Fondazione Ricerca
Fibrosi Cistica - Onlus
italian cystic fibrosis research foundation

ITALIAN CYSTIC FIBROSIS RESEARCH FOUNDATION (FFC)
CALL FOR GRANT APPLICATIONS YEAR 2021

December 15th, 2020

The Italian Cystic Fibrosis Research Foundation (FFC) funds a limited number of research projects that have the ultimate aim to improve the health status of cystic fibrosis (CF) patients. Research proposals in which translational objectives are clearly evident will be prioritized. Accordingly, research projects dealing with either clinical studies or pre-clinical studies exploiting animal models of CF are encouraged. Multi-centre applications that combine different expertises in one project will be given a higher priority only if there is convincing evidence that the expected output will be more effective than the sum of individual projects.

1. Priority areas

1.1. Pathophysiology of the basic defect in cystic fibrosis and pharmacological approaches designed to correct defective CFTR or to compensate for its deficient function with the following particular indications:

- Novel modulators or combinations of modulators for the treatment of F508del mutation and particularly of mutations not sensitive to current modulators;
- Ancillary supports to modulator therapy;
- Targeting alternative chloride channels;
- Development of cystic fibrosis therapies based on gene or RNA editing.

1.2. Identification and validation of new and appropriate *in vivo* and *ex vivo* models and assays to predict and monitor the potential efficacy of new therapies finalized to correct the CFTR defect, with special reference to CFTR mutations not sensitive to current modulators.

1.3. Lung infection in CF: development of innovative diagnostic and antimicrobial strategies (studies clearly oriented towards clinical applications) with special indication for the rapid and accurate diagnosis of infections and the treatment of difficult-to-treat microrganisms

1.4. Inflammation in CF: really innovative strategies to contain the inflammation-based pathology (studies with evident translational potential).

1.5. Clinical applications in CF prevention, diagnosis, therapy, care and health organization: clinical trials, with special regard to phase IV clinical studies (post-marketing studies in the real life) and those to improve the outcomes of lung transplantation in CF; review and update of traditional therapies that involve a heavy burden on sick people; epidemiological studies (with reference also to the database of the Italian CF Registry) and systematic reviews.

Important Notes:

- FFC will support studies aimed at identifying drugs already used in the clinic to treat other diseases for their potential in the treatment of CF patients **provided that there is a strong rationale to test them in the context of CF pathology**.
- Studies aimed at identifying new therapeutical compounds will also be taken into consideration, **provided that they suggest new strategies** to affect mutated CFTR function and/or CFTR-

dependent mechanisms of cell pathology, also including modification of DNA and RNA. Both types of studies may exploit *in vitro* or *ex vivo* primary cell models.

- FFC will give very low priority to studies aimed at identifying hit compounds derived from lead molecules previously reported to potentiate/correct mutated CFTR **unless the proposal will provide clear evidence that standard preclinical studies will be supported by the host institution, private companies or other sources**. FFC will not fund formal preclinical studies, with the exception of those addressing the drug/compound effects on animal models of CF pathology, when existing and available, and limited to provide the proof of concept that they work in the animal models without toxic effects. **Lack of toxicity should also be documented in projects included in other priority areas.**
- Studies aimed at identifying new antimicrobial strategies will only be considered if original strategies are proposed, along with enough preliminary data, to support a potential advantage vs. conventional treatment protocols. FFC will not consider studies aimed at the identification or preliminary characterization of hit compounds active against multidrug-resistant pathogens unless a clear advantage over current agents (even at the pre-clinical stage) is expected for treating CF infections.
- Collaboration and transferring of knowledge and expertise from basic to clinical research is particularly recommended. To this aim **a clinical referring consultant for basic research projects and a basic research consultant for clinical projects** and her/his role must be clearly highlighted in the application cover letter.
- By "**translational research**" this call means not only "bench-to-bedside" studies. Research projects considering the translation of results from clinical studies into everyday clinical practice and health decision making are also welcome. Topics to be considered include clinical epidemiology, communication, behavioral science, organizational theory, quality monitoring and quality improvement research.

