aviesan
alliance nationale
pour les sciences de la vie et de la santé

ITMO Cancer

FRFT Programme

Support for training in basic and translational research in oncology

Ex post Analysis 2011-2017

(July 2019)

Introduction

Since 2011, the Multi-Organization Thematic Institute (ITMO) Cancer of the Alliance for Life Sciences and Health (Aviesan) is responsible for thematic calls of proposals to support emerging research domains. These funding instruments, whose operational management falls to Inserm, are launched in the frame of the research part of the French Cancer Control Plans, which are coordinated by the French National Cancer Institute (INCa).

In addition to these thematic calls, ITMO Cancer-Aviesan launches generic calls to fund laboratory equipment and the cancer research training of young clinicians. In this context, ITMO Cancer-Aviesan holds the call *Support for Training in Basic and Translational Research in Oncology* yearly since 2011.

Elements Taken into Account in the Analysis

- Key figures of the number of submissions, success rate, average budget over time
- Analysis of the submissions (*using the submitted information and the selection committee reports*):
  - ✓ laureate profile: training*, demographic data;
  - ✓ projects: type of research, cancer type;
  - ✓ main reasons for rejection of non-selected candidates.
- Impact of the funding (*based on the final reports and on discussions with former laureates during the restitution seminar)*:
  - ✓ career paths of laureates;
  - ✓ dissemination and publications;
  - ✓ scientific and medical knowledge advances.

**Medicine, pharmacy, odontology, veterinary medicine*

In accordance with the recommendations of INCa's international scientific advisory board and the 3rd Cancer Control Plan objectives, a discussion about programme evaluations took place at the national level. In parallel, ITMO Cancer-Aviesan started to elaborate assessments of its own programmes, for which a sufficient hindsight exists, using a generic analytical grid.

Here, the analysis methodology has been adapted to the specificities of a call financing persons instead of projects.

This document recapitulates the main elements of the *ex post* analysis of the *Support for Training in Basic and Translational Research in Oncology* Programme (FRFT) over the 2011-2017 period (7 editions).

Context and Objectives of the Programme

The FRFT call was organized by INCa since its creation in 2007. From 2011 onwards, the call has been organised by ITMO Cancer-Aviesan. The original name (*Training for Translational Research*) was modified in 2017 to include basic research, in order to encourage applications in this area essential for medical professions training.

The programme allows physicians, pharmacists, veterinarians and dental surgeons to take part to a full-time training for and by research, in order to acquire the knowledge and methodology of basic and translational research in oncology. The programme is based on the principle of alternation between training and clinical practice, meant to foster a two-way exchange of knowledge between clinical care and research.

In the frame of the 3rd French Cancer Control Plan (2014-2019), the programme corresponds to the objective 13: "*To provide the means for an innovative research*". One mean to achieve this is "*to promote professional curricula that take into account cancer research evolutions*". These evolutions must "*insure breaking down barriers between science and medicine, and, biology and other disciplines, as well as fostering double trainings, while making them attractive to students*". These actions should ultimately "*strengthen the attractivity of research in oncology*" (action 13.4 of the 3rd French Cancer Control Plan).

Scope of the *FRFT* Programme

Fields covered

All fields of fundamental and translationnal research in oncology.

Type of funded training

- Master degree in research (M2)
- Doctorate
- Postdoctoral fellowship (in France or abroad)

Targeted public

- M2: students in medicine, pharmacy, odontology or veterinary medicine holders of a Master 1 diploma.
- Doctorate: students in medicine, pharmacy, odontology or veterinary medicine holders of a Master 2 diploma or a fundamental veterinary studies diploma.
- Post-doctoral fellowship: students in medicine, pharmacy, odontology or veterinary medicine holders of a doctorate since less than 3 years.

