Research evaluation

EVALUATION REPORT OF THE UNIT

Dynamo - Dynamique moléculaire de la transformation hématopoïétique

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université Paris Saclay
Institut national de la santé et de la recherche médicale — Inserm
Institut Gustave Roussy — Cancer campus grand Paris

EVALUATION CAMPAIGN 2024-2025
GROUP E

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High Council for evaluation of research and highter education

On behalf of the expert committee:

Philippe Kastner, chairman of the committee

For the Hcéres:

Stéphane Le Bouler, acting president

In accordance with articles R. 114-15 and R. 114-10 of the Research Code, the evaluation reports drawn up by the expert committees are signed by the chairmen of these committees and countersigned by the president of Hcéres.

To make the document easier to read, the names used in this report to designate functions, professions or responsibilities (expert, researcher, teacher researcher, professor, lecturer, engineer, technician, director, doctoral student, etc.) are used in a generic sense and have a neutral value.

This report is the result of the unit's evaluation by the expert committee, the composition of which is specified below. The appreciations it contains are the expression of the independent and collegial deliberation of this committee. The numbers in this report are the exact certified data extracted from the deposited files by the supervising body on behalf of the unit.

MEMBERS OF THE EXPERT COMMITTEE

Chairperson:	Mr Philippe Kastner, Université de Strasbourg
Experts:	Mr. Thierry Fest, (CNU), Ms. Marie-Bérengère Troadec, Inserm CSS2)

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Mr. Kamel Benlagha

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Ms. Anne-Hélène Monsoro-Burq, Université Paris-Saclay VP recherche Déléguée Santé Science de la Vie

Mr. Eric Deutsch, vice doyen Faculté de Médecine, coté recherche, Université Paris-Saclay,

Ms. Anne Paoletti, directrice de la Fondation GR (représente Fabrice André)

Ms. Emma Pailler, suivi des projets de recherche, Institut Gustave Roussy

CHARACTERISATION OF THE UNIT

- Name: Dynamique moléculaire de la transformation hématopoïétique
- Acronym: Dynamo
- Label and number: num
- Composition of the executive team: Olivier Bernard

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement
SVE6 Physiologie et physiopathologie humaine, vieillissement

THEMES OF THE UNIT

The two teams of the unit study normal and malignant haematology. The unit notably addresses the molecular mechanisms of leukaemia initiation, and also engages in more translational and clinical studies that aim to identify relevant biomarkers and novel therapies. Team 1 focus is on the transformation process of myeloid cells and mature B cells, and notably with respect to the role of mutations of epigenetic modifiers (isocitrate dehydrogenase; IDH1/2, Tet2) and transcription factors (Spi1). Team 2 is interested in paediatric acute myeloid leukaemias, with a strong focus on acute megakaryocytic leukaemia (AMKL).

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The unit is located in the "Pavillons de Recherche" buildings at the Institute Gustave Roussy site (IGR, Villejuif). It is the remnant of a previously larger U1170 entity which split into the current unit after two teams (headed by F. Porteu and H. Raslova) formed a separate unit at Gustave Roussy. A third team (headed by Camille Lobry) was originally planned to be part of the unit, but this team was not created and C. Lobry left Gustave Roussy.

RESEARCH ENVIRONMENT OF THE UNIT

The Unit is membership of the Gustave Roussy Siric Epicure funded by INCa for the period 2024-2029.
It is fully integrated into the Gustave Roussy Institute, which includes ten technology platforms grouped in the AmmiCa Joint Service Unit, jointly supervised by CNRS UAR 3655, Inserm US23 and the University of Paris-Saclay.
As part of Gustave Roussy, the team is open to the Paris-Saclay Cancer Cluster (PSCC), which offers opportunities for personalized medicine.

UNIT WORKFORCE: in physical persons on 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	4
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	7
Sous-total personnels permanents en activité	**14**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	10
Post-doctorants	3
Doctorants	3
Sous-total personnels non permanents en activité	**16**
Total personnels	**30**

DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: in physical persons on 31/12/2023. Non-tutorship employers are grouped under the heading "others".