2. Eligibility

Any individual with the role of Principal Investigator (PI), Coordinator or Partner **must be clearly qualified and effectively involved to play that role. Personal prestige and authority alone are not qualifying criteria**. Eligibility criteria are:

- **Scientists with proven scientific independence** with at least 3 experimental/clinical papers as last Author or first Author in the last 5 years (these papers have to be highlighted in the P.I./Coordinator's curriculum vitae in Form 2) are eligible to apply as PI or Coordinator of a multicenter project.
- The **PI or Coordinator must have a permanent position**. The FFC will also consider applications from RTD researchers ("fixed research contract", as stated in the Italian Law 240/2010, article 24, clause 3, for the University system): this type of applicants must meet the criterion of scientific independence provided that their contract **completely** covers the intended duration of the funding period (a copy of the contract must be submitted).
- The **PI or Co-ordinator of a multicentre project**, as a rule, should reside and work in Italy. However, the role of Coordinator of a multicentre project can also be assumed by researchers who live and work in another country of the European Community, provided that the project includes at least one partner who lives and works in Italy. Partners of a multicentre project may be co-opted by an Italian coordinator even among scientists living and working in any country outside of Italy.
- **Partners** are those scientists providing an autonomous (though co-ordinated), active and substantial contribution to a specific part of the project. The FFC Foundation does not consider as Partners those working as collaborators in the PI's, Co-ordinator's or Partner's group nor in their laboratory or hospital ward. Individuals involved in supplying biological materials, or clinical and biological data are not eligible as Partners and should rather be enlisted as **internal or external Collaborators.**
- **Partners** must have a permanent position. Also RTD researchers (with "fixed research contract" as stated by the Italian Law 240/2010, article 24, clause 3, for the University system) are eligible: in that case they must attach a copy of their contract with a declaration of the legal representative of the host institution, as specified above for PI (see also point 5).

- **PI (or Coordinator)** cannot be Partner or PI or Coordinator in other FFC projects simultaneously, including projects funded by FFC which are in progress, unless they will be concluded on 31st August 2021 and are not "pilot projects" (see also paragraph 7). A researcher can be a simultaneous partner in no more than two FFC projects as long as he/she is not a PI/Coordinator in another project.
- The **position and function of partner** should not be confused with that of **external collaborator**. External collaborators are usually researchers with limited roles and functions in the specific project, functions that are not to be confused with "provision of external services", which have their own specific position and specific treatment in the identification of costs. An external collaborator cannot be involved in more than two FFC projects.

3. Budget

The budget description **(Form 10)** must be accurate and every item must be justified and detailed per each Partner and per each year in the case of 2-year projects. **Inadequate budget description will lead to rejection of the project**. The maximum budget request cannot exceed € 130.000,00 for 2-years projects and € 70.000 for one-year projects.

Eligible costs (all must be clearly related to the project):

a. Fellowships or research contracts (for graduated and technicians). See also point 9 of the Call
b. Consumables and animals
c. External and occasional professional or technical services for not more than 15% of the total budget)
d. Small research equipment or accessories and softwares (justified and related to the current project): not more than 7% of the total budget
e. Travel and meeting/congress participation (International Conferences on CF), training sessions: not more than 4% of the total budget
f. Costs for patients participating in clinical trials
g. Publication expenses, with clear reference to the project assigned in 2021 (max 2.5% of the budget)
h. Overheads (general expenses not provided for in the previous items, but in any case compatible with the admitted expenses): cannot exceed 3% of the total budget

Ineligible costs:

1. Salary and wages for PI, Co-ordinators, Partners and internal or external Collaborators (with the exclusion of personnel above mentioned for FFC fellowship or research contract)
2. Furniture and stationery articles
3. PC and other hardware
4. Software not specifically related to the project
5. Basic lab or clinical equipment
6. Equipment repairing or technical assistance fees
7. Office materials

