

EVALUATION REPORT OF THE UNIT
TAGC - Théories et Approches de la Complexité
Génomique

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

Aix-Marseille université - AMU,
Institut national de la santé et de la recherche
médicale - Inserm

EVALUATION CAMPAIGN 2022-2023
GROUP C

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In the name of the expert committee¹ :

Susan Chan, Chairwoman of the committee

For the Hcéres² :

Thierry Coulhon, President

Under the decree n° 2021-1536 of 29th November 2021:

¹ The evaluation reports "are signed by the chairperson of the expert committee". (Article 11, paragraph 2);

² The president of the Hcéres "countersigns the evaluation reports established by the expert committee and signed by their chairperson." (Article 8, paragraph 5).

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 certified exact data extracted from the deposited files by the supervising body on behalf of the unit.

MEMBERS OF THE EXPERT COMMITTEE

Chairperson:

Ms Susan Chan, Inserm, Illkirch, université de Strasbourg

Experts :

Mr Thomas Clouaire, Inserm, université de Toulouse (representative of the Inserm's CSS1)

Ms Thérèse Commes, université de Montpellier (representative of the CNU 65)

Mr Yohann Couté, Inserm, Grenoble (representative of supporting personnel)

Mr Antonin Morillon, CNRS, Université Paris Cité

HCÉRES REPRESENTATIVE

Ms Marie José Stasia

CHARACTERISATION OF THE UNIT

- Name: Theories and Approaches of Genomics Complexity
- Acronym: TAGC
- Label and number: UMR 1090
- Composition of the executive team: Director for the current contract: Pr Pascal Rihet (01/01/2018–31/12/2023); Director for the next contract: Dr Christophe Chevillard (01/01/2024–31/12/2029)

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement

SVE3 Molécules du vivant, biologie intégrative (des gènes et génomes aux systèmes), biologie cellulaire et du développement pour la science animale

THEMES OF THE UNIT

The unit is dedicated to understanding complex biological systems through: 1) bioinformatics and genomics of molecular networks, and 2) genetics and genomics of multifactorial diseases. At the end of 2021, the single-team unit consisted of 68 members, including eighteen permanent researchers (4 DR, 5 CR, 5 MCU, 2 PU, 1 MCU-PH, 1 PU-PH), twelve permanent technical staff (ITA), eight CDD ITA, six postdocs, and 24 PhD students. During the evaluation period, the unit recruited 14 new members to its research axes.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The unit is situated on the Luminy campus (Faculty of Sciences, Marseille). It was created at the CIML (Center of Immunology of Marseille-Luminy) as a genomics team involved in the development of high-throughput technologies (1997), and then became a full-research unit focused on technological and methodological innovation. The unit developed and expanded under the direction of Catherine Nguyen, first as an ERIT (research unit of technological and methodological innovation), then ERM, and finally a joint Inserm-university unit in 2008. In 2018, Pascal Rihet became director of the unit, which was renamed TAGC; he will lead until the end of 2023. The next DU will be Christophe Chevillard (2024–2029).

RESEARCH ENVIRONMENT OF THE UNIT

The unit is part of the Aix-Marseille University (AMU), where it is implicated in the research on 1) immunology, 2) genetics, rare diseases and development, and 3) cancer. It is a member of the AMU Institutes for Rare Diseases (MarMaRa), Cancer and Immunology (ICI), and the interdisciplinary Turing Centre for Living Systems (Centuri), the latter a Convergence institute (funded within PIA2). The unit is affiliated with the genetics, genomics and bioinformatics institute at Inserm, and is involved in the Inserm national consortium GenOmics variability in health and disease (Gold). The unit is an associated team of the French Bioinformatics Institute (IFB), and hosts a sequencing facility that is recognised IBISA and France Génomique.

The unit maintains links to the clinics by interacting with the Haematology & Cellular Therapy Unit at Conception Hospital in Marseille, and via its translational research in haematology, which addresses: 1) tumour escape mechanisms to chemo- and immunotherapy; 2) prognosis factors regarding sepsis in neutropenic patients; and 3) novel treatments via the collaboration with innovative Biotech companies (Advanced BioDesign, BioCytex).

UNIT WORKFORCE: in physical persons on 31/12/2021

Permanent personnel in active employment	
Professors and associate professors	3
Lecturer and associate lecturer	6
Senior scientist (Directeur de recherche, DR) and associate	4
Scientist (Chargé de recherche, CR) and associate	5
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	12
Subtotal permanent personnel in active employment	30
Non-permanent teacher-researchers, researchers and associates	3
Non-permanent research supporting personnel (PAR)	10
Post-docs	2
PhD Students	21
Subtotal non-permanent personnel	36
Total	66

DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: NON-TUTORSHIP EMPLOYERS ARE GROUPED UNDER THE HEADING 'OTHERS'.

Employer	EC	C	PAR
Aix-Marseille Université	9	0	5
Inserm	0	5	7
CNRS	0	4	0
Total	9	9	12

UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	998.0
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP idex, i-site, CPER, territorial authorities, etc.)	2108.0
Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	3786.0
Own resources obtained from international call for projects (total over 6 years of sums obtained)	1079.0
Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.).	1181.0
Total in euros (k €)	9152.0

GLOBAL ASSESSMENT

Profile, resources and organisation

The TAGC unit is a single-team unit that is dedicated to understanding physiology through: 1) bioinformatics and genomics of molecular networks, and 2) genetics and genomics of multifactorial diseases. It benefits from the complementary expertise of its 68 members to develop an ambitious research program that integrates bioinformatics with experimental approaches, and runs the Transcriptomic and Genomic Marseille Luminy (TGML), IBISA-labelled, core facility that provides the unit and the greater community with advanced expertise in transcriptomics and genomics.

