Telethon Research Projects
- Call for Applications 2019 -

FONDAZIONE Telethon

Università degli Studi di Milano

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Agenda

- Telethon in a nutshell
- The peer review process: Actors and roles & Review phases
- Evaluation criteria
- The 2019 Call for Research Proposals
- General considerations
- The Application in Tetra – *live* (Aldo Borrè)

Telethon in a nutshell

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Telethon

About us

- The **Telethon Foundation** is an Italian biomedical research charity founded in 1990 out of the will of a group of patients
- We rely on **donations** from the general public through **fund raising**

MISSION	VISION
To advance biomedical research towards the cure of genetic diseases	**To convert results of excellent, selected, and sustained research into available therapies**

We give **priority** to **rare genetic diseases** that are **neglected** by major public and private investments

Our Stakeholders	Telethon's Responsibility
RESEARCHERS	
	← **SCIENTIFIC RESULTS** (Research monitoring and development)
PATIENTS	
	← **FUNDRAISING** (Financial accountability and expenses control)
DONORS	
	← **FUND ALLOCATION** (Merit-based selection of research)

The Telethon research portfolio

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Intramural research

209 M€ research investment
294 research grants

Telethon Institute of Genetics and Medicine
Naples/Pozzuoli

San Raffaele - Telethon Institute of Gene Therapy
Milan

Dulbecco Telethon Institute
Career development program

KEY FIGURES 1990-2017

498 M€ research investment
2,629 research grants
1,611 PIs awarded
571 genetic diseases studied
10,717 scientific publications
6 Industrial partnerships
1 Marketing authorization

Excellence-driven grant allocation

Extramural research

288 M€ research investment
2,335 research grants

EXTERNAL RESEARCH: PROJECTS

- General projects
- Neuromuscular clinical projects
- Program projects
- Exploratory projects
- Collaborative projects