Ex post Analysis of the Programme

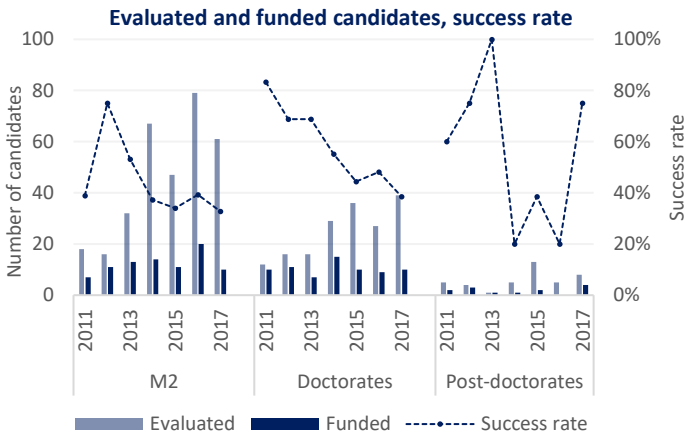
KEY FIGURES

The analysis covers the candidates evaluated, selected and funded between 2011 and 2017, as well as the final reports that were available at the end of 2018. In complement, ITMO Cancer-Aviesan organised a seminar dedicated to this programme in May 2019. Former laureates, selection committee members, and PhD school directors held discussions about the programme and the more general question of medicine/research double trainings.

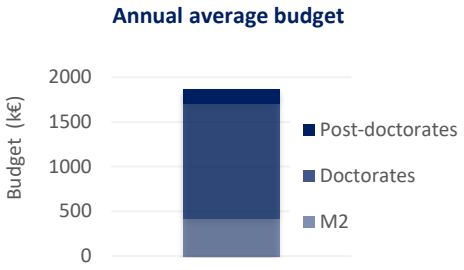
Main figures of the *FRFT* Programme (2011-2017)

- 538 submissions evaluated
- 240 submissions selected
- 171 laureates funded:
  - ✓ 86 M2 (average 12/y)
  - ✓ 72 doctorates (average 10/y)
  - ✓ 13 post-doctorates (average 2/y)
- % of women laureates:
  - ✓ M2: 68 %
  - ✓ doctorates: 56 %
  - ✓ post-doctorates: 41 %
- total budget: €13.1M
- average budget per laureate:
  - ✓ M2: €33.6k
  - ✓ doctorates: €49.5k
  - ✓ post-doctorates: €68.7k
- median age of laureates:
  - ✓ M2: 28 yo
  - ✓ doctorates: 30.5 yo
  - ✓ post-doctorates: 34 yo

Each year between 2011 and 2017, the FRFT programme funded on average 12 M2, 10 doctorates and 2 post-doctorates (including some abroad). The average success rate to the calls for proposals was 45% for all types of training. The increase of the number of candidates from 2014 onwards caused a decrease in the success rate which reached 36% for M2, 46% for doctorates, and 38% for post-doctorates over the 2014-2017 period, compared to 56 %, 74 %, and 78 %, respectively, between 2011 and 2013.



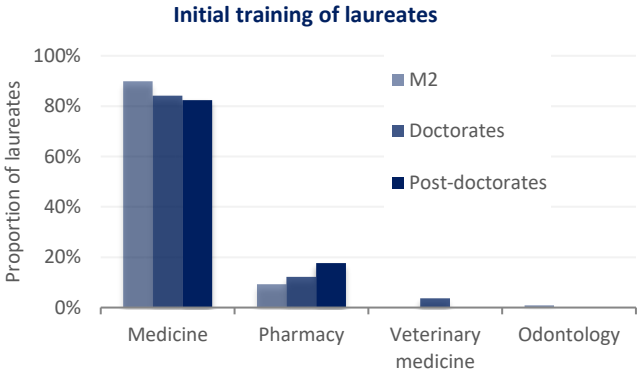
The rates of grant waiver were significant over the whole period (30% on average for all types of trainings), especially for masters (33%) and post-doctorates (35%). A bit more than one fifth (22%) of doctorate laureates did not take the funding. Withdrawals made possible for all candidates on supplementary list to receive *in fine* a grant proposal.



The budget was mainly attributed to doctorates, as their training last longer than masters and post-doctorates, and their annual cost (€49.5K) is higher than for masters (€33.6K).