Nom de l'employeur	EC	C	PAR
Inserm	0	5	3
Inst. Gustave Roussy	0	0	3
Autre	0	1	1
U Paris Saclay	1	0	0
Total personnels	**1**	**6**	**7**

GLOBAL ASSESSMENT

The overall assessment of the unit is excellent. The aim of the unit is to understand the mechanisms involved in the transformation of haematopoietic cells and validate or implement its findings in the clinic. Its members have strong ties with other haematology teams locally (founding member of the Paris-Saclay Haematology Federation), nationally (active roles in the Société Française d'Hématologie and the Club Hématopoïèse et Oncogenèse) and internationally (active participation in the activities of the European Hematology Association).
The unit members have been very successful in securing funding, and have leveraged a total of 5.8 M€ during the evaluation period. Its resources originate mainly from national programs dedicated to cancer research (e.g.as PI, obtained during the evaluation period, two INCa, one Cancéropole…) or charities (three LNCC, one Equipe FRM…). It has also been very active in coordinating large national consortia in the field of paediatric cancers (notably coordination of the Pediac program, which was awarded 3.7 M€ (around 10% for the unit).
The unit is excellent in its visibility. It has been extensively involved in organizing scientific events (participation in organization meeting of the European Hematology Association, EHA), and is strongly involved in numerous evaluation bodies (e.g., Inserm CSS2, grant evaluation committees from ANR, FRM or EHA). It is also involved in training activities, having hosted seventeen PhD students during the evaluation period (fourteen theses defended), five postdocs, and recruited by mobility one researcher CRCN Inserm. It benefits from the excellent network of technological facilities at Gustave Roussy, and has itself contributed to improving this ecosystem through the creation of a novel facility dedicated to Crispr-Cas9 mutagenesis.
The number and quality of the publications are excellent. Members authored 27 papers as senior authors, of which the majority are in prominent journals such as Cancer Discovery, Blood, Nature Medicine, Leukaemia, Nuc Acids Res, etc. Topics range from fundamental studies to clinical ones. One major achievement is the maintenance, with high efficiency, of the exploration of genetic and molecular abnormalities in haematological disorders over the years, starting with Tet2 abnormalities more than a decade ago in myeloid cancers, then moving to Tet2 mutations in B-cell lymphoma and finally opening new questions on PU1 mutations in the chronic B cell Waldenström disease. The unit has made major discoveries pertaining to the roles of epigenetic modifiers (e.g. the isocitrate dehydrogenases IDH1/2) and transcription factors (PU.1) in myeloid and B cell malignancies, and has generated novel mouse models for paediatric acute megakaryocytic leukaemia (AMKL) to understand the mechanisms of disease development and validate combinatorial therapeutic options.
The unit has an excellent engagement with society. Its teams have strong links to pharmaceutical companies to test novel drugs in preclinical and clinical settings (notably with Forma Therapeutics for the IDH1 inhibitor Olutasidenib, an anticancer medication used to treat relapsed or refractory acute myeloid leukaemia with a susceptible IDH1 mutation, now in the clinic. They are very active in engaging the general public, notably patient associations for paediatric leukaemias.
Despite its scientific success and the strong ties between the teams, the unit will be dissolved due to the retirement of the head of the lab and the teams integrated into separate units at Gustave Roussy. This reflects the general restructuring of research teams at Gustave Roussy. They will become key elements and take leadership roles in their respective future host units. Team 2 will federate the Gustave Roussy research team working on paediatric cancers into a novel unit dedicated to paediatric oncology, while team 1 will integrate an existing unit dedicated to translational research and biomarker discovery.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

(i) The previous evaluation recommended that the unit increases its interaction with other onco-haematology teams on the sites. It was stressed that promoting such interactions was particularly important for the junior team of the unit (Team 3; Camille Lobry). Since C. Lobry left Gustave Roussy early during the mandate as his team was not created, this recommendation becomes irrelevant. To improve internal communication between the haematology teams, an annual lunch meeting has been organized to discuss important orientations.
(ii) The previous evaluation committee had strongly recommended to continue and strengthen the focus on epigenomic aspects, and to recruit an engineer in bioinformatics for that purpose. This point was addressed since 2 bioinformatician positions were obtained, funded respectively by Siric Epicure (for team 1) and by an individual grant to team 2.
(iii) The committee had also suggested applying to European grants to increase funding and networking. While no European funding was obtained by the teams (an application to an ITN program as partner was unsuccessful), it is worth stressing that members of the unit have a good visibility on the European stage, as some unit members are very active in the EHA network, participating in meeting organization and
International (Associate editor American Journal of Haematology, The Lady Tata Memorial Trust International Scientific Advisory Committee) and national (Member of the Avenir selection committee, member of CSS2 Inserm…) scientific boards.