GENETIC BIOBANKS AND RESEARCH SERVICES

UNDIAGNOSED DISEASES PROGRAM

FELLOWSHIPS

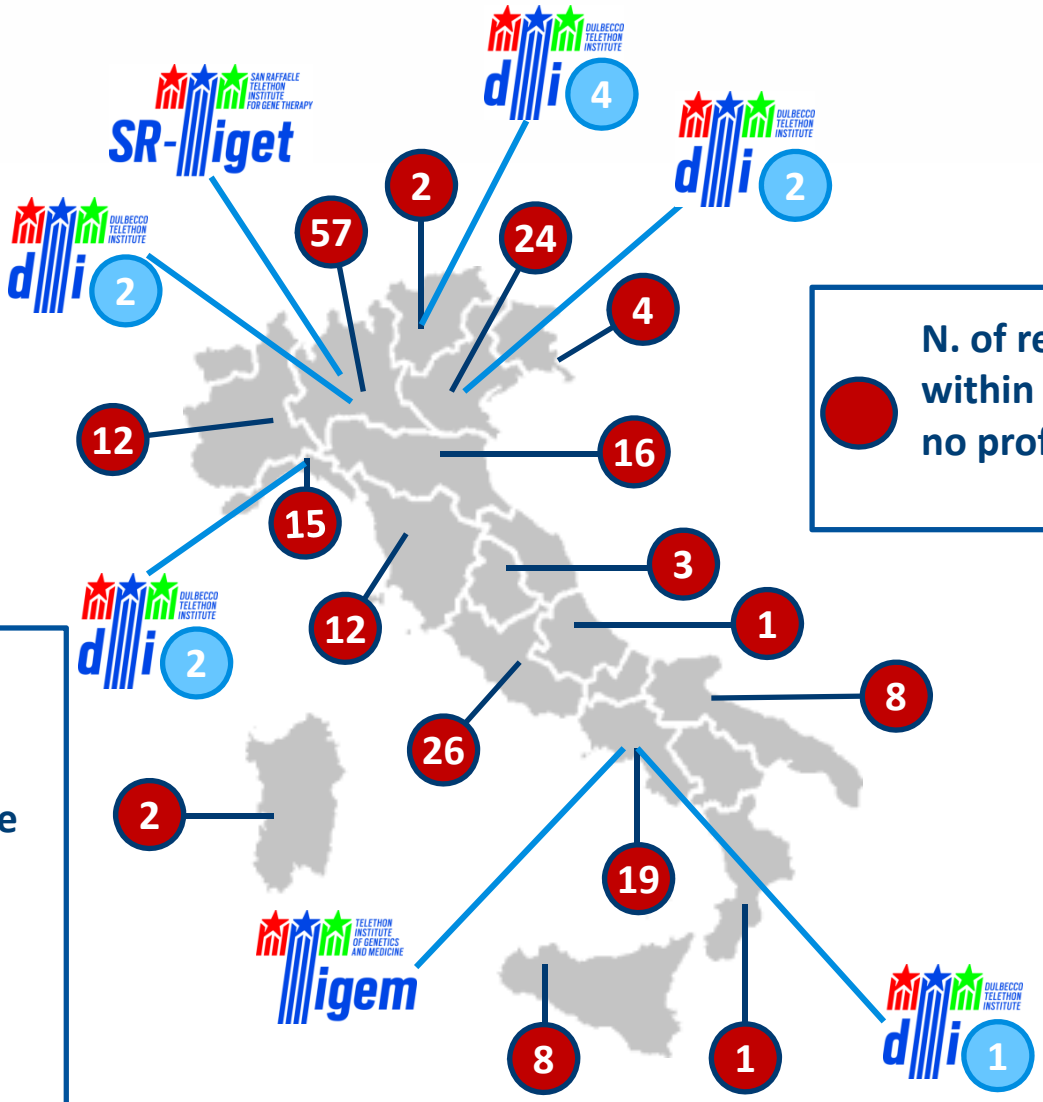
Steering and management

TELETHON'S ROLE

Funding and support

Research funded by Fondazione Telethon

On going Telethon-funded research
March 2018



N. of research projects within universities and no profit institutes

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Fondazione Telethon Institutes

Telethon's investment in research

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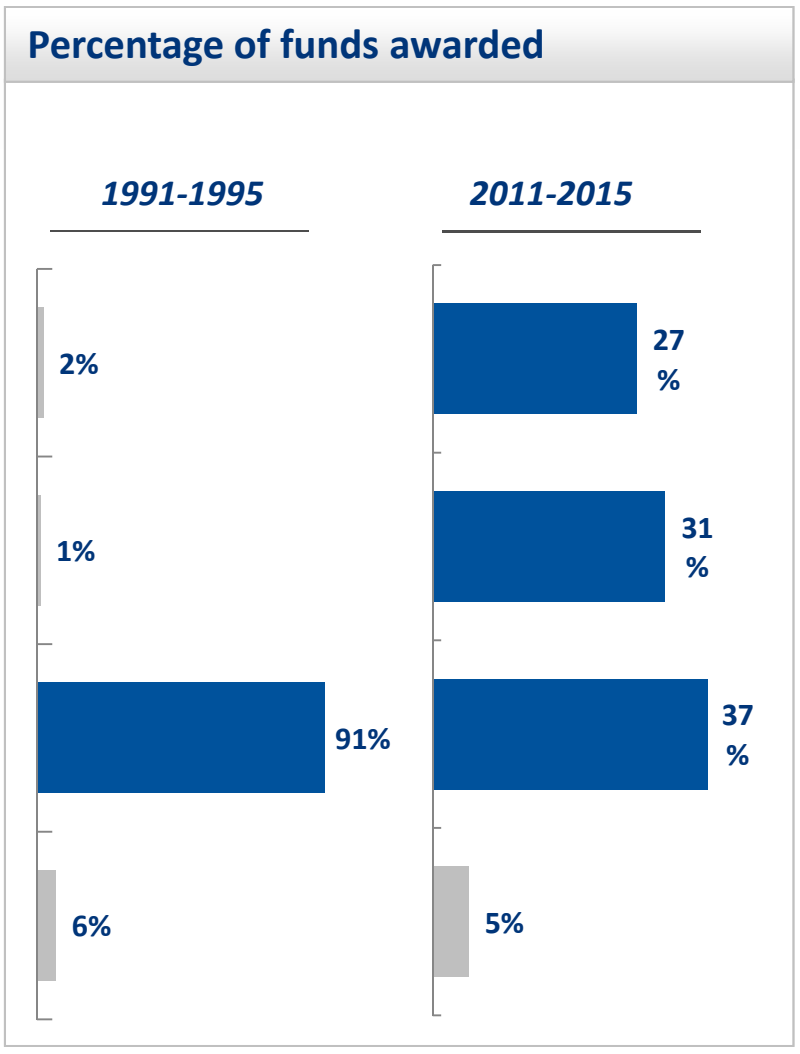
The research ladder