The human and financial resources of the unit were excellent and in line with its scientific objectives. About 90% of the unit's budget (~1.5M €/year) came from competitive grants, contracts with companies, and fees for service of the TGML core facility. This consolidated budget fully supported the scientific activities of the unit. The human resources were evenly distributed between the two axes, and allowed each to develop an ambitious program that is both fundamental (gene regulation and the organisation of molecular networks) and translational (biomarker and therapeutic target identification in multifactorial diseases like leukaemia, malaria, sepsis and Chagas) with high quality results and bioinformatics tools that are the state-of-the-art in its field.

The functioning of the unit in terms of human resource management was very good. The staff was fully involved in the organisation and execution of the unit's research activities, though administrative burdens were heavy. The measures taken by the unit to prevent risks to its scientific assets and information systems were excellent, and adapted to the team's activities in bioinformatics.

Attractiveness

The attractiveness of the unit was excellent. Unit members organized national and international meetings, held editorial responsibilities and contributed to research strategy. Two teacher-researchers were recruited from Aix-Marseille University (MCU, MCU-PH) and five CR researchers from CNRS and Inserm joined the unit. Numerous PhD students (45) and postdocs (12) were trained.

However, the current size and state of the premises, together with the unit's difficulties in securing key permanent engineers and technical positions, put the scientific policy of the unit at serious risk, as it will be less attractive to young ERC and ATIP-Avenir candidates. In addition, the unit did not seem to have an active policy to compete for European grants (ERC Starting, Consolidator, Advanced or Synergy), which is important for the visibility and recognition of TAGC.

Scientific production

The unit had an excellent to outstanding scientific production with a total of 193 publications (total citations 4325) in high standard journals (Nat Genet, Nucleic Acids Res, Cell). The scientific production of the unit was the result of research activities that comply with quality rather than quantity. Two publications where the unit members were main authors were cited more than 100 times (Nat Genet, Nucleic Acids Res). Considering the size of the unit and each subgroup, the scientific production was balanced across researchers and teacher-researchers, and 84 of the publications featured PhD students as co-authors. In addition, the unit produced six internationally recognised softwares (Pygfftk, ReMap, RSAT, MultiXrank, WopMars, Tagoos), free of charge, that are important tools for the scientific community.

Contribution of research activities to society

The involvement of the unit with non-academic partners was excellent. Most prominently, the unit established a contract of collaboration with Advanced BioDesign (ABD) to develop new treatments for acute myeloid leukaemias. This collaboration was initiated by a scientist from the unit, and has been ongoing for seven fruitful years. This collaboration led to a phase 1 clinical trial (Odyssey) which will soon start to evaluate the efficacy of an aldehyde dehydrogenase inhibitor for the treatment of acute myeloid leukaemias and myelodysplastic syndromes. More recently, two additional PIs became involved in collaborative research.

The output of the unit regarding products for the socio-economic world was excellent. The unit was granted a patent for its methods to predict the risk of developing sepsis or systemic inflammatory response syndromes. The bioinformatics tools or databases developed by the unit is freely available to the socio-economic world.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous committee made six comments (in bold and italics).

1/ Focus on key and challenging problem:

The unit was recommended to further strengthen the combined experimental and bioinformatics approaches, to refocus the research axes on key problems on which the unit can make a difference in a strongly competitive environment.

Efforts were made with the ongoing projects. The unit indicated that it made major efforts with co-publications between the 'two axes' (Axis 1: Bioinformatics and genomics; Axis 2: Genetics and genomics of multifactorial diseases) as proof of its reinforcement of combined approaches concerning experimental development and methodology (see also publications list). The links between these axes as well as the projects between biologists and bioinformaticians were clearly apparent in the oral presentations, with real added value for most of the research projects.

2/ Personal recruited/strategy for long-term software maintenance:

The unit was recommended to continue its successful recruitment of permanent staff, to focus efforts on attracting postdoctoral researchers and MD-PhDs, to better valorise the cohorts. The committee recommended defining explicitly a strategy for long-term software maintenance and distribution, and, at least, the tracking of software downloads possibly by requesting academic registration.

- **Define a strategy for Long-term software maintenance and distribution**

The answer to this question is not straightforward. The researchers detailed the number of software used and the citations of the publications which used them. Software downloading, usage and citations (p.46) gave a good idea of their usefulness (for example a total of 39,394 downloads for RepMap and 28,658 for WopMars, 15,000 jobs/month for RSap). Impressively, RepMap is now offered as an available software by the UCSC genome browser. However, it was unclear how these tools are maintained and updated. Additional engineer support could provide the unit with more visibility for these important tools.

- **Personnel recruited**

The unit was active and recruited four researchers or assistant professors in this **period (two per axis)**. One more person, as CR CNRS, will arrive in 2023. The unit also hosted twelve postdoctoral researchers. The team indicated that it had difficulty recruiting researchers in general. For example, candidates for ERC or ATIP grants cannot come because of lack of space. In addition, because the unit does not have a permanent engineer, it cannot obtain ELIXIR support for long-term software maintenance. Support for the TGML platform would be a plus but depends on Inserm-DR-Paca. The unit hoped to have a positive decision from Inserm-DR-Paca for space and permanent/CDI positions.

3/ Technology transfer opportunities

The unit was recommended to investigate opportunities for the transfer of technologies to local companies or start-ups, including the deposit of patents or other IP protection measures

The unit established a scientific collaboration with the start-up company Advanced BioDesign (ABD) in 2015 on acute myeloid leukaemia, with a phase 1 approved clinical trial on the drug candidate ABD-3001, a powerful ALDH inhibitor (authorisation from ANSM). The company now also collaborates with several researchers of the unit. A partnership with the company BioCytex was also mentioned without more details. It should be noted that bioinformatics tools are difficult to transfer or patent as they are open-source tools.