B - EVALUATION AREAS

EVALUATION AREA 1: PROFILE, RESOURCES AND ORGANISATION OF THE UNIT

Assessment on the scientific objectives of the unit

The unit is excellent to outstanding in its scientific objectives. It aims to understand the mechanisms involved in the transformation of haematopoietic cells and validate or implement its findings in the clinic. Its members have strong ties with other haematology teams locally (founding member of the Paris-Saclay Haematology Federation), nationally (active roles in the Société Française d'Hématology and the Club Hématopoïèse et Oncogenèse) and internationally (active participation in the activities of the European Hematology Association). Its make-up of both scientists (six) and clinicians (three) has provided an excellent environment to reach these objectives.

Assessment on the Unit's Resources

The unit is excellent in its resources. It has leveraged a total amount of 5.8 M€ in grants. Its resources originate mainly from national programs dedicated to cancer research (e.g. INCa,..) or national cancer charities (Ligue contre le Cancer, FRM,..). It is worth stressing that both team leaders and team researchers are main investigators of the unit's grants, indicating an excellent capacity of the unit's members to fund their research.

Assessment on the Functioning of the Unit

The unit's functioning is excellent. As part of a general policy of the Gustave Roussy site, it has implemented strong guidelines for gender equality and the fight against sexual harassment and sexist behaviour (gender equality plan, referents to whom incidents can be reported). The unit is also active in promoting young scientists, who are provided with opportunities to present their work. Issues like safety and security, and IT resources and security are well taken care of. Finally, the unit has established a "Green research group" to promote sustainability within its activities.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The unit studies the mechanisms underlying normal and malignant haematology, and addresses both fundamental aspects of leukaemia initiation, and translational aspects like biomarker identification, and development and implementation of novel therapies. Team 1 is particularly interested in myeloid leukaemias and is building on its pioneering research involving isocitrate dehydrogenases (IDH1/2) with relation to the Tet2/Dnmt3 axis. It also works on mature B cell malignancies (Waldenstrom and diffuse large B cell lymphoma), and hosts two prominent clinicians who are specialists of these diseases. Team 2 focuses on paediatric leukaemias, notably acute megakaryocytic leukaemia (AMKL). The questions addressed by both teams and their scientific approaches are highly relevant and have led to significant advances on both the cognitive and translational fronts.

Weaknesses and risks linked to the context

No weaknesses identified

2/ The unit has resources that are suited to its activity profile and research environment and mobilizes them.

Strengths and possibilities linked to the context

The unit receives recurrent funding from Inserm and Université Paris-Saclay which amount to 141 k€ for 2023. This institutional funding has significantly diminished between the beginning and the end of the evaluation period (362 k€ in 2018 and 140 k€ starting in 2021). The bulk of the resources is obtained through grants from INCa and from Ligue contre le Cancer. One CRCN joined the Unit in 2023 by mobility.
The unit also hosts 6 permanent technical and administrative staff members, and has access to the state of the art technological and animal facilities at the Gustave Roussy site.

Weaknesses and risks linked to the context

The unit has not obtained international funding.

3/ The unit's practices comply with the rules and directives laid down by its supervisory bodies in terms of human resources management, safety, environment, ethical protocols and protection of data and scientific heritage.

Strengths and possibilities linked to the context

The unit and Gustave Roussy are active in promoting gender equality. The leader of team 1 is a woman. For health and safety, Gustave Roussy is responsible for the general supervision. The unit is represented by an H&S manager and prevention assistants who are responsible for implementing H&S-related procedures (use of radioactivity and genetically modified organisms). Gustave Roussy is also responsible for managing the IT infrastructure and data safety and conservation issues, through a dedicated "Digital Transformation and Information Systems Department" (DTNSI). Gustave Roussy also hosts a Green research group, formed by volunteers from the research staff, to discuss and provide advice about sustainable development. The unit has a detailed protocol to welcome new staff, which provides the necessary information regarding safety and administrative issues. Students appear to be well trained, with regular (weakly) interactions with their supervisors. The unit also meets on a weekly basis, and members present their projects.