Percentage of funds awarded



Source: TRic database, Telethon, October 2015

The Telethon peer review process

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The ‘selection’ process at a glance

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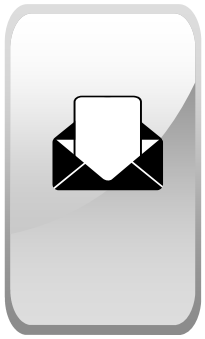
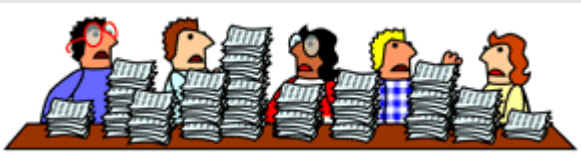
Phase		Responsibility	
1	Call for application and examinations of projects		Telethon Research Program Managers
2	Evaluation of the projects		*Triage*: 3 members of the Scientific Committee *Full Review*: 3 members of the Scientific Committee + 2 external reviewers
3	Plenary review meeting		All 30+ members of the Scientific Committee
4	Approval of funding		Telethon Board of Directors

Actors & Roles - 1
The Telethon Scientific Office

- **Manages the entire peer review process**
- **Provides the necessary distance between Applicants and Reviewers**
- **Duties:**
  - Preparing the Calls for applications
  - Defining the composition of the Telethon Scientific Committee by inviting members from the academic community
  - Selecting External Reviewers and ad-hoc members of review panels
  - Organizing the review sessions
  - Providing feedback to Applicants

Key figures in the Office are **Research Program Managers**: former researchers with a strong background in biomedical research

Actors & Roles - 2
The Scientific Committee



- **Conducts the review process** and **provides funding suggestions** on the basis of shared criteria
- All members participate in a final **plenary review meeting** to discuss the proposals
- Members are **internationally recognized leaders** in their field of expertise
- Italian members: max 2 Italy-based and/or foreign-based Italian members
- Participation on a **4-year rotation basis**, regulated by a **contract with Telethon**
- **Composition may vary** according to the type of Applications being reviewed (Call)
- Although the list of members is publicly available (website), **the identity of Reviewers** involved in each application **is not disclosed to the Applicants**

Actors & Roles - 3
External Reviewers

- Necessary because of the **diversity of the Applications** received within the General Call

- Their support is meant to provide members of the Scientific Committee with **specific comments on each Application**

- **Chosen by Research Program Managers** from among the international scientific community on the basis of:
  - **Specific scientific expertise** related to each individual Application
  - **Absence of conflicts of interest** with the Applicant
  - Other criteria (e.g. suggestions / exclusion by Applicants)

- External Reviewers remain **anonymous** to the Applicants

Conflicts of Interest

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In order to minimize conflicts of interest, Reviewers should not:

- have **published** together **with the Applicants in the past 5 years**
- be engaged in **active collaborations** with the Applicants
- be **employees** of the Applicant's institution
- have **close relatives** involved with the Applicant
- have/had longstanding **scientific or personal differences** with an Applicant
- be **professional associates** of the Applicants **(5-year limit)**

During the plenary review meeting, Reviewers with a conflict of interest with any Applicant/Application will leave the room during the relevant discussion

The Telethon General Grant Call Review Phases

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Admission of Applications to the Review Process

- **Immediately after the Call's deadline, Applications are assessed by the Scientific Office for compliance with the Call's criteria, including:**
  - Administrative requirements
  - Applicant's and Host Institution's eligibility
  - Eligibility of the disease/topic being addressed

Second half of February

- **Applicants whose Application is excluded are notified soon afterwards**

- **Accepted Applications are distributed among the Research Program Managers**

Beginning of March

Triage

March

- An **initial screening** (i.e. **Triage**) of accepted Applications is necessary to optimize the peer review process

- **All Applications** are subject to the **triage screening, irrespective of their past history** (e.g. Revised Applications, Renewals)

- Each Application is assigned to **3 members of the Scientific Committee**, who **provide a triage score**. A threshold is set and exclusion/inclusion criteria based on the scores are applied to determine the outcome of the triage step.