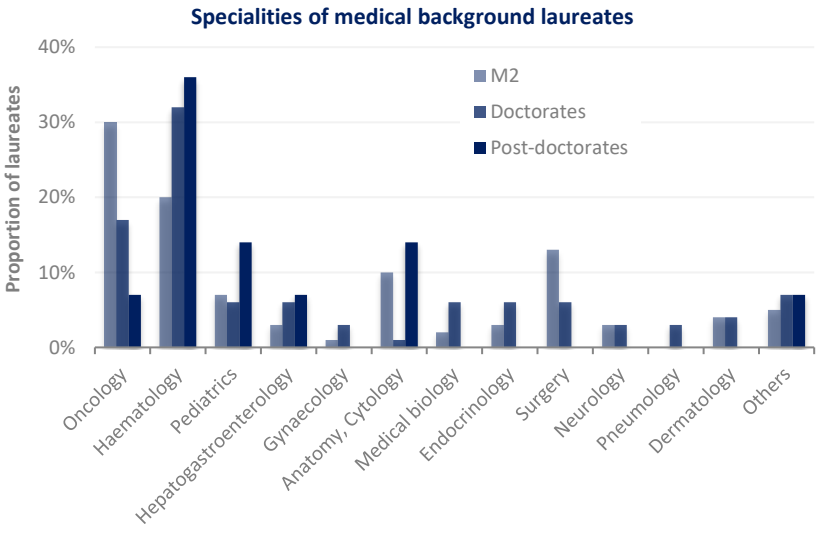
A Majority of Candidates and Laureates From a Medical Background, Mainly Oncology and Haematology

The vast majority of candidates and laureates were stemming from medical studies: around 90% of M2 candidates and laureates, around 70% of candidates and 80% of laureates -on average- for doctorates and post-doctorates. Furthermore, for doctorates and post-doctorates, candidates with medical backgrounds had a better success rate than those with a pharmacy background.



Among the whole programme, oncology and haematology were the most salient medical specialities among the candidates and laureates, followed by paediatrics, hepato-gastro-enterology, gynaecology, medical biology, pathological anatomy and cytology, surgery, and dermatology.

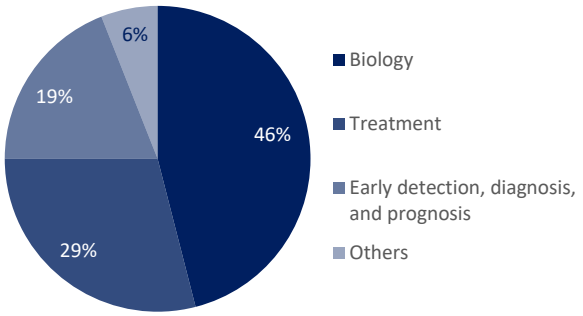
However, oncology-specialised candidates and laureates were less present at the end of the curriculum than at its beginning: they were representing 30% of medicine laureates for M2 level, but 7% of post-doctoral fellowships, with a success rate of only 20%. Inversely, specialities such as haematology, paediatrics, hepato-gastro-enterology, gynaecology, and medical biology were more represented in the programme later in the curriculum, although their absolute numbers in the programme remained low.



CANCER BIOLOGY, ESPECIALLY FUNCTIONAL ANALYSES, AT THE HEART OF RESEARCH PROJECTS

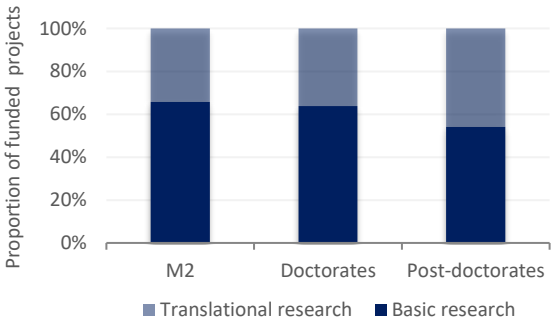
FRFT-funded projects were mainly belonging to the CSO[1] categories "*Biology*" (almost half of the projects), "*Treatment*", and "*Early detection, diagnosis and prognosis*". Other CSO categories ("*Aetiology*", "*Scientific models*", "*Cancer control, survivorship, outcomes research*", and "*Prevention*") were representing all together only 6% of the projects.