4/ A clear policy:

The unit was recommended to formulate a clear policy for co-authorship of technical and engineering staff, and to improve internal communication of decisions by the management team. Permanent research staff was encouraged to assist the new Director in his tasks, and the new director as full professor at Aix-Marseille University (PU) should inquire about obtaining a significant 'décharge d'enseignement'.

- **A new policy**

The team adopted a new policy in 2018 to announce manuscripts in preparation in electronic form, which had a positive impact on the communication between researchers and technical staff. Manuscripts in preparation must now be announced on the unit's internal website (intranet) by indicating: 1) the content, and 2) the list of authors. The announcement is then sent to all unit members by email. If a member feels wronged, then they can discuss it with the project leader and eventually the direction.

- **Assisting the new Director in his tasks**

The director obtained a partial 'décharge d'enseignement' of 48 hours per year, and has been assisted by two deputy directors, who meet every week with a 'board of directors' to make decisions. The future director is an Inserm researcher, and should have less teaching duties.

5/ Young researchers (HDR and training):

The unit was recommended to: - encourage young researchers to defend their HDR; - increase attractiveness for MD-PhD staff and contribute to MD-PhD programs; —train young experimental biologists in computational approaches, but conversely give computational biologists an experience in experimental biology.

- **HDR defence**

Between 2018 and 2021, four researchers or researcher-teachers obtained their HDR. Among the eighteen researchers or researcher-teachers, fourteen have HDRs (78%). Additional HDR theses are in preparation. For recruitment, see Point 2.

- **Training of experimental biologists**

Efforts were made to train students (M2, PhD) and postdocs in computational biology and genomic data analyses in this period. Moreover, PhD students and postdoctoral fellows recruited through the Centuri calls were trained and prepared to be at the interface of disciplines such as biology and mathematics, or computational science and biology.

6/ Limited high-priority scientific objectives/selected pathologies/cohesiveness:

The unit was recommended to: - persevere in the strategy to develop and apply both computational and experimental approaches within the context of pathologies, and continue the training of researchers in these interdisciplinary approaches; - focus efforts on a limited number of high-priority scientific objectives, bring the experimental and computational tools developed by the unit to bear on selected pathologies where the unit can make an impact; —maintain efforts to hire permanent research staff with additional competencies that are complementary to those already present and increase the cohesiveness of the research axes; - define a technology transfer and IP protection strategy.

- Concerning the training, much effort was made. The professors and assistant professors were very active and involved in complementary training like masters, and specific training (IFB). However, it was mentioned that the cohesion of the Master in Bioinformatics was compromised by the lack of permanent positions and the high turnover of the Ater contracts that made it difficult to maintain a continuity in the teaching, and placed the burden of training on a small number of permanent staff.

- Concerning the scientific objectives, there was an effort to select some pathologies and to limit to high priority scientific objectives. Many links to other Aix-Marseille University communities (Centuri, Marmara, Onco-immunology ICI) or with international collaborations were mentioned as a strong effort to maintain high quality projects.

B - EVALUATION AREAS

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

Assessment on the unit's resources

The human and financial resources of the unit were excellent and perfectly in line with its scientific objectives. These resources allowed the unit to implement its research projects in the two thematic axes described and to run a core facility. The human resources were evenly distributed between the two axes, allowing each to develop an ambitious research program. The financial resources were mainly obtained through numerous successful applications to various calls for projects.

Assessment on the scientific objectives of the unit

The scientific objectives of the unit with regards to the state of the art in its field were excellent. The unit offered a unique combination of bioinformatics and experimental approaches to characterise the molecular functions of biological systems under physiological and pathological conditions. The level of integration of the unit in local, national and international scientific networks was excellent. The contribution of its research policy to the resolution of societal challenges was very good, with the ambition to transfer the knowledge acquired in the field of personalised medicine.

Assessment on the functioning of the unit

The functioning of the unit in terms of human resource management was very good. The staff was fully involved in the organisation and execution of the unit's research activities. Administrative burdens, external to the organisation of the unit, prevented its optimal functioning. The measures taken by the unit to prevent risks to its scientific assets and information systems were excellent. These measures were perfectly adapted in view of the team's activities in the field of bioinformatics. The unit's commitment to environmental preservation was very good, with efforts made to reduce waste and save energy. The adequacy between its internal organisation and the operational implementation of its strategy was very good. Internal communication could still be improved.

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

Strengths and possibilities linked to the context

The unit benefited from the complementary expertise of its 68 members, including 30 permanent staff, to develop an ambitious research program integrating bioinformatics and experimental approaches along two scientific axes (Axis I: Bioinformatics and genomics of molecular networks; Axis II: Genetics and genomics of multifactorial diseases), operate one core facility (TGML), and participate in a multicenter platform (for CRISPR screening).

In this period, the unit recruited fourteen new staff members (+25%), including six permanent people. The permanent staff was composed of employees from Aix-Marseille University (9 teacher-researchers, 5 engineers/technicians), Inserm (4 researchers, 7 engineers/technicians) and CNRS (5 researchers). The two scientific axes benefited from comparable and well-balanced permanent human resources (Axis I: 9 researchers/teacher-researchers, 3 engineers/technicians; Axis II: 9 researchers/teacher-researchers including 2 physicians, 5 engineers/technicians).