- Triaged Applicants are notified before the end of the peer review process

Full Review

- Triage-approved Applications are re-distributed among members of the Scientific Committee (continuity with the Triage assignments is preserved where possible)

  Beginning of April

- Research Program Managers also assign two **External Reviewers** to each project

  April - May

- Written comments by External Reviewers are directly forwarded to the relevant Scientific Committee Reviewers

  By beginning-mid of June

- The Scientific Committee Reviewers provides scores and written comments

  By mid-end of June

- Based on the mean scientific scores provided by the Scientific Committee, the Telethon Scientific Office selects top-ranking projects to be discussed during the plenary review meeting

  End of June

The Plenary Review Session

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1-2 July 2019

- **Chairman & Vice-Chairman**: conduct, moderate/steer
- **The 3 assigned Reviewers**: present and discuss the project
- **All Committee Members**:
  - participate in the discussion
  - score all discussed Applications (consensus vs. open statement of different positions is recorded)
- **Chief Scientific Officer** and **Research Program Managers**:
  - safeguard the coherence of the whole process
  - prepare the final ranking based on the overall scores
  - set the funding threshold (based on funds availability)

The ‘selection’ process at a glance

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Phase		Responsibility	Average 2013-2015
1	Call for application and examinations of projects	Telethon Research Program Managers	100%
2	Evaluation of the projects	*Triage*: 3 members of the Scientific Committee	59%
		Full Review: 3 members of the Scientific Committee + 2 external reviewers	
3	Plenary review meeting	All 30+ members of the Scientific Committee	30%
4	Approval of funding	Telethon Board of Directors	14%

Feedback to the Applicants the Review Report

Beginning of August

- **Prepared by the Research Program Managers**

- **Provides**:
  - a clear outline of the whole selection process
  - a coherent explanation of the outcome for the Applicant's project
  - integral anonymous written comments by Reviewers (both Committee Members and External Reviewers)

- **Aims:**
  - preserving transparency
  - providing helpful indications for re-submission

The Evaluation - Criteria and scores

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Triage evaluation

- 3 members of the Scientific Committee / Application
- Evaluation of the Core project - ‘Scientific merit’
- Scores (1.0 – 5.0), supported by brief written justification

	Project Evaluation	Recommendation
	Outstanding: no concerns	Suggested for full review
*	Good to Excellent: some concerns	Could undergo full review
	Poor to average: major problems	Not suggested for full review

* Triage threshold

Full Review evaluation - criteria

Reviewers of the Scientific Committee are asked to separately evaluate and score the following two aspects of each Application:

Scientfic Merit

Relative weight: 90%

Question: Is the proposed research scientifically excellent?

Evaluation parameters

- Significance
- Originality of science
- Appropriateness of design and methods
- Preliminary results
- Feasibility/safety
- Link to the disease

Other evaluation criteria:

- Comments on Applicant
- Comments on Budget Allocation
- Evaluation of the Previous Grant's Scientific Report - for former grantees only

Impact on Patients

Relative weight: 10%

Questions:

- What is the potential of the proposed project to make progress towards therapy or to provide any other impact on patients' clinical management and/or quality of life?
- How close in time is such a development envisaged?

Full Review evaluation - Scoring range

Scientific Merit
90%

Impact on Patients
10%

OVERALL SCORE	VALUE	DESCRIPTION	RECOMMENDATION
4.6 - 5.0	Outstanding	No concerns	Highest priority for funding
4.0 - 4.5	Excellent	No substantial issues need discussion	Funding is recommended
3.0 - 3.9	Good	Only one or a few addressable points	Funding is deemed appropriate, if funds are available
2.0 - 2.9	Average	Several concerns in one or more Aims	Not fundable
1.0 - 1.9	Poor	Major concerns in one or more Aims	Not fundable

* Funding threshold

The 2019 Telethon Call for Research Proposals

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Projects' features and Applicants

One or Two center-projects only **'Center'**= Laboratory, working group, PI

Roles: Lead Applicant + Partner

Applicants can apply to the present Call for Applications with **one research project only**, **irrespectively of the role** (Lead Applicant or Partner).