CSO categorie of funded projects



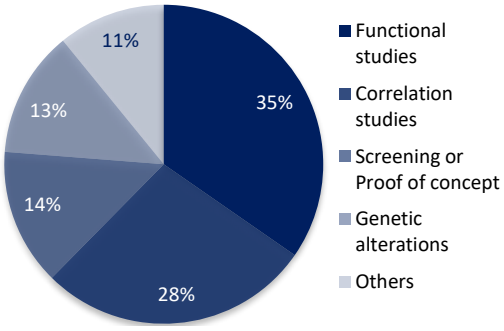
Projects involving basic research (development of knowledge on cancers, oncogenesis or resistance mechanisms, primary proofs of concepts on cell lines for potential therapeutic approaches) were representing around 60% of the funded projects. The remaining 40% of projects were translational research (determination of the prognostic or predictive value of responses to therapy based on cohorts of patients, or testing of therapies on mice harboring human tumors).

Proportion of basic vs translational research



Research works described in the final reports of laureates were -in more than a third of the cases- functional studies of genes, signalisation pathways, or genetic and epigenetic alterations involved in oncogenesis. Correlations between a biomarker, a genetic or epigenetic variant, and characteristics of the tumour (its aggressiveness, sensitivity to therapies or to hormones) were also well represented. The remaining projects were screenings, proofs of concepts for therapeutic approaches, or descriptive studies identifying new genetic alterations or assessing their frequencies.

Projects research types



Funded projects were studying a variety of organs, including the hematopoietic system (33% of funded projects), the lung and upper aerodigestive tracts (14%), the central nervous system (8%), the uro-genital apparatus and the digestive system (7% each). Only 9% of the projects were research concerning several types of tumours. In the vast majority of the cases (90%), the type of cancer studied or the type of research was in line with the specialisation of the laureate.

As for the research model or material used, it was mainly human patient samples and cell lines. Mouse models, primary cells and data from other laboratories were also used.

[1] CSO Categories (*Common Scientific Outline*) are a universal scientific classification system covering the full spectrum of research on cancer.

Tangible Benefits and Long-Lasting Projects

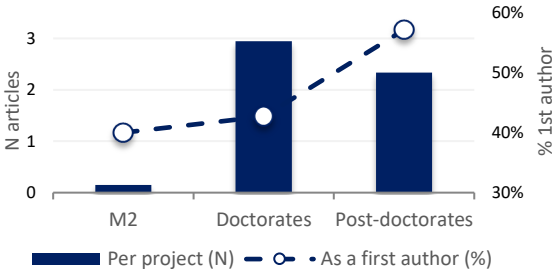
Concerning results dissemination, 15% of the M2 laureates had one accepted publication at the time of the final reporting. The vast majority of doctorates and all post-doctoral fellows had accepted publications (2.9 and 2.3 articles on average, respectively). The proportion of scientific papers with the laureate as first author increased with the curriculum to reach 57% for post-doctoral fellows.

Outcomes and impacts of the FRFT Programme

(107 final reports)

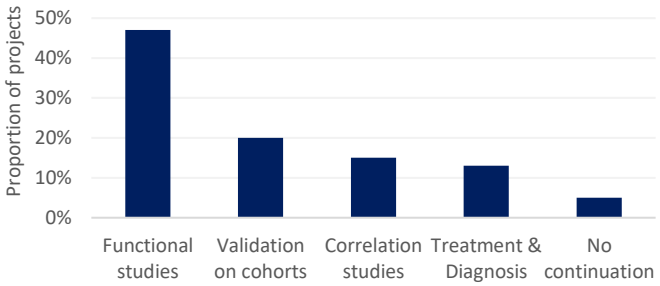
- Distinction (price or grant): 7% of M2, 18% of doctorates
- 7 patent requests, for therapeutic (5) or diagnostic (2) approaches, and one licencing
- International and national collaborations going beyond the end of the projects
- Launch of 2 clinical trials (M2 laureates)
- Changes in the clinical practices regarding diagnosis and cancer management in 2 hospital services
- 141 publications, including 127 original articles

Publication average



In line with the French Cancer Control Plan objective "*sharing knowledge and data nationally and internationally between professionals [and with the lay public]*", the majority (67%) of the publications stemming from the work done in the frame of the programme was available in open access.