Weaknesses and risks linked to the context

No weaknesses were identified

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The unit is excellent in its visibility. It has been extensively involved in organizing scientific events, and is strongly involved in numerous evaluation bodies (e.g. Inserm CSS2, grant evaluation committees from ANR, FRM or EHA). It is strongly involved in training activities, having hosted seventeen PhD students during the evaluation period, five postdocs, and recruited one CRCN researcher by mobility. The unit members have been very successful in securing funding, notably large grants as principal investigators (three INCa, two LNCC, one equipe FRM).
They benefit from the excellent network of technological facilities hosted by Gustave Roussy, and have themselves contributed to improving this ecosystem through the creation of a novel facility dedicated to Crispr-Cas9 mutagenesis.

1/ The unit has an attractive scientific reputation and is part of the European research area.

2/ The unit is attractive because for the quality of its staff support policy.

3/ The unit is attractive through its success in competitive calls for projects.

4/ The unit is attractive for the quality of its major equipment and technical skills.

Strengths and possibilities linked to the context for the four references above

The unit has been extremely active in organizing national and international scientific events, notably: the annual meeting of the Société Française d'Hématologie, a workshop within the annual meeting of the EHA Research conference, the annual congress of the Club Hématopoïèse et Oncogenèse (CHO). Unit members have also editorial responsibilities (associate editor of the American J of Haematology; Editorial board of Hemasphere). Most staff researchers are very active as members of research steering bodies and funding agencies evaluation committees, such as Inserm CSS2, Fondation Arc CN1, ANR CE17, etc. Unit members have won several prizes during the evaluation period (David Grimwade award; Roy-Vaucouloux National Science Academy awards, Prix Brigitte Mérand,..). The unit trained seventeen PhD students during the evaluation period, and fourteen of them have defended their thesis between 2018 and 2023. About two third of them were women. Eight international students or postdocs were hosted. The unit has been reinforced by the integration of a CRCN previously associated with another unit, into Team 2. The unit has obtained 5.8 M€ from grants during the evaluation period. These include many large grants from INCa or charities (labellisation Ligue and FRM) (seven grants>100k€ as PI, obtained during the mandate), as well as smaller ones (twenty 100k€; Gefluc, ALF, Fondation ARC). All the unit's staff researchers were successful in securing funding as principal investigators. Team members have also acted as coordinators of multi-team grants.
In particular, one leader coordinated a grant on paediatric cancers (Pediac) which was funded for 3.7 M€ in total (10% for the unit). The unit benefits from ten state-of-the-art platforms hosted by Gustave Roussy (AmmiCa). The unit has also set up a facility dedicated to Crispr/Cas9 mediated mutagenesis, which is open to all Gustave Roussy teams. This facility is supervised by an engineer from the unit. Since 2021, this facility has already performed twelve non-unit projects. Thus, the unit benefits from, and contributes to, an excellent technological environment at the Gustave Roussy site.

Weaknesses and risks linked to the context for the four references above

It is unclear if unit members had been invited as speakers to high visibility international conferences

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The number and quality of the publications are excellent. Members authored 27 papers as senior authors, of which the majority are in prominent journals such as Cancer Discovery, Blood, Nature Medicine, Leukaemia, Nuc Acids Res, etc. Topics range from fundamental studies to clinical ones. Senior authorship is well distributed among unit members. Unit members have also published several reviews or meeting reports, further bolstering their visibility.

1/ The scientific production of the unit meets quality criteria.

2/ The unit's scientific production is proportionate to its research potential and properly shared out between its personnel.

3/ The scientific production of the unit complies with the principles of research integrity, ethics and open science. It complies with the directives applicable in this field.

Strengths and possibilities linked to the context for the three references above

Unit members authored 70 publications, of which 27 were authored as senior authors by unit members. Papers were published in a prominent journal like Nature Medicine, Cancer Discovery, Blood, Leukaemia or Nucl Acids Res. Notably, eight papers were published as collaborations between both teams. Topics broadly covered the molecular and genetic mechanisms of leukaemia and lymphoma development. The unit published several highly visible clinical papers (eg, Nat Med 2023; Am J of Hematol 2023), highlighting its potential to conduct both fundamental and clinical research. Major achievements include the discovery and modelling of novel mutations of the transcription factor PU. One in Waldenström's macroglobulinaemia, clinical studies targeting IDH1/2 mutations, and mechanistic and preclinical studies of paediatric acute megakaryocytic leukaemia in mice. The number and quality of the publications are outstanding for the unit size. Senior authorship is well distributed between the unit staff researchers and associated clinicians. Most PhD students are the first authors on one or several publications, often in high quality journals. All projects received the proper authorization for experimental work (e.g. use of patient samples). The unit follows the general rule at Gustave Roussy and is committed to open science.

