff (technicians and administrative personnel)	27 (23,7)	26 (22,7)
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	7 (4,66)	
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	12	
N6: Other contractual staff (technicians and administrative personnel)	26 (24,9)	
N7: PhD students	29	
TOTAL N1 to N7	**140 (116)**	
Qualified research supervisors (HDR) or similar positions	35	

Unit record	From 01/01/2010 to 30/06/2015
PhD theses defended	22
Postdoctoral scientists having spent at least 12 months in the unit	10
Number of Research Supervisor Qualifications (HDR) obtained during the period	11

2 • Overall assessment of the interdisciplinary unit

Introduction

The 4 existing units are merging around a new project. The project is truly multi-disciplinary with epidemiology and biostatistics, imaging, animal models, preclinical biology, chemistry and radiochemistry.

The team "Cancers & Preventions" UMR1086 Inserm-UNICAEN covers a large domain of cancer epidemiology, from public health to clinical research. In order to investigate cancer risk factors, and in particular those associated to agriculture and to asbestos exposure, it sets and follows cohorts, including the largest cohort of farmers in the world (AGRICAN). The follow-up of AGRICAN, via the MSA (“Mutuelle Sociale Agricole”), a complementary health insurance dedicated to farmers, guarantees an almost exhaustive long-term follow-up of this large cohort. This cohort is included in the very structured international collaborative network AGRICOH, which is an additional guaranty for future results of high quality standards. Other cohorts allowed demonstration that asbestos environmental exposure is associated with several digestive cancers and further exploration will be possible through the international network

on mesothelioma under the team coordination. In secondary prevention, the demonstration, during the previous contract, that the immunochemical faecal occult blood test is best suited for screening for colorectal cancer has been very innovative, and is now nationally implemented in France. Unit members have recently conducted further work to identify the best immunological test, and further collaborations are ongoing to develop screening procedures for lung cancer in persons at risk. A new area of research, concerning tertiary prevention, is survivorship, and in particular the decrease of cognition associated with brain cancer treatment. Interestingly, some clues for a role of angiogenesis have generated the first collaboration with team 3 (LDM-TEP).

The team CERVOxy "Hypoxia, cerebrovascular and tumor pathophysiology" (constitutive team of UMR 6301-CNRS-CEA-ISTCT UNICAEN), has an expertise in the field of hypoxia and cerebral pathologies, and particularly ischemia and brain tumors. As a general matter, the objective of this team is to develop new preclinical models pertinent for the clinic, to develop a new therapeutic strategy focusing on hypoxia, and to propose and develop new biomarkers using MRI and TEM imaging (MRI, TEP), permitting to better target and to short term evaluate treatments of cerebral pathologies. It investigates the impact of hypoxia in the treatment of brain tumors, in particular the role of erythropoietin in the growth of glioma and its resistance to treatments. The work done is clearly highly original and often inter-disciplinary in nature. The team has established a niche with nice models for research concerning imaging of the brain in small live mammals and patients, as well as the emerging use of a novel animal model based on marmosets that they are beginning to exploit.

The team LDM-TEP “Methodological Developments in Positron Emission Tomography "(team constitutive of the UMR 6301 CNRS-CEA-ISTCT-UNICAEN) is centered on the development and evaluation of radiopharmaceuticals for PET imaging, rather than the development of PET technology *per se*. These developments in radiopharmaceuticals for clinical imaging are focused on Alzheimer's disease, psychiatry, and oncology. The team has established a very specific and desirable expertise in radiochemistry (C11, Fluorine 18, Gallium 68) and in the development of radiotracers (automated radiosynthesis, *in vivo* evaluation, POC) with an activity of production of radiopharmaceuticals for PET imaging (investigational medicinal products, programmed production, clinical trials). About 20% of the activity is dedicated to service production of radiopharmaceuticals and 80% is dedicated to research. More than 500 patients have been treated with radiopharmaceuticals produced by the team since 2010.

The team BIOTICLA "Biology and Innovative Therapies of Locally Aggressive Cancers", Inserm UMR 1199 UNICAEN, is positioned in the field of ovarian cancers, with two themes: pharmacological modulation of apoptosis and role of miRNAs, in the response to treatment or as biomarkers. This team is conducting world-leading research in evaluating Navitoclax, a BH3 mimetic, in ovarian cancer. This team is the first having shown that Navitoclax has single agent activity in ovarian cancer and collaborates with Abbvie, the pharmaceutical company behind this BH3 mimetic. The team works also on biomarkers to identify patients likely to respond well to Navitoclax, on inhibitors of Mcl-1, which endows resistance to Navitoclax, and on the identification of the intracellular signalling pathways that may be pharmacologically manipulated to inhibit Mcl-1. The team is also conducting novel work to understand how miRNAs and lncRNAs contribute to drug resistance, the goal of these investigations being to identify novel therapeutic targets as miRNAs have the potential to modulate the expression of multiple genes.

During the next 5 years, collaborative research will be centered on 2 main axes: cognitive function after radiation therapy of brain metastases or brain primary cancer, and prognosis factors and treatment of ovarian cancer.

Global assessment of the unit

The unit project is truly multi-disciplinary with epidemiology and biostatistics, imaging, animal models, preclinical biology, chemistry and radiochemistry.

The evaluation committee has been impressed by the multidisciplinary aspect and the quality of the previous works and of the projects for future. As a general matter, the evaluation committee has been convinced by the interest and by the huge potential of the collaborative multi-disciplinary project of Cancer and Cognition platform, in particular given the expertise and achievements available within the various teams, and the geographic presence of France Hadron in Caen. Nevertheless, although marmoset is a nice model, the clinical impact of the research is not totally clear. It may be to the unit’s advantage to establish collaboration with medical physicists, neuro-oncologists, and neuro-psychiatrist specialized in the domain.

Strengths and opportunities in the context

- the development of a Cancer and Cognition platform is a true opportunity for very productive collaboration between the different teams of the unit on an issue, the cognitive decline after brain irradiation, which is one of the major issues in cancer survivorship;

- the structured management of the unit and the attractiveness for academics and PhD students, which has constantly increased during the current period, has proved effective for the team success;
- the location of the unit in the Centre François Baclesse, its strong interaction with the clinicians of this cancer treatment Centre, as well as the important support from this Centre, and the facilities it offers in term of team management facilities.

Weaknesses and threats in the context

- the difficulty to find resources for post-docs and to attract students from other universities is somewhat a limitation;
- there is a risk if preclinical and clinical strategies are not rapidly integrated into the long-term plan;
- the strong association of BIOTICLA in the development of Navitoclax could force a significant portion of the team to realign its research if clinical trials are unsuccessful;
- most or the publications of the unit are either as non-leading authors in high impact journals (IF>10), or as leading authors in lower-impact journals;
- with the exception of the "Cancer and Prevention" team, and to a certain extent the BIOTICLA team, the other teams of the unit have too much focus on local, rather than international collaborations.

Recommendations

- the team "Cancer and Prevention" should develop a strategy to make the most benefit of the interaction with other teams in term of sample selection;
- patient specification for validation of biomarkers would be an asset to predict successful and optimized transfer from preliminary clinical to clinical population prognosis studies;
- considering the already strong expertise of Cervoxy and Bioticla teams in biology, the LDM-TEP team should consider consolidating its expertise in chemistry and biochemistry, in order to maintain a unique edge;
- the unit is encouraged to make all attempts to increase its number of post-doctoral positions;
- the unit should attempt to publish in more renowned journals than is currently the case;
- the unit should increase its collaboration with leading groups in Europe and the other areas of the world.