4. Guidelines to fill in the forms

The research project must contain all the following information, which must be followed very carefully.

a. General information (**Form 1**). Project title, name of the Principal Investigator, or Co-ordinator for multicentre studies, host Institution, project duration (1 to 2 years); type of application (new, resubmitted, extension of a 2020 one-year pilot project, extension of a project both concluded or in progress, (the ongoing project must be in very advanced phase) previously funded by FFC; priority research area; name/s of the Partner/s, their host Institutions, names of Collaborators (internal and external) really involved in the project (in the case of multicentre study specify the Collaborators for each research team) and their host Institution and specific

roles in the project. The acceptance of collaboration must be supported by personal declaration (see also point 5: "Additional documents"). Also, the main personal data have to be included in the form, both for PI and Partner/s: residence, personal e-mail address, personal phone (even mobile) and fax numbers, tax code.

b. Curriculum vitae (**Form 2**). Education and training, previous job and research experiences, significant publications in the last 5 years (only in peer-reviewed journals). For multicentre study enclose also Partners' CV and publications (last 5 years).

c. Project overview (**Form 3**). It must be included: background/rationale, aims, preliminary results relevant to the project, design and method description, anticipated output, relevance for CF Foundation.

d. Aims, background and rationale (**Form 4**). The originality of the project must be clear from these items.

e. Preliminary results (**Form 5**). They must be proved and convincing and refer to the results obtained by the applicant in preliminary investigations bearing the rationale and the justification of the proposal. The preliminary results will serve to demonstrate that the candidate has the capacity to carry out the proposed project This part will be regarded as absolutely necessary and decisive for the evaluation of the project.

f. Experimental plan and methods (**Form 6**). In this part it must be specified in detail: the research plan, methodology, materials intended to use, justified numerousness of the samples (whether patients or animals) which are going to be examined and the statistical methods that are going to be applied for results evaluation. Moreover, it is requested a description of the development phases of the project, even temporal (timeline), quality controls, and whole pertinent references. Also, the organization and the management to assure quality and feasibility of the project have to be described. It would be interesting if the critical points of the experimental plan are detailed, and the eventual "B plans" indicated in case problems are found.

g. Host Institution/s facilities (**Form 8**). Spaces, equipment, technical systems, technologies and services available for the realization of the project must be detailed, indicating their specific relevance to each phase of the experimental plan.

h. Outside Collaborations/Services (**Form 9**). They have to be considered as external technical services or professional consulting/performances and constitute only an accessory part of the project.

i. Budget and its duration (1-2 years) (**Form 10**). Specify the expenses both overall and per each year; in case of multicentre study, also per each Partner (see point 3).

j. Roles and contribution of the Partner(s) in the multicentre project, coordination and management (**Form 7**). The Coordinator has to fill in this part with a detailed description of the specific contribution of each Partner in the project. Description of the Coordinator's strategies to monitor each team activities, to facilitate communication among one another, to promote exchanges of ideas and methods, to integrate research phases and results.

k. Lay summary (**Form 11**). This must be written both in English and Italian (including Italian title), in a popular and well comprehensible style. This summary is meant to serve as a succinct and accurate description of the proposed work; if the application is funded, this summary will be published in the FFC Bulletin and in other media. The summary must state clearly the relevance of the proposed study to the FFC Mission (to promote innovative treatment and care for CF).

5. **Additional documents** (See point 13 in the application platform)

Each project must be accompanied by a **Cover Letter** that summarizes the overall project plan and the reasons why it falls within the priorities indicated in the call for applications, in line with the Foundation's mission objectives. Resubmitted projects (previously submitted to FFC and not approved) require extensive explanation (see point 6), and cannot be resubmitted with only minor tweaks. Resubmissions must include point-by-point answers to the reviewers' critiques. In the Cover Letter the applicant must declare (specifying the details) any **patent registration**, completed or in progress, for an invention referring to the proposed project.