The unit ran and benefited from TGML, an IBISA-labelled core facility with advanced expertise in transcriptomics and genomics, that was part of the France Génomique Infrastructure. TGML is equipped with state-of-the-art instrumentation, notably next-generation sequencers, and provided the community and the TAGC unit with a variety of expert solutions. For its bioinformatics activity, the unit took care to continuously improve the computing and storage capacities, and the security of its infrastructure. The unit also took part in a multicenter CRISPR screening platform that was supported by the Cancéropôle Paca.

The unit demonstrated a significant capacity to mobilise financial resources in addition to the recurring endowment of Inserm and Aix-Marseille University. About 90% of the unit's budget (~1.5M €/year, excluding salaries of permanent staff) came from grants from local, national and European agencies and foundations, contracts with companies, and fees for the service of the TGML core facility. This consolidated budget fully supported the scientific activities of the unit.

A common stock of reagents and materials was provided by the unit to its members thanks to the recurring endowments from Inserm and Aix-Marseille University, and a 15% overhead from grants. This policy made it possible to obtain preliminary results in new and existing projects for the next round of grant applications.

Weaknesses and risks linked to the context

Several researchers and teacher-researchers will retire in the next few years, which could negatively impact the functioning of the unit.

The current size of the unit was perceived as insufficient to support the development of the unit, and its ability to host new researchers. Moreover, the staff have complained that the advanced age of the building prevented them from working properly.

The unit is not labelled by CNRS, and the career development of the five CNRS researchers, who represented >50% of the researchers in the unit, may be negatively affected.

There was no bioinformatics engineer to maintain the software tools developed by the unit.

2/ The unit has set itself scientific objectives, including the forward-looking aspect of its policy.

Strengths and possibilities linked to the context

This single-team unit explored the function of complex biological systems in physiological and pathological conditions using bioinformatics and experimental approaches. The unit developed an ambitious research program that produced high quality scientific results and bioinformatics tools, as software and databases, that are state-of-the-art in its field of research.

At the local level, the unit was involved in different academic research structures operated by the Aix-Marseille University — the Marseille Institute for Rare Diseases (MarMaRa) and the Institute for Cancer and Immunology (ICI). The unit was part of the Turing Centre for Living Systems (Centuri), and was a member of the Marseille Immunopôle research cluster. At the national level, the unit was an associated team of the Institut Français de Bioinformatique (IFB, programme des investissements d'avenir - PIA). The TGML core facility was part of France Génomique (PIA) and IBIISA-labelled. The unit was also part of the Inserm transversal program Gold (GenOmics variability in heaLth & Disease). Finally, unit members have built a strong network of local, national and international collaborators to enrich its ambitious research program and reach its scientific objectives. The unit also established scientific collaborations with two biotech companies, Advanced BioDesign and BioCytex.

The ambitious research program of the unit involved the use of interdisciplinary approaches to answer fundamental questions in gene regulation and the organisation of molecular networks. It tackled the goal of personalised medicine for multifactorial diseases like leukaemia, malaria, sepsis and Chagas, by searching for molecular events that drive disease development, and led to biomarker and therapeutic target identification. The scientific objectives of the unit are in line with the policies of Aix-Marseille University and Inserm.

The management board was composed of the director and two deputy directors. It relied on a strategic advisory council, consisting of all the PIs, that met monthly to discuss the scientific strategy of the unit and the scientific projects developed within the unit. This assembly made possible the emergence of synergies between PIs. The decisions concerning the unit were presented to and validated by the laboratory council that met twice a year.

Weaknesses and risks linked to the context

The modalities behind the decision-making processes in the different instances of the unit (management board, PI, laboratory councils) were unclear.

The organisation as a single-team unit may dilute the personal achievements of the PIs on their main projects, the visibility of the PIs outside the unit, and hinder the capacity of the unit to attract ambitious young researchers.

The administrative delays at the level of the supervisory authorities complicate the administrative management of the unit.

3/ The functioning of the unit complies with the regulations on human resources management, safety, the environment and the protection of scientific assets.

Strengths and possibilities linked to the context

The unit had a defined organisation that complied with the different regulations. The Management board (director and deputy directors) was responsible for the proper management of human resources, safety, the environment and the protection of scientific assets. Specific members responsible for administration and finances, informatics, health and safety, scientific culture and communication, doctoral school and gender parity were clearly defined. Important information was disseminated through the intranet. The laboratory council met twice a year. The unit's research support staff felt strongly involved in the unit's research projects and its organisation.

Staff career development had been effective. Seven permanent staff members (3 women, 4 men) were promoted during the 2016–2021 period: one TCN to TCE, two TCS to TCE, one IR2 to IR1, one CRCN to CRHC, one CRCN to DR2, and one DR2 to DR1. Unit members were encouraged to develop their skills in various training courses. In the evaluation period, a total of 186 training courses were given by Inserm, CNRS or Aix-Marseille

University, and followed by 48 permanent and non-permanent staff members. Further, all members of the unit were invited to attend scientific congresses. A survey on psychosocial risks was submitted to the unit's members in 2019. The participation rate was very high (75%). The results indicated a positive situation concerning the overall well-being at work.

The unit ensured a strict protection of its scientific assets and computer systems through the control of the physical access to unit premises by a personal badge system. The IT system was effectively protected and the use of private computers was not allowed.

The unit implemented a proactive policy to apply the recommendations on environmental risk prevention and the pursuit of sustainable development goals, by recycling paper, cardboard, toner and plastics, installing water fountains, and switching off computers at night.

Weaknesses and risks linked to the context

The gender distribution of the permanent staff was not well balanced, especially in the category of researchers and teacher-researchers (67% men vs. 33% women). The difference was even greater among research directors and professors (78% men vs. 22% women).

The precise involvement of the engineers and technicians in the different axes and sub-axes was unclear, which may impact their career development.