Weaknesses and risks linked to the context for the three references above

No weaknesses identified

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

Assessment on the inclusion of the unit's research in society

The unit has an excellent engagement with society. Its teams have strong links to pharmaceutical companies to test novel drugs in preclinical and clinical settings (notably with Forma Therapeutics for the IDH1 inhibitor Olutasidenib, which is now used in the clinic) and is collaborating with several pharmaceutical companies for this aim (Servier, Agios Pharmaceutical, Forma Therapeutics, Foghorn). They are engaged in the general public, notably patient associations for paediatric leukaemias.

1/ The unit stands out for the quality and the number of its interactions with the non-academic world.

2/ The unit develops products for the cultural, economic and social world.

3/ The unit shares its knowledge with the general public and takes part in debates in society.

Strengths and possibilities linked to the context for the three references above

The unit has shown a strong commitment to collaborate with industrial partners. It is affiliated with the Carnot Opale institute, an ANR-funded structure aimed at facilitating and funding common projects between research labs and private companies. One project of Team 2 has been funded in this context (therapeutic potential of the combined inhibition of Bcl2 and Mcl1 in Eto2-Glis2 leukaemias). The unit has also direct collaborations with several pharmaceutical companies (Agios Pharmaceuticals, Forma Therapeutics, Foghorn, Remix Therapeutics, Servier), for projects that aim to test the potential of several drugs (notably IDH1/2 inhibitors as Olutasidenib), an anticancer medication used to treat relapsed or refractory acute myeloid leukaemia with a susceptible IDH1 mutation. The unit is also very active in its engagement with the general public, notably with patient organizations for paediatric leukaemias.

Weaknesses and risks linked to the context for the three references above

The unit has no patent, start up, or Cifre fellowships.

ANALYSIS OF THE UNIT'S TRAJECTORY

The unit will cease to exist at the end of the current mandate. The two teams will follow separate paths and integrate different structures, both located at Gustave Roussy. The heads of both teams will become directors of their respective new units.
The disbanding of the unit makes sense, as the current unit is rather small and may not have had the critical mass to create real intra-unit synergies. It also reflects an ongoing remodelling of the research team organization at Gustave Roussy, and notably reflects a strong will of Gustave Roussy to promote the visibility of its research on paediatric cancers. The new structures into which both teams will integrate will be larger, and have a diverse set of expertise. Both teams will also be reinforced by the integration of new groups.
Team 1 will join Inserm unit U981, currently headed by Fabrice André. Virginie Penard-Lacronique will become director of the unit, which will host 5 teams. The leading theme of the unit will be to leverage high throughput approaches to identify novel biomarkers for therapy response in several types of cancers. The scientific interest of team 1 will take an interesting new turn, as it will explore the role of Tet2 in RNA modifications and translational remodelling. This team will be joined by the groups of Lydie da Costa (ribosomopathies) and Jean-François Emile (malignant histiocytoses). These groups will certainly bring new expertise that will be useful to the current focus on the mechanisms of malignant hemopoiesis, and the team's new venture into RNA and translation.
Team 2 will integrate a new unit that will be created and headed by Thomas Mercher, which will host 3 teams dedicated to the study of paediatric cancers. The other two teams are headed by David Castel (gliomas and ependymomas) and Birgit Georger (therapy resistance in osteosarcomas). Team 2 itself will be co-led by T. Mercher and ML Arcangeli. The three teams of the new unit will find common ground as they all plan to use approaches involving induced pluripotent stem cells and organoid, and Crispr-Cas9 screening strategies. The new unit will have numerous ties to larger programs coordinating research on paediatric cancers such as the Pediac program (coordinated by T. Marcher), the Foster and ITCC consortia, and the Paris Kids Cancer integrated center for research on paediatric oncology. Team 2 will also be reinforced by the groups of Pr. Hélène Cavé (paediatric leukaemias) and Dr. Charlotte Rigaud (MD, paediatric lymphomas).

RECOMMENDATIONS TO THE UNIT

Recommendations regarding the Evaluation Area 1: Profile, Resources and Organization of the Unit

No specific recommendations are given to the unit, as it is closing.