Projects continuation beyond funding

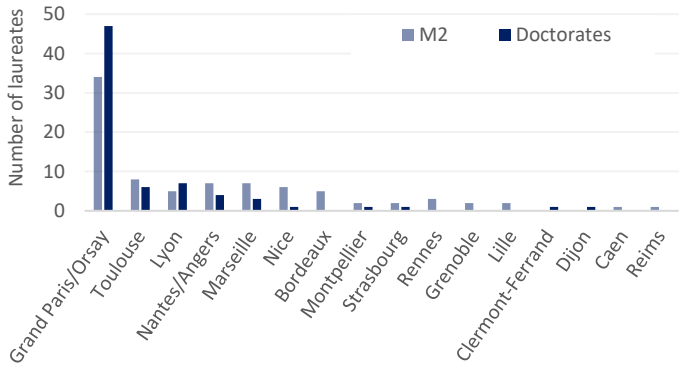


Projects were almost all (95%) continuing beyond the end of the grant, mostly with functionnal studies, or validations of preliminary results on larger cohorts. Laureates also mentionned ongoing correlation studies, or assessments of the therapeutic or diagnostic potential of various molecules or approaches.

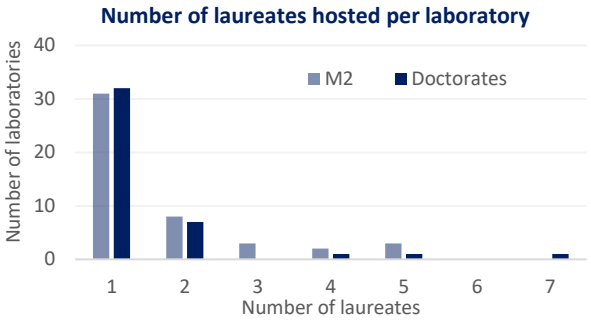
Host Laboratories all over France, and a Few Well-Represented Research Centres

M2 and doctorate laureates were hosted in laboratories in the whole metropolitan France, but with a high concentration in Paris, Toulouse, Nantes-Angers, Lyon, and Marseille areas. Postdoctoral fellows were hosted in laboratories in United States, Canada, and Germany, as well as in Marseille and Paris for France.

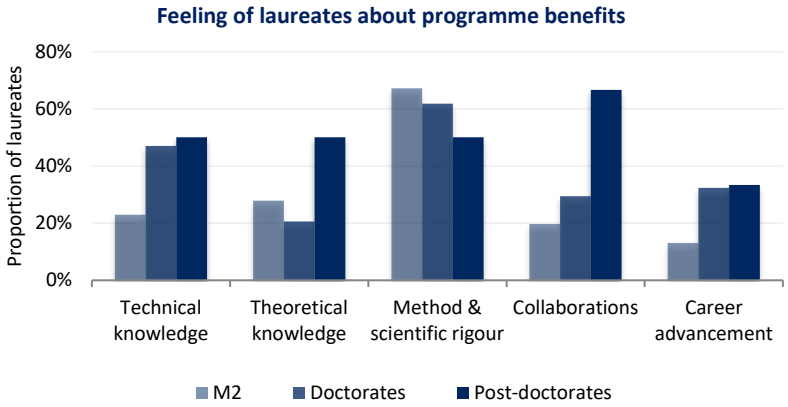
Localisation of hosting laboratories



A vast majority of laboratories receiving M2 (40/47) and doctorates (39/42) had hosted 1 or 2 laureates over the analysed period. However, 5 research centres hosted over a quarter of M2 and doctorate laureates. Hence, the Centre de recherche en cancérologie de Marseille (CRCM), the Centre de recherche en cancérologie de Toulouse (CRCT), and the Centre de recherche en cancérologie et immunologie Nantes/Angers (CRCINA), with 5 grants each, collectively hosted 19% of the M2. The Institut Cochin in Paris, the CRCT, and the Centre de recherche en cancérologie de Lyon (CRCL), with 7, 5 and 4 grants, respectively, hosted 26% of the doctorates in the FRFT Programme[2].