With an important number of non-permanent staff, the training of the newcomers to important issues, like health and safety, protection of environment, prevention of psychosocial risks, and protection of scientific assets and computer systems seemed to be too loosely organized.

Some omissions in the inclusion of research support staff in the list of authors of certain publications were noted.

The minutes of the PI council were not made available to all staff in a timely manner.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness of the unit was excellent. Unit members organized national and international meetings, held editorial responsibilities and contributed to research strategy (ITMO GGB, Inserm, FIB). One MCU and one MCU-PH were recruited at Aix-Marseille University, five CR (CNRS and Inserm) joined the unit, and 45 PhD students and twelve postdoctoral fellows were trained. The unit was very successful with external competitive calls (90% of its budget) and hosts the IBISA-labelled TGML core facility.

However, the size and state of the premises, together with the difficulties in securing key permanent positions, put the scientific development of the unit at risk.

1/ The unit has an attractive scientific reputation and contributes to the construction of the European research area.

Strengths and possibilities linked to the context

The scientific reputation of the unit and its impact on research were excellent. Unit members contributed to the scientific reputation of the unit at both the national and international levels. TAGC researchers were invited to 29 national and international seminars, conferences and meetings. Unit members organized or co-organized 8 national and European workshops and conferences in France or Spain, including the JOBIM conference of the French Society of Bioinformatics (>450 attendees). Several members had editorial responsibilities in internationally recognised journals (i.e. F1000, Front Bioinform, Int J Mol Sci, Front Mol Sci, Front Immunol), contributed to the national research strategy (ITMO Genetics, Genomics and Bioinformatics, Scientific Council of Inserm, French Institute of Bioinformatics), and were parts of internationally recognised scientific institutions (Italian Bioinformatic society, Steering Committee of Centuri Institute, Scientific Committee of the MarMaRa Institute). Important scientific prizes ('Coup d'Élan pour la recherche française' Bettencourt Schueller

Foundation, Roche and Mexican Health Society 'Basic Science Award', 'Young Investigator' award of the French Society of Human Genetics) were awarded to unit members.

Weaknesses and risks linked to the context

There was an imbalance between members in establishing the scientific reputation of the unit. In the long-term, this may negatively impact the career development of less visible members.

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

Strengths and possibilities linked to the context

The unit's quality of staff hosting was excellent, as attested by the steady growth of the unit, and hosted many early-stage researchers. In the past period, 45 PhD students and 12 postdoctoral fellows were trained, and the unit currently hosts >20 PhD students. The unit strongly benefited from its participation in the Centuri, Onco-Immunology and MarMaRa institutes which allowed it to recruit seven PhD students and two postdoctoral fellows. Students and postdocs were given the opportunity to present their work in weekly seminars, and were encouraged to attend conferences and meetings in France and abroad. Indeed, the unit was described as welcoming and supportive by the PhD students and postdocs during the interview with the committee.

In the last period, four researchers applied for Inserm CRCN positions (none successful yet), two applied and were awarded MCU and MCU-PH positions (at Aix-Marseille University in 2020 and 2021), and five CR from CNRS and Inserm joined the unit (2018, 2022, another one expected in 2023).

The unit had a policy of supporting exploratory projects to obtain preliminary results for future grant applications, which allowed PIs to develop further lines of research. The work of the technical staff was shared among projects in a coordinated manner, according to the needs of each project.

Important resources were available through the intranet, such as the charter for co-authorship of scientific publications or proceedings from the monthly PI or laboratory council meetings. News of manuscript preparations were shared early across the unit to discuss and ensure rightful co-authorship ahead of potential submissions. The vast majority of publications (around 90%) are deposited on Hal.

The unit therefore hosted a significant number of early-stage and established researchers, implemented an efficient policy to ensure accurate authorship, and made its publications available in public repositories.

Weaknesses and risks linked to the context

The weaknesses and risks for this item largely came from external factors.

The state of the premises and the interactions with the governing bodies did not seem to provide the best working environment for TAGC members. For example, the internet network, a central part of the activity of the unit, had been defective for over a month at the time of the Hcéres visit. More generally, recurrent problems in the relationships with Inserm and Aix-Marseille University were shared with the committee (hiring process, management of European funds, TGML pricing list, etc.). The friendly and collegial internal interactions of the unit allowed members to maintain a good spirit so far, but this situation led to additional unnecessary work and exposed unit members to potential psychosocial risks in the short and long run.

Moreover, the current size of the premises prevents any future scientific development of TAGC as space limitations already limits the number of trainees that can be hosted by the unit each year. This situation also prevents the unit from implementing a policy for welcoming promising new scientists with innovative lines of research. In its current state, the unit cannot host Atipe or ERC starting grant laureates. In the short term, this risk damages the positive dynamic established by the unit, as attested by its continual growth in recent years. In the long run, this situation threatens the ability of the unit to maintain a critical mass and/or could trigger the departure of key members from TAGC, thereby causing an existential threat to the unit.

3/ The unit is attractive because of the recognition gained through its success in competitive calls for projects.

Strengths and possibilities linked to the context

The unit had been very successful in its applications to competitive calls for projects. This included international and European calls (>1.2M €), IBI SA and France Genomics (PIA1, >2.5M €), ANR (>1.5M €), Aix-Marseille Université,

Inserm (e.g. TAGC was part of the Inserm transversal program GenOmics variability in health and Disease) and charities (>4.7M €). Because of this, the unit was able to fund PhD and postdoctoral contracts (South region council, Centuri Institute, etc.) and 90% of its budget came from external grants.