See below for recommendations to the teams.

Recommendations regarding the Evaluation Area 2: Attractiveness

NA

Recommendations regarding Evaluation Area 3: Scientific Production

NA

Recommendations regarding Evaluation Area 4: Contribution of Research Activities to Society

NA

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: Haematopoietic transformation, transcription factors and epigenetics

Name of the supervisor: Virginie Penard-Lacronique

THEMES OF THE TEAM

Team 1 works on oncogenesis in onco-haematological diseases, with a focus on mature myeloid and lymphoproliferative syndromes. The team has a long track record in its research areas and has published original reference articles in haematology.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has met the expectations of the previous evaluation in that international links have been maintained and the unit has created a position for a bioinformatics engineer and hired an administrative officer.

WORKFORCE OF THE TEAM: in physical persons on 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	1
Directeurs de recherche et assimilés	3
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	**9**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	3
Post-doctorants	2
Doctorants	1
Sous-total personnels non permanents en activité	**6**
Total personnels	**15**

EVALUATION

Overall assessment of the team

Overall, an excellent team, which had been publishing, through international collaborations, outstanding and landmark papers in 2019 & 2020 Cancer Discov. & Blood concerning the Waldenström's disease as well as 2 clinical studies on IDH2 mutations in Nature Med 2018 & 2023. The team hosted twelve PhD students, PIs are in French steering committees (Siric, ANR, SFH and FRM) and participated in the French and European haematology societies. There have been no reports of international invitations to speak or of steering committees. The team has secured funding from national institutions (FRM, LNCC), and maintained international collaborations (e.g. Ari Melnick, NY).
Interaction with the socio-economic world is very good. The team is interacting with private/pharmaceutical companies (e.g. Agios & Servier) and is in contact with R&D Department (Gustave Roussy) and IP structures (no patent deposit so far).

Strengths and possibilities linked to the context

The team continued to build on the discoveries made under the previous contract.

On the "B cell side" of the team, the investigations are focused on the functional role of the PU.1/SPI1 mutation identified in Waldenström's macroglobulinaemia (WM) using an original knock-in mouse model showing abnormalities in plasma cell differentiation currently under investigation with insights in the continuum of differentiation from B to plasma cells, the specific site of abnormalities in WM disease. This murine model is a good option for mechanistic analyses of the disease, especially when crossed with mice expressing the MYD88L252P mutant (orthologue to human L265P mutant). Finally, molecular studies of the Pitié Salpêtrière WM cohort are continuing, which is very positive (first paper Blood 2020) to further characterize the heterogeneity of the WM. One major achievement is the maintenance, with high efficiency, of the exploration of genetic and molecular abnormalities in haematological disorders over the years, starting with Tet2 abnormalities more than a decade ago in myeloid cancers, than moving to Tet2 mutations in B-cell lymphoma and finally opening new questions on PU1 mutations in the chronic B cell Waldenström disease. The team published in outstanding collaborative papers on all these topics, notably in Cancer Discovery and Blood journals. Other findings are involved in IDH and Tet2 loss-of-function abnormalities in acute myeloid leukaemia, opening a new research program on the epitranscriptome and RNA methylation profile disorders that induce translation machinery dysfunction, with the hypothesis of an impact on the leukaemia proliferation. An internal collaboration has been established at Gustave Roussy (CNRS UMR 9019) to develop this new approach and two new researchers are integrating the team. Major achievements on these topics are translational papers in Nature Medicine published in 2018 and 2023. Overall, all findings were published in outstanding papers as first and/or corresponding authors in Cancer Discovery and Nature Medicine. The team hosted twelve PhD students from 2018-2023. The team contributed to the open science HAL database and encouraged student participation in scientific meetings, integrity committees and Ecole Doctorale meetings. The team is interacting with private/pharmaceutical companies (e.g. Agios & Servier) and is in contact with R&D Department (Gustave Roussy) and IP structures (no patent deposit so far). The involvement of the team within the ANR Carnot/Opale project bridges the healthcare industry and the research lab to develop innovative therapies. The team has a strong and effective relationship with the Gustave Roussy haematology clinical department.