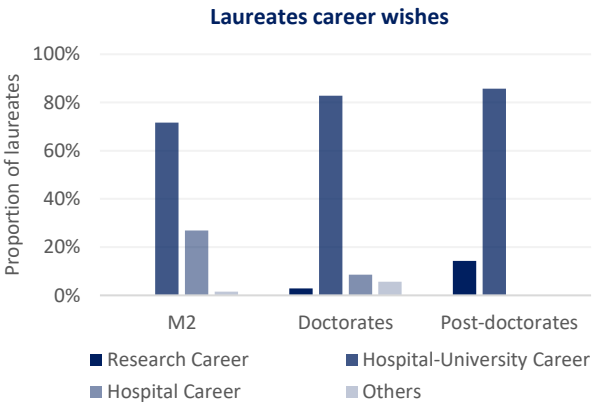
TANGIBLE OUTCOMES AND IMPACT ON LAUREATES PRACTICE AND CAREER



When asked about outcomes of the grant on their practice and career, M2 laureates have indicated a better knowledge of the scientific research process that helped the development of a critical thinking and the understanding of scientific papers. Many doctorate laureates mentioned a better scientific rigour and new technical knowledge. Post-doctoral fellows cited the development of collaboration networks that were continuing beyond the funding period, acquisition of further theoretical and technical knowledge, as well as experience in conducting scientific research.

Almost a third of the doctorate grantees and post-doctoral fellows have reported a significant impact of the funding on their career.

Laureates career wishes, as expressed in their final reports, have been compared with the laureate's actual careers, 3 years on average after the end of the funding[3]. The wish to pursue a hospital-university double career increased with the curriculum, going from 72% of M2 laureates to 86% of postdoctoral fellows. Inversely, M2 were still 27% to envision a purely

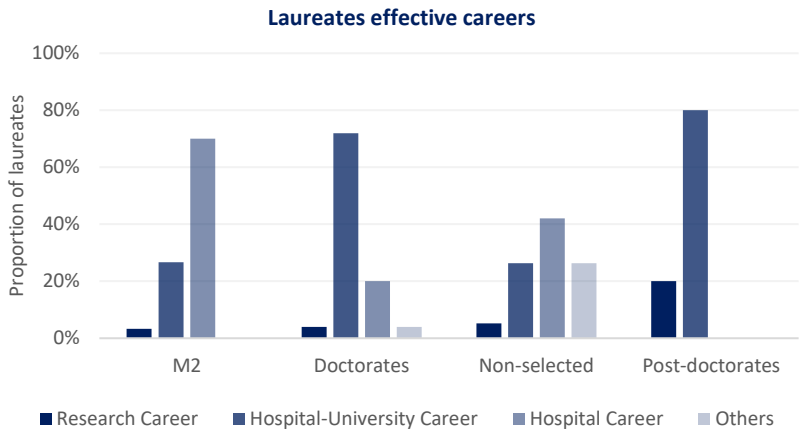


[2] Institut Cochin Inserm U 1016 – CNRS UMR 8104; CRCT Inserm U 1037 - CNRS ERL 5294; CRCM Inserm U 1068 - CNRS UMR 7258; CRCINA Inserm U 1232 – CNRS ERL 6001; CRCL Inserm U 1052 – CNRS UMR 5286

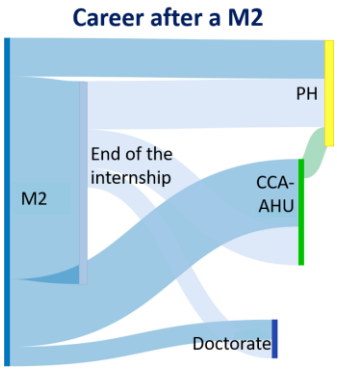
[3] Sources: Hospitals and research laboratories websites, ResearchGate, LinkedIn, etc.