Weaknesses and risks linked to the context

The unit did not seem to have developed an active policy to compete for European grants (e.g. ERC Starting, Consolidator, Advanced or Synergy). Securing these grants usually have the domino effect of boosting the unit's visibility and providing a scientific quality label that can have a substantial impact on its interactions with the governing bodies. The risk here is that the visibility and recognition of TAGC will remain below the level of its real scientific quality.

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

Strengths and possibilities linked to the context

The unit was host to the TGML (Transcriptomic & Genomic Marseille Luminy) facility for transcriptomics, epigenomics, and genomics analysis, which is a great asset to the unit and directly contributes to the unit's attractiveness. TGML was labelled by IBISA, France Genomics and Aix-Marseille University, certified ISO 9001:2015 and NFX 50-900:2016 and was composed of 6 staff members (3 permanent staff and 3 engineers on fixed-term contracts). TGML is an open facility performing experiments for public and private laboratories. Equipment and IT infrastructure were regularly renewed.

Weaknesses and risks linked to the context

Key personnel in the facility were on fixed-term contracts. Indeed, one of these contracts was reaching the end and will not be renewed because of the Sauvadet law. In general, the possibilities for securing permanent positions or converting fixed-term contracts to CDI ones for TGML personnel appeared limited, and no solutions had been proposed by the governing bodies.

The relationship between the local governing bodies and the facility did not seem to be ideal. For example, the facility's prices took over a year to be validated and there was incomprehension regarding the economic model of TGML in general.

Altogether, there is a significant risk for a loss of expertise and recurrent issues in the day-to-day operations at TGML that can negatively impact the quality of the services provided by this great asset to the unit.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The unit had an excellent to outstanding scientific production with a total of 193 publications (total citations 4325) in high standard journals (Nat Genet, Nucleic Acids Res, Cell), with two publications, where the unit members were main authors, cited more than 100 times. The scientific output was well balanced in terms of quality and quantity. It is to note that 8/10 of the most cited publications were collaborative works with no leading activity by unit members. The scientific production was very well balanced between different staff categories (i.e. 84 for PhD students, only 1/24 had no publication yet). The unit also produced six internationally recognised softwares (as ReMap or RSAT).

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

Strengths and possibilities linked to the context

The unit had an excellent to outstanding scientific production with a total of 193 peer-reviewed publications (involving the 2 axes of the unit, and including 13 reviews). The total number of citations for the period was 4325 for publications in high standard journals (Nat Genet, Nucleic Acids Res, Cell). Two publications where the unit members were main authors were cited more than 100 times within the period (Nat Genet, Nucleic Acids Res),

and eight as collaborative partners (Nucleic Acids Res, Circulation, Cell, Sci Rep, Mol Cell). Considering the size of the unit and each subgroup, the scientific production was rather balanced across researchers and assistant professors. In addition, the unit produced six internationally recognised softwares (Pygfftk, ReMap, RSAT, MultiXrank, WopMars, Tagoos) free of charge that are important tools for the scientific community.

Weaknesses and risks linked to the context

In this period, the majority (8/10) of the highly cited publications (>100 times) were collaborative works for which the members of the unit were not main authors.

2/ Scientific production is proportionate to the research potential of the unit and shared out between its personnel.

Strengths and possibilities linked to the context

The unit had an excellent commitment to PhD training, with 84 publications where PhD students were co-authors (only 1 of the 24 PhD defending students did not publish in the period). The scientific production was very well balanced among the different groups (84 for PhD students, 25 for Post-docs, and on average 11 publications per researcher, 12 for assistant professors and 13 for physicians). Several of these works could be grouped within topics of 'Clinical medicine' (48), or under 'Biology and biochemistry' (41), and finally within 'Molecular Biology and genetics' (36).

Weaknesses and risks linked to the context

No major weaknesses were detected in this section. However, the distribution of the publications among the researchers and teacher-researchers was uneven, with more publications from the basic science projects than the translational ones. This difference was probably amplified by the distinct opportunities to produce collaborative versus main author-signed publications for the 2 axes. The risk would be a decrease in visibility for the translational research of the unit.

3/ The scientific production of the unit complies with the principles of research integrity, ethics and open science.

Strengths and possibilities linked to the context

The scientific production of the unit was the result of research activities that comply with quality rather than quantity to warrant rigorous publications.

The traceability of the work was very good with all members receiving a laboratory notebook. Since 2018, an electronic form to announce the preparation of a new manuscript has been available online (intranet) to communicate: 1) the content, and 2) the list of authors for each manuscript.

The unit had an excellent traceability for the ethical conduct for preclinical experimentation. Indeed, the research on cohorts of biological samples from various countries were performed after receiving the authorisation of the French or foreign ethical committees. Investigations conformed to the principles outlined in the declaration of Helsinki. In addition, the unit performed experimentation at the PSEA, Celphedia. All the projects were submitted to the ethical committee for experimentation.

The scientific production of the unit respected the principles of open science by sharing publications, methods, data, codes and other elements as broadly and quickly as possible. For instance, a significant part of the unit work was based on transcriptomic and epigenomic studies, for which data were systematically deposited in public databases (Geo or array express).

Weaknesses and risks linked to the context

No weaknesses were detected.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The unit made an excellent contribution to society through its research. The most impressive effort resided in the very fruitful collaboration between the unit and Advanced BioDesign, which involved three PIs, four PhD projects (with 2 ongoing) and a phase 1 clinical trial. Thus, the unit's research may directly benefit patients in the near future. The unit also holds a patent, and its bioinformatics tools and databases are freely available to the socio-economic world, which has the potential of contributing to impactful discoveries. The unit also showed an excellent contribution in sharing its knowledge with the general public (Fête de la Science, Declics, Nuit des chercheurs) and participating in scientific debates (blogs, radio show, science to society debates in a theatre in Marseille).