Weaknesses and Risks Linked to the Context

A possible weakness is the lack of models to decipher the molecular mechanisms involved in malignant proliferation, especially for the group involved in myeloid leukaemia. The knock-in mouse models developed for Tet2 and PU1 mutants are the only one that offers the hope of making significant contributions to the study of lymphoid malignancies, such as aggressive lymphoma and Waldenström's macroglobulinaemia.
Regarding the study of myeloid proliferation, the study of patient samples is interesting, but there are no developments around PDX, for example. It would be important to find a researcher to take over Olivier Bernard's research in the field of lymphomas and WM.

Analysis of the Team's Trajectory

The transfer of Team 1 to the Inserm U981 unit involves a certain risk. In fact, this team is limited in terms of the number of its members, given the wide range of research activities. The scientific leadership and dynamism of the team are highly dependent on the two Inserm DRs, one of whom will take over the management of the future U981 unit, which could weaken the team. It will be necessary, if not essential, to open up the team to attract new scientists and future leaders.

RECOMMENDATIONS TO THE TEAM

Attract young scientists and future leaders to give new perspectives to the team

Team 2: Paediatric Leukaemia Biology

Name of the supervisor: Thomas Mercher

THEMES OF THE TEAM

The main focus is acute paediatric myeloblastic leukaemia (AML), in particular acute megakaryocytic leukaemia (AMKL) and acute erythroleukemia (AEL), known as poor-prognosis diseases. The team investigates the functional interplay between oncogenes and ontogeny during leukemogenesis. This novel knowledge will drive the identification of therapeutic targets.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations on scientific production, collaborations, recruitment of bio-informatician and researchers have been followed. Regarding the recommendation of getting European grants: the team did not get European grants but participated in applications to European calls. However, it has developed many other actions with the European dimension such as participation to the board of EHA or being a member of the Scientific Committee of Cancer Core Europe Summer School.

WORKFORCE OF THE TEAM: in physical persons on 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maitres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**4**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	7
Post-doctorants	1
Doctorants	2
Sous-total personnels non permanents en activité	**10**
Total personnels	**14**

EVALUATION

Overall assessment of the team

The research axes are of major interest for the paediatric population, as well as for basic research in haematology. The team has an excellent visibility by obtaining funding (one Canceropole, one Carnot Opale, and one LNCC) and hosting a CRCN Inserm, one postdoctoral fellow, and six PhD students. The team leader has been awarded the National Sciences Academy Award in 2019. The team organized scientific congresses of European scale (EHA, SFH) or national ones (CHO, colloque INCa). The committee recognizes the leadership of the team and its dynamics in the structuration of the national landscape of paediatric cancers. The team's non-academic activity is also excellent, with multiple participation in patient association's events (SFCE, Ligue contre le cancer...). The team has an excellent scientific production (nineteen articles as peer-reviewed, including eight as PDC, for instance in Cancer Discovery, 2019, Mol Cancer, 2024, Blood, 2024).

Strengths and Possibilities Linked to the Context

The team obtains very regularly grants from competitive calls from national agencies (for instance one Canceropole, one Carnot Opale, one LNCC,) and from charity associations (one from La Ligue contre le Cancer and SFCE). Members of the team participate to boards/committees of national and European scientific committees or associations (CHO, Laurette Fugain, EHA, SFH, Fondation ARC) are at the origin of an important consortium (national Pediac program, funded by INCa, eleven teams), coordinates a WP of the more local Paris Kids Cancer (Centre Intégré de Recherche d'Excellence en Oncologie Pédiatrique (2024-2028)), demonstrating the leadership of the team in the structuration of the national paediatric landscape in cancer and particularly paediatric myeloid leukaemia. The team is involved in the national network Conect-AML, the Carnot Opale Institute and the Fédération d'Hématologie de l'Université Paris- Saclay. Junior researchers obtained regularly prizes for their research results, from national institutions (Fondation de France, Bettencourt Foundation, CHO, Gustave Roussy). The team has been joined by a CRCN Inserm), in 2022 and by one postdoctoral fellow. The team has supervised six PhD students (two theses ongoing). The team leader has been awarded the National Sciences Academy Award in 2019. The team organized scientific congress of international scale (EHA, SFH, CHO) or national ones (colloque INCa).
The success of the research projects of the team is illustrated by the publication of 38 publications including eight peer-reviewed papers with first/last authors from the team during the last five years in very high quality generalist journals and the very best specialized journals (Nature Medicine, Cancer Discovery, Blood, Science Adv, Leukaemia, Molecular Cancer…). For instance, they deciphered, using a murine model, the pathogenic effect of Eto2-Glis2 in paediatric AMKL (Cancer discovery, 2019). Subsequently, the understanding of Eto2-Glis2 downstream pathways allowed them to identify the combination of drugs to which Eto2-Glis2 cells are sensitive to (Leukaemia, 2023).
The extensive contribution to society is also exemplified by regular interactions with patient associations and the general public (SFCE, Ligue contre le cancer, React4Kids Parents-Researcher summer school, Colloque "Cancers pédiatriques, des causes aux traitements", Rendez-Vous Laurette Fugain…). Since 2012, the team leader is a member of the scientific and medical committee of Association Laurette Fugain. One patent on the treatment of anaplastic large cell lymphoma has been submitted.