5.1 Individual project

- Acceptance by the host Institution of the P.I.
- Copy (a scanned copy is OK) of the contract and its duration (see point 2), in case the PI or Partner has no permanent position.
- Consent for use of personal data, according to the Italian Law 196/2003.
- Declaration of commitment (signed, scanned copy) by each internal and external collaborator involved in the project and listed in the application.
- PI declaration of adherence to provisions governing laboratory animal care, if required.

5.2. Multicentre Project

The Coordinator of a multicentre project is the only responsible for both the accuracy and the completeness of all the documentation submitted to the Italian CF Research Foundation (including those of Partner Centres).

Coordinator: see documents required for individual project.

Partners: each Partner has to transmit to the Coordinator (who will send them to FFC) the following documents:

- Acceptance of Partnership (along with personal data and consent to use them, address, telephone and fax number, e-mail and fiscal code)
- Copy (just scanned copy) of the time contract, in case of not permanent position
- Declaration of acceptance by the host institution
- Partner's declaration of adherence to provisions governing laboratory animal care, if required
- Declaration of commitment (signed, scanned copies) by each internal and external collaborator involved in the project and listed in the application. A single pre-compiled form to fill in with the names and signatures of all collaborators is available in the "Administrative documentation - Upload Area" of the platform.

5.3. Clinical project

A clinical or mixed project (a project implying, even just in part, diagnostic, therapeutic or rehabilitative interventions on humans, not provided for in common standard or from the personal plan of diagnosis, care and rehabilitation) must provide the following documentation, in accordance with the provisions of the Italian Ministero della Salute (D.M. 15/07/1997, D.M. 18/03/1998, D.M. 19/03/1998, DL 26/05/2000 and DL 24/06/2003):

a. Ethical Committee Approval (for each Partner/Centre, if multicentre study) to be sent to FFC after award of the grant and not later than October 31st, 2021;

b. "Parere Unico", released by the Ethical Committee of the Principal Investigator/Coordinator/Partner's centre (if applicable) (not later than 31st October 2021 if the project will be funded);

c. Informed consent form (for interventions and for use of personal data, in anonymous form, for research purpose, released by patients or people involved in the study) plus patient information leaflet;

d. Good Clinical Practice declaration by the Applicant.

5.4. Projects including use of animal models

Any project which includes experiments on animals must be accompanied by a specific authorization of the Ethical/Technical Committee of the Institute hosting the animal facility to be submitted only after award of the grant and not later than October 31st, 2021.

Moreover, the PI or Co-ordinator must declare that the procedures concerning those experiments will follow the instructions included in the legislative decree 2014, n. 26, "Attuazione della direttiva 2010/63/UE sulla protezione degli animali utilizzati a fini scientifici (14G00036) (GU n. 61 del 14-3-2014)"

NOTE: *If the approval of Ethical Committee (for clinical trials) or Ethical / Technical Committee (for animals) and "Parere Unico" are not available by October 31st, 2021, a follow-up report on the ongoing application either to the Italian Ministero della Salute or the Local Ethical Committee must be sent to this Foundation by email. Providing this information to the FFC Foundation is crucial for the correct management of the grant.*

6. Resubmitted projects

Researchers who are going to resubmit a project previously not funded by FFC, even with a different title and improvements, must follow these recommendations:
- The Cover Letter must highlight the year of the previous submission and the relevant modifications of the revised one.
- If the previous application underwent full review, the Cover Letter must also include detailed, point by point, reply to the critiques of the referees and FFC Scientific Board.
- In case the Revised Application is submitted by a different PI, an explanation must be provided in the Cover Letter.
- The same research project can be resubmitted only once, even if substantially modified.