1/ The unit stands out by the quality of its non-academic interactions.

Strengths and possibilities linked to the context

The involvement of the unit with non-academic partners was excellent. The unit established a contract of collaboration with Advanced BioDesign (ABD) to develop new treatments for Acute Myeloid Leukaemias. This collaboration was initiated by a scientist from the unit, and had been ongoing for seven fruitful years, with two PhD students already defended. More recently, two additional PIs became involved in collaborative research with ABD, leading to two more ongoing PhD projects. Furthermore, three ABD scientists are currently being hosted in the unit. These collaborations have led to a phase 1 clinical trial (Odyssey) which will start very soon to evaluate the efficacy of an aldehyde dehydrogenase inhibitor for the treatment of acute myeloid leukaemia and myelodysplastic syndromes.

The unit also collaborated with BioCytex for the development of cell-based assays to evaluate the potential in vitro value of drugs undergoing clinical evaluation. This was part of an ongoing PhD funded by the South region council.

Weaknesses and risks linked to the context

No weaknesses were detected in this section.

2/ The unit develops products for the socio-economic world.

Strengths and possibilities linked to the context

The output of the unit regarding products for the socio-economic world was excellent. The unit was granted a patent for its methods to predict the risk of developing sepsis or systemic inflammatory response syndromes, though the method was not yet used in the clinic. The research output from the unit, in the form of bioinformatics tools or databases, was freely available to the socio-economic world.

Weaknesses and risks linked to the context

No particular weaknesses were detected here.

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

Strengths and possibilities linked to the context

The involvement of the unit in sharing its knowledge with the general public, and its participation in scientific debates in society was excellent. Many members of the unit took part in events aimed at the general public (Fête de la Science, Declics, Nuit des chercheurs). Members of the unit also contributed to scientific outreach through blogs, science to society debates at a theatre in Marseille and a radio show.

Weaknesses and risks linked to the context

There were no strong weaknesses detected on this criterion.

C - RECOMMENDATIONS TO THE UNIT

Recommendations regarding the Evaluation Area 1: Profile, resources and organisation of the unit

- Prepare for the future of the unit by establishing a recruitment strategy for young researchers.
- Strengthen the communication with staff members, particularly with regards to the decisions taken in the IP council and the decision-making procedures regarding the implementation of telework.
- Set up a functional organisation chart to show the involvement of the different unit members in the different research groups.
- Allow support staff to present their work at internal seminars.
- Pursue efforts to have the unit labelled by CNRS.
- Prioritise the recruitment of an engineer for the maintenance of the unit's tools and databases in order to free up time for research of other staff members.
- Continue to be vigilant about co-authorship of support staff.
- Further strengthen interactions with other units on the site to negotiate with the building owner (Inserm).

Recommendations regarding the Evaluation Area 2: Attractiveness

- To reduce the imbalance among unit members in establishing the scientific reputation of the unit, the unit should encourage all members to regularly contribute to the visibility and reputation of the unit (meeting participation and organisation, research steering committees, etc.)
- The unit is recommended to continue its dialogue with its supervising bodies and neighbouring units to find a workable solution to reasonably increase the size of its premises and allow for scientific development.
- The unit should apply to European grants, which may have a positive impact on its discussions with supervising bodies.

Recommendations regarding Evaluation Area 3: Scientific Production

The balance of the scientific production could be improved by targeting more impactful journals for the translational research axis, in which the already high quality of research produced by the unit could be more systematic.

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

The unit may seek to diversify its non-academic partners to develop more products for the socio-economic world.

CONDUCT OF THE INTERVIEWS

Date

Start: 13 décembre 2022 à 8 h 30

End : 13 décembre 2022 à 17 h 30

Interview conducted: online

INTERVIEW SCHEDULE

TAGC – Tuesday 13 December 2022

8:00 - 8:15 Testing Zoom connections

8:15 - 8:30 Closed session Expert Committee (EC) – Scientific Officer (SO)

Assessment of the Unit, Scientific Plenary session

8:30 - 8:45 Presentation of the EC to the staff members by SO

8:45 - 9:15 Presentation of the unit by Pascal Rihet (20 + 10 min questions)
Attending: EC, SO, all the unit members

Presentation of the Axis

9:15 - 9:40 Bioinformatics approaches to study genomic complexity, **Benoit Ballester**
(15 min presentation + 10 min questions)
Attending: Team members, EC, SO, director of the Unit

9:40 -10:05 Network biology, **Christine Brun**
(15 min presentation + 10 min questions)
Attending: Team members, EC, SO, director of Unit

10:05-10:30 Systematic study of cis-regulatory functions: from mechanistic insights to the assessment of regulatory variants in disease, **Salvatore Spiguglia**
(15 min presentation + 10 min questions)
Attending: Team members, EC, SO, director of Unit

10:30-11:00 Break – Closed session with EC and SO

11:00-11:25 Deciphering physio-pathogenic process in cardiac aging cardiomyopathies and malaria, **Christophe Chevillard**
(15 min presentation + 10 min questions)
Attending: Team members, EC, SO, director of Unit

11:25-11:50 From the bench to the patient's bed, an Odyssey, **Régis Costello**
(15 min presentation + 10 min questions)
Attending: Team members, EC, SO, director of Unit

11:50-1:30 p.m. Lunch Break

Closed session with EC and SO from 1 p.m. to 1:30 p.m. (if needed)

1:30 p.m.-2:15 p.m. Meeting with the technical and administrative personnel

Attending: Technicians, Engineers, Administrative staff, EC, SO

2:15 p.m.-2:30 p.m. Break – Closed session with EC and SO

2:30 p.m.–15:00 Meeting with the representatives of Inserm and University

Attending: expert committee, representatives of Institutions, SO

3 p.m.-3:30 p.m. Meeting with the researchers and professors

Attending: Researchers except group leaders, EC, SO

3:30 p.m.-4 p.m. Meeting with the thesis students and postdocs

Attending: PhD students and postdocs, EC, SO

4 p.m.-4:30 p.m. Break – Closed session with EC and SO

4:30 p.m.–17:00 Meeting of the Committee with the head of the unit

Attending: Unit Direction, expert committee, SO

5 p.m. – 6 p.m. Meeting of the Committee – Finalisation of the report (closed hearing)

PARTICULAR POINT TO BE MENTIONED

None.