Weaknesses and risks linked to the context

The major weakness of the team is its relatively small size with few permanent researchers and technician/engineers.

Analysis of the team's trajectory

The team trajectory is to become a constitutive team into a new unit. Paediatric cancers will be the common topic between the three teams of the new unit that is planned to be created. The three teams have similar workforce with about ten ETP. Beyond the general topic of paediatric cancers- that will give the unit an excellent visibility, a challenge will be to imagine the environment and shared research programs that will make this new unit a success. A synergy between those heterogenous cancers of interest (osteosarcoma, gliomas, ependymomas, and myeloid leukaemia), should be found beyond the techniques and methods. The strengthening of human resources in the new unit is expected to be effective since a computational biologist will be recruited on a chair in paediatric oncology research.

RECOMMENDATIONS TO THE TEAM

The committee encourages the team to maintain this very positive dynamics and leadership to bring them to a European and international level, in terms of collaborations, grants and research strategy. The committee also recommends continuing their effort to attract young researchers. An attention point will be to create a real synergy between the different PIs of the team to succeed to fully integrate the group of clinicians/biologists on Juvenile Myelomonocytic Leukaemia (JMML) and the research objectives of the newly arrived CRCN.

CONDUCT OF THE INTERVIEWS

Date(s)

Start: 17 January, 2025 at 10h00

End: 17 January, 2025 at 17h45

Interview conducted: online

INTERVIEW SCHEDULE

10h00-10h10 Zoom connection and committee presentation

10h10-10h35 Overall presentation of the organizational unit UMR 1170 and trajectory by Olivier Bernard (15 min + 10 min of questions)

10h35-11h45 Teams' presentations:

Team 1: Haematopoietic transformation, epigenetic and transcription factors

10h35-10h45 Presentations of key scientific facts and trajectory: past (2018-2023)
Virginie Penard-Lacronique (10 min)

10h45-10h55 Trajectory: future unit led by Virginie Penard-Lacronique
Virginie Penard-Lacronique (10 min)

10h55-11h10 Questions (15 min)

Team 2: Biology of paediatric leukaemia

11h10-11h20 Presentations of key scientific facts and trajectory: past (2018-2023)
Thomas Mercher (10 min)

11h20-11h35 Trajectory: future unit led by Thomas Mercher
Marie-Laure Arcangeli (5 min), Birgit Geoerger (5 min), David Castel (5 min)

11 h 35 - 11 h 50 Questions (15 min)

Coffee break (15 min)

12h05-12h25 in camera session with thesis students

12h25-12h45 in camera session with researchers/professor and post docs

12h45-13h00 Debrief of the committee

Lunch break (1 hour)

14h00-14h25 Meeting with the managing bodies (only for the committee)
Inserm: Alain Eychène : directeur adjoint de l'IT Cancer

Université Paris Saclay: Anne-Hélène Monsoro-Burq: VP recherche Déléguée Santé Science de la Vie Univ. Paris-Saclay
Eric Deutsch: vice doyen Faculté de Médicine, côté recherche Paris Saclay

Gustave Roussy : Anne Paoletti: représente Fabrice André, directrice de la Fondation GR
Emma Pailler: suivi des projets de recherche de GR

14 h 25 - 14 h 40 Debrief of the committee

14 h 40 - 15 h Meeting with the director

Coffee break -: 10 min

15h10-17h30 Working session on the report of the committee

17h45 End of the evaluation day

GENERAL OBSERVATIONS OF THE SUPERVISORS

- The institution responsible for submitting the application, which is also responsible for coordinating the response on behalf of all the research unit's supervisors, did not submit any general observations."

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