Duration: 1-3 years

Budget: For single-center Applications a maximum of **100,000 €/year** is allowed.

For two-center Applications a total budget of **160,000 €/year** is allowed; the Coordinator may ask for a maximum of 100,000 €/year.

Revised projects

A maximum of two revisions is allowed

Young applicants

Scientific independence needs to be assessed
(Note: if the Applicant is not the *Chief of the Laboratory*, he/she had to provide an Independence statement in the dedicated section)

Dual Appointments Any external appointment at a foreign Institution must be clearly indicated in the Host Institution section and in the related "Host Institution Agreement" document

Application form

The Full Application comprises the Core Project and the Supplementary Contents.

Only the Core Project is made available to Reviewrs for the Triage phase.

Core Project:

- General information
- Overview (Abstract and Role and contribution of participants)
- Cover Letter (for Revised Application only)
- Preliminary Results
- Scientific Approach (Central Hypothesis, Background and Rationale; Overall Objectives, Specific Aims)

[NOTE: from within this section, the Detailed Experimental Plans and the Figures will be made available to Reviewers only for the Full review phase, not in the Triage.]

- Cited Literature

Supplementary Contents:

- Previous Achievements (for former Grantees – New and Renewal Applications only)
- Feasibility, timing, clinical protocols
- Next Generation Sequencing and High Performance Computing (NGS and HPC)
- Administrative details, for Lead Applicant and Partner
  - Personal data and CV
  - Collaborations
  - Budget and Personnel
  - Other Financial Support
  - Host Institution
- Reviewers
- Notes

Scientific content (1)

- **Relevance to Telethon**: state how the goals of your project fit with Telethon's Mission
- Focus on a single or a group of **diseases of proven genetic origin**
- Identify the chosen Disease(s) **(OMIM, ICD-10 code and Orpha Number)**
- **Impact on Patients**: address how your proposal will advance progress towards therapeutic development, or will have any other potential impact on patients

Telethon DOES NOT fund studies on:

- **Cancer**
- **Multiple sclerosis**
- **Acquired immunodeficiency**
- **Amyotrophic Lateral Sclerosis (ALS)**
- **Multifactorial diseases (identification of genetic risk factors e.g. SNPs or other predisposing variants)**

Scientific Content (2)

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Background, Rationale & Overall Objectives

- Clearly and concisely **introduce the genetic disease(s)** involved in your proposal (Relevance & Impact on patients)
- Put the attention on **what is still missing** in the comprehension of the pathogenetic mechanism, identification of the disease, management, and therapy of the disease
- Stay on **one single story**, avoid to develop more stories because they are not conclusive
- Your **hypothesis** should be **provable** and **aims doable** with the **resources** you are requesting
- In the **rationale** put all the steps necessary to understand **what you want to achieve**
- **Do not propose too much**

Most common reasons cited by Reviewers for an Application's failure

- **Problem not important** enough
- **Not significant** to health-related research
- **Lack of original ideas**
- Study **not likely to produce useful information**
- Problem more **complex** than investigator appears to realize
- Issue is scientifically premature
- **Fishing expedition** lacking solid scientific basis (i.e. no basic scientific question being addressed)
- **Proposal driven by technology** (i.e. a method in search of a problem)
- **Rationale** for experiments **not provided** (why important / how relevant to the hypothesis)
- **Alternative hypotheses not considered**

Scientific Content (3)

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Preliminary data

- You need **solid preliminary results**
- Your results should **sustain key points** in your grant proposal **suggesting** that **you may obtain results in all of your Aims**
- If you are starting from zero, **ask for a pilot grant for one year**. **Not having preliminary data** is, in general, considered **highly risky**
- If your **proposal** is **highly innovative**, you'll need to **make a very strong case** for why you are challenging the existing paradigm and have data to support your innovative approach

Most common reasons cited by Reviewers for an Application's failure

- Studies based on a **shaky hypothesis or data**
- **Investigator too inexperienced** with the proposed techniques
- Proposal **lacking enough preliminary data** or **preliminary data do not support project's feasibility**
- **Not clear which data were obtained by the investigator** and which reported by others

Scientific Content (4)