7. Submission of applications by former FFC grant recipients

A former FFC grant holder may submit a new project or a proposal of development of a project already funded by FFC ("extension project"). In both cases all of the following must apply:

7.1 The previous project has been completed and its final scientific report has been already submitted to FFC. The scientific report must include details of the project's achievements, the contribution of each Partner (for multicentre projects) and a list of the resulting publications and congress presentations (abstracts).
7.2. Applications can be considered exceptionally for an extension even before the conclusion of a previous project (only for project expiring on August 31st, 2021 and are not "pilot projects" *) provided that the PI or Co-ordinator is able to show results that convincingly support the extension. However, this opportunity is offered exclusively for two-year projects at their second year.
7.3 The application for extension of a 1-year ongoing project clearly approved by FFC as a "pilot project"* in 2020 may be submitted exceptionally with a deadline postponed to May 31, 2021, provided that at that date the project has really achieved its objectives (with adequate and convincing documentation).
7.4 Partners in a multicentre project financed by FFC may submit a new research proposal as PI or Coordinator (see the conditions in 2.) provided their previous projects were completed or that the ongoing project expires on August 31st, 2021, and that they are not involved in other FFC projects in accordance with the provisions of point 2.

* *It is up to the Scientific Committee to define "pilot project" a project previously submitted and evaluated with the final decision to be approved (duration 1 year) but only in some of its goals, whose results are considered indispensable to carry out the entire project, upon request for its extension in the following year call.*

8. Evaluation of applications

Incomplete or behind schedule applications will not be processed for evaluation.

Procedures

Grants will be awarded on a priority basis. Specific factors that will play a major role in determining a successful outcome of the application are:

- relevance to the Italian CF Research Foundation's mission and to the priority areas (see point 1);
- soundness and originality of the study;
- relevance of the preliminary results;
- potential value to improving the clinical and care strategies;
- potential value to stimulating further studies, mainly on translational basis;
- appropriateness of the whole design;
- scientific record of the participants and the host institutions/laboratories;
- methods reliability;
- feasibility within the estimated time;

- facilities appropriateness.

All accepted applications will undergo a preliminary review by the Scientific Committee of the Italian CF Research Foundation on the basis of their relevance to the Foundation's mission and overall quality. Projects selected in this triage step will undergo full peer review by an international panel of experts. In the final step, the projects will undergo evaluation by the Scientific Committee, taking in due consideration the independent referees' comments. The Scientific Committee will also review the budget, which may be reduced with respect to the original request. **The evaluation of the Committee is final,** with the approval of the Board of Governors.

Due to the limited budget available, even projects that have received a positive evaluation by the external reviewers may be denied funding. Co-funding of projects, which must be declared and accurately described in the appropriate section of the application (see Form 10)**, is strongly encouraged and may increase the chances of approval of projects with an adequate rating.**

9. Fellowship and research grants

No more than one scholarship or contract with full salary can be admitted for each year of the entire duration of the project and the related cost (which can even be divided between two collaborators) cannot exceed 40% of the total amount of the grant, recalling that the project must be conducted mainly with the direct involvement of PI/Coordinator, partners and internal and/or external collaborators as indicated in the application. The sum set aside for such fellowship cannot exceed 31.000 Euros gross per year for graduated personnel and 23.000 Euros gross per year for technicians or other not graduated personnel (in any case the amount must be indicated in the budget, specified per year and per each partner centre).
The life of the research grant (including the part concerning scholarships and contracts) cannot exceed the duration of the project and will expire at its end date.
Normally, the Italian CF Research Foundation will directly assign and manage the research grant (including scholarship or contract). Exceptionally, other modes of administration of the grant and research collaborators must be discussed on a case by case with the FFC Foundation. On assignment of the grant, FFC will furnish to the PIs or Coordinators detailed information about the procedure to follow.
Fellows or contract holders have to be mentioned in any documents or publications as "Italian CF Research Foundation fellow/contract holder". The Italian CF Research Foundation reserves the right to have direct contacts with the fellows or contract holders, to ask for periodical progress reports on their work in the project (however, the scholar or contractor must send a report on the activity performed at the end of his term) and to call them to participate in the annual Convention of the Italian CF Researchers in which also the Principal Investigators/Co-ordinators and Partners must participate as FFC guests. The attendance to the whole Convention is mandatory because it is a working time on research funded by FFC and not just a general update conference.