GENERAL OBSERVATIONS OF THE SUPERVISORS

Le Président de l'université

au

Département d'Évaluation de la recherche -
Hcéres

Objet : Observations de l'unité relatives au
rapport d'évaluation des experts Hcéres

N/Réf. : VPR/LS/AMS/CM – 23-07

Dossier suivi par : Cécile Merle

Tél : 04 13 94 95 90

cecile.merle@univ-amu.fr

Vos réf :

DER-PUR230023363 - TAGC - Théories et approches de la complexité génomique

Marseille, le mercredi 21 juin 2023

Madame, Monsieur,

Je fais suite au mail que vous nous avez adressé le 22/05/2023 dans lequel vous me communiquez le rapport d'évaluation Hcéres de l'Unité TAGC - Théories et approches de la complexité génomique.

Comme demandé dans ledit mail, je vous fais part des observations de portée générale en reportant les commentaires de la direction de l'unité :

We would like to thank the committee for its thorough and constructive assessment of our laboratory. This evaluation encourages us to consolidate our strengths in terms of organization, attractiveness, scientific output and relationship with society. We will also be paying close attention to the committee's recommendations for the coming years.

In particular, the committee recommends that we actively compete for European grants to increase our visibility. We would like to mention that TAGC members either led or participate to three H2020 funded projects during the evaluation period, and we will continue this effort. The committee also noted our attractiveness, particularly in terms of researchers, which has exacerbated the lack of both technical staff and space to accommodate all the staff. As far as staffing is concerned, we will continue to put forward requests for permanent technical staff. With regard to the size of the premises, we will have the opportunity to reorganize the use of the areas in 2024 when two teams from a neighbouring laboratory will leave the building. The directors of the units that will occupy the building in 2024 have agreed on a distribution in principle and have communicated this to the Inserm delegation.

Vous souhaitant bonne réception des présentes,

Je vous prie de croire, Madame, Monsieur, l'expression de mes respectueuses salutations.



Eric BERTON



The Hcéres' evaluation reports are available online:
www.hceres.fr

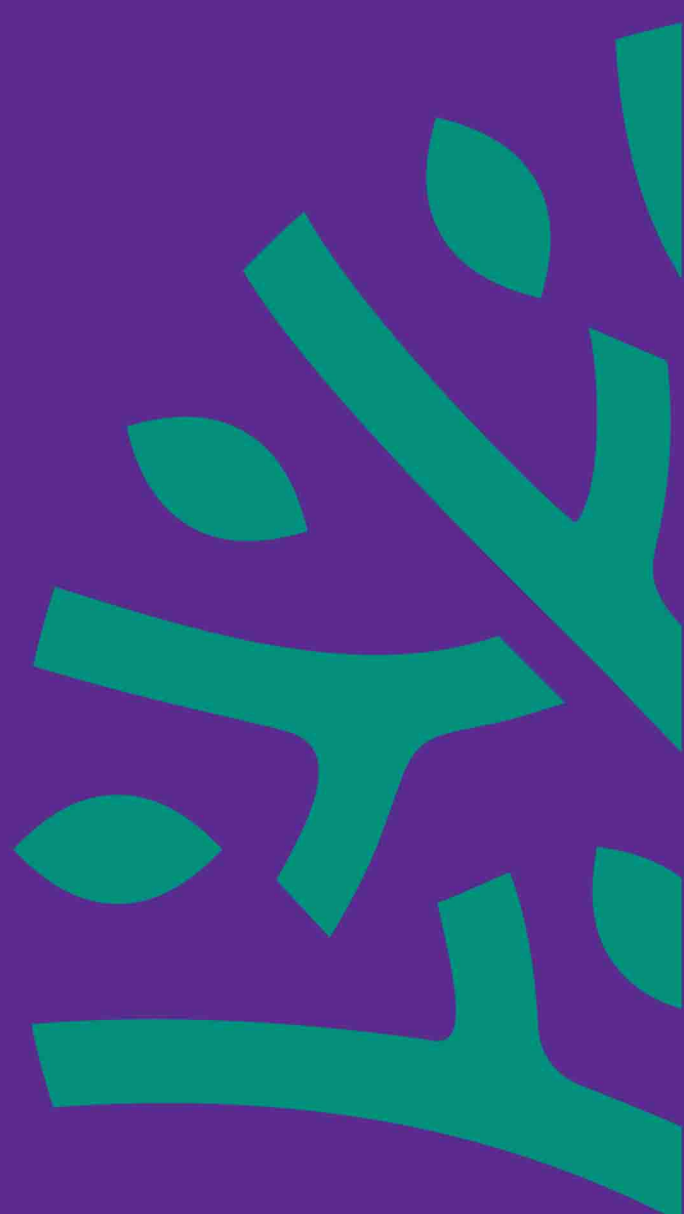
Evaluation of Universities and Schools

Evaluation of research units

Evaluation of the academic formations

Evaluation of the national research organisms

Evaluation and International accreditation



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