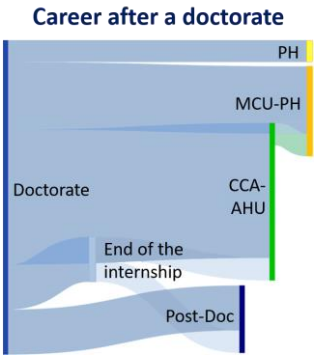
hospital career while no post-doctoral fellows were having that wish, 14% of them even contemplating a purely research career.

Data showed a different reality for M2 laureates, as 75% of them were being in a purely hospital career path and only 21% were having a hospital-university double career. The percentage of hospital-university double careers increased with the curriculum, as 65% of the doctorates and 80% of the post-doctoral fellows went into that path. Postdoctoral fellows were 20% to have a purely research career, and none of them were in a purely hospital career. Wishes were therefore closer to reality as grantees went further in the curriculum, going from 50% of fulfilled wishes for M2 laureates to 100% for the post-doctoral fellows. Interestingly, non-selected doctorate candidates who did a PhD thesis through another funding appeared to have less followed the hospital-university path than the FRFT-funded laureates (26% *vs* 65%).

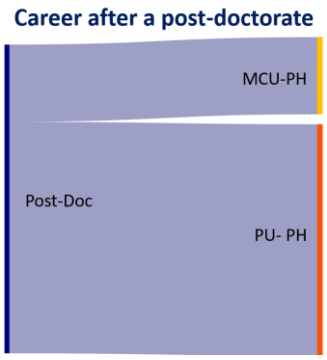


The career path of the medical laureates subpopulation has been specifically investigated[4]. About 12% of M2 laureates did a PhD thesis afterwards, a number that is likely an underestimation due to the limited hindsight (3 years minimum and 4.5 years on average). In fact, in 80% of the cases, there was a return to clinical work for 3 years on average between the M2 and the PhD thesis. In terms of career, around a quarter (26%) of M2 laureates had obtained a hospital practitioner permanent position (PH) at the moment of the analysis.





The doctorate laureates were for 21% of them pursuing with a post-doctoral fellowship, in most cases directly after their thesis. For their career, they were 29% to have a lecturer-hospital practitioner (MCU-PH) position at the moment of the analysis (hindsight of 3 years on average). The others (43%) were often in a position of clinical assistant head or university-hospital assistant (CCA-AHU).



The vast majority (75%) of the laureates for a post-doctoral fellowship was in a university professor-hospital practitioner position (PU-PH) at the time of the analysis (hindsight of 4.5 years on average).

[4] Sources: Laureates final reports, *Curriculum vitae* or public data collected on Internet

Conclusion

The *ex post* analysis of the FRFT programme over the 2011-2017 period provides us with the following insights:

- The attractiveness of the programme never dropped, with submissions increasing until 2014, and becoming stable afterwards;
- Laureates went to laboratories all over metropolitan France, but 5 research centres concentrate a quarter of the M2 and doctorates laureates;
- Physicians were the main grantees of the programme before pharmacists. The programme could not strengthen the research in veterinary oncology, as there were not enough candidates. The programme attracted only one student in odontology;
- Programme's physician laureates were mainly oncologists or haematologists. Oncologists were however less present in the programme as moving further in the training curriculum. This might be related to the high workload in oncology services at hospitals that hinders the availability of oncologists to further their scientific training. Inversely, haematology, hepato-gastro-enterology, medical biology, and paediatrics were more and more present along the curriculum: the objective of strengthening the attractivity of research in oncology is therefore attained in part;
- M2 laureates went only in a small proportion further in their training by and for research, although a quarter of them have continued research activities afterwards;
- In addition to theoretical and practical knowledge, laureates have pointed out the impact of the FRFT programme on their clinical practice:
  - ✓ By a better understanding of the scientific process and of the various aspects of research (including for laureates that have not pursued research activities);
  - ✓ By the development of collaboration research networks in France or abroad that went beyond the end of the funding, mainly for postdoctoral fellows;
  - ✓ By the translation in the clinical practice of some research results, underlying the importance of exchanges between the two communities ("Clinics" and "Research") to foster innovation translation into healthcare.