10. Awarding and management of research funds

The awarding of funds will be formally decided by the Italian CF Foundation Board of Governors and communicated on assignment. As a rule, funds are given to the PI and not to the Institution where he/she intends to carry out the funded project.
The Italian CF Research Foundation will manage directly the funds according to the PI's or Co-ordinator's indications. Approved PI/Co-ordinators and Partners have to keep an accurate and update account, in parallel to CF Foundation. With reference to budget indications, expenses will be administered per year and per each partner centre.
In case of 2-year projects, award recipients will be expected to provide a detailed yearly administrative report by September 30th, 2021 to obtain subsequent payments.
Any changes of the original destination of budget formalized on assignment, occurring during the fulfilment of the project, must be exceptional and formally asked and agreed with FFC.

The Italian CF Foundation will not pay any expenses made after the date of conclusion of the project or exceeding the budget assigned. No expense orders can be issued in the last month of the project. Any costs in excess of the budget will be charged personally to the PI or Co-ordinator.

11. Scientific and administrative reports, publications

At the end of the first year of a two-years project, the PI or Coordinator must provide a detailed scientific and administrative progress report, which is necessary to decide the continuation of the financing. At the conclusion of the project, investigators are asked to submit, together with the administrative report, a Final Scientific Report including any publications and congress presentation abstract referring to the project. Every publication or congress abstract relevant to the FFC funded project must be forwarded promptly to the Foundation even before those reports. The Italian CF Research Foundation must be acknowledged in all publications arising from the funded project (congress abstracts, book chapters, scientific articles, congress slides, press releases…) by specifying the code of the related grant and by inserting the FFC logo both on congress slides and posters. Also, the adopters of a project, as indicated by FFC (see in www.fibrosicisticaricerca.it/area-ricercatori/i-progetti-di-ricerca/), have to be mentioned.
FFC may ask investigators to collaborate to public engagement and dissemination of their research results in order to support the FFC fundraising. For this purpose, it is up to FFC the task of contacting investigators.

12. Research results, intellectual property and patents

One of FFC's goals is to translate research results into clinical applications available to CF patients. Sometimes, this can be achieved by establishing partnerships with industry, so that the most promising research results can be fully developed into drugs, therapies, devices and diagnostics.
For this reason, FFC requests that all scientific results derived from a FFC funded project, that have importance for a possible development, are assessed for patent protection and/or commercial valorization. This can be performed by the funded scientists' institutional dedicated offices (for example Technology Transfer Offices), providing support and assistance on intellectual property matters and technology transfer activities. In any case, the request for a patent relating to results from projects funded by FFC must first be discussed with FFC and authorized by it. The FFC reserves the right to negotiate in good faith with the funded scientists' institutions its participation in the ownership of intellectual property of inventions derived from funded projects. The funded scientists must promptly inform FFC in writing of any new patent filings and execution of agreements with for-profit entities related to FFC funded research results.

FFC is confident that FFC-funded researchers will operate with clarity and honesty concerning the attribution of merits relative to any work, invention or discovery. FFC is confident that FFC researchers will always remember that all funds supporting CF research are coming from voluntary donations.

13. Writing and submitting applications

Applications must be written in detail and submitted only through the dedicated online platform **https://forms.fibrosicisticaricerca.it**, other options are not available. For first time access a registration is required to create a personal account and allow applications submission. Attention must be paid to not exceed the indicated number of characters in each form. Any images (photos, graphs, tables) must be low-resolution version and inserted in the text near the point to which they refer. Applications must be submitted through this platform **by midnight of February 15th, 2021.**