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Research plan

- Begin each paragraph with a great lead sentence. Then elaborate on that
- Follow the **same order** presented in the background/rationale and preliminary results (makes the review easier), but don't be redundant with the content
- Define **one single story**, go in details in each aim in order to achieve definitive result and answer to your questions
- Explain always the **rationale of each sub-aim** (experiment), what you expect to find, and what is your **alternative approach** if you fail to obtain a result
- Whenever possible suggest experiments that give rise to **quantitative results**, define the **statistic analysis** and **power for significance**
- Avoid/limit experiments too dependent on success of an initial proposed experiment

Most common reasons cited by Reviewers for an Application's failure

- **Methods unsuited** to the objective
- Relevant **controls not included** in the study design
- Proposed **model system not appropriate** to address the proposed questions
- **Over-ambitious** research plan with an unrealistically large amount of work
- **Direction or sense of priority not clearly defined**, i.e., the experiments do not follow from one another, and lack a clear starting or finishing point
- Experiments too dependent on success of an initial proposed experiment. **Lack of alternative methods** in case the primary approach does not work out
- **Too little detail** in the research plan to convince reviewers the investigator knows what he or she is doing (no recognition of potential problems and pitfalls)
- **Insufficient consideration of statistical needs**

Scientific content (5)

If Next Generation Sequencing experiments are envisaged, the Applicant is asked to provide the following information:

- **Organism name** (e.g. Mus musculus, Homo sapiens…)
- **Estimated number of samples to be sequenced and/or the number of sequencing runs foreseen in the project**
- **Type of experiment** (i.e. type of sequencing approach, e.g. WES, WGS, Epigenome…)
- **NGS platform to be used** (e.g. Illumina, Ion Torrent…)

High Performance Computing [HPC] bioinformatics resources at Cineca:

Telethon's partnership with Cineca offers the Applicant the possibility to exploit the HPC tools (as listed on the Cineca website: *http://www.hpc.cineca.it/services*) for the analysis of NGS data or to perform computer simulations of biological systems.

If the Applicant intends to take advantages of such services, he/she is asked to provide information as described in the Guidelines of the 2019 Call.

Personal data & CV

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➢ Knowledge and skills

The Reviewers use this part to see whether the PI is a leader in the field and has experience with the proposed techniques

- Important to have **good records in the topic**, or at least **in the methods** you propose to use
- **List any experience in foreign laboratories**

➢ Independence

The CV should allow to determine also the independence of young investigators

- **Papers** as **First/Corresponding** author
- Other "recognized additional products, such as datasets, as important research outputs" (as indicated by the Dora Declaration http://www.ascb.org/dora/)
- **Other/previous grants**
- How large is your group?
- Will you have the **authorship of the proposed study**?

State how this work will differentiate your own research from that of your former boss

Provide your **Personal author ID** (ORCID, ResearcherID, Scopus author ID)

Administrative forms

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- **Personnel**. **Be consistent** between the amount of work proposed and the number of persons (Full Time Equivalent). Ask for a salary appropriate to cover a fellowship ***(ask the Telethon grant office for support)***

- **Collaborations**. Indicate if you need to set up collaborations for key experiments in your grant proposal (identify people with recognized record in the field; request letter of collaboration detailing the topic of the interaction)

- **Budget**. Make a **realistic**, **consistent** budget, especially for consumables; indicate the **role and name of the personnel for whom salary is requested** (consistency with 'Personnel')

- **Other Financial Support**. Indicate if you are holder of **other grants** and those you have submitted; **if related to the proposal, report possible areas of overlap or synergy** with the current request

Administrative section - Reviewers

Suggested Reviewers

- Must **not currently work in Italian Institutions**
- **Avoid** Reviewers with **Conflicts of Interest**
- Choose **highly qualified Scientists**, with expertise in the subject of your proposal

Excluded Reviewers

- You can also **indicate people you deem not appropriate to assess your Application** - a motivation is required!

General considerations and suggestions

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General considerations

- **Make life easier to Reviewers** - Peer review puts a big burden on Reviewers, so they truly appreciate an application that is **neat, well organized, and easy to read**

- **Give the big picture** (think to your audience) and don't drown reviewers in too many details

- **State well the Rationale for each aim**: why do these experiments need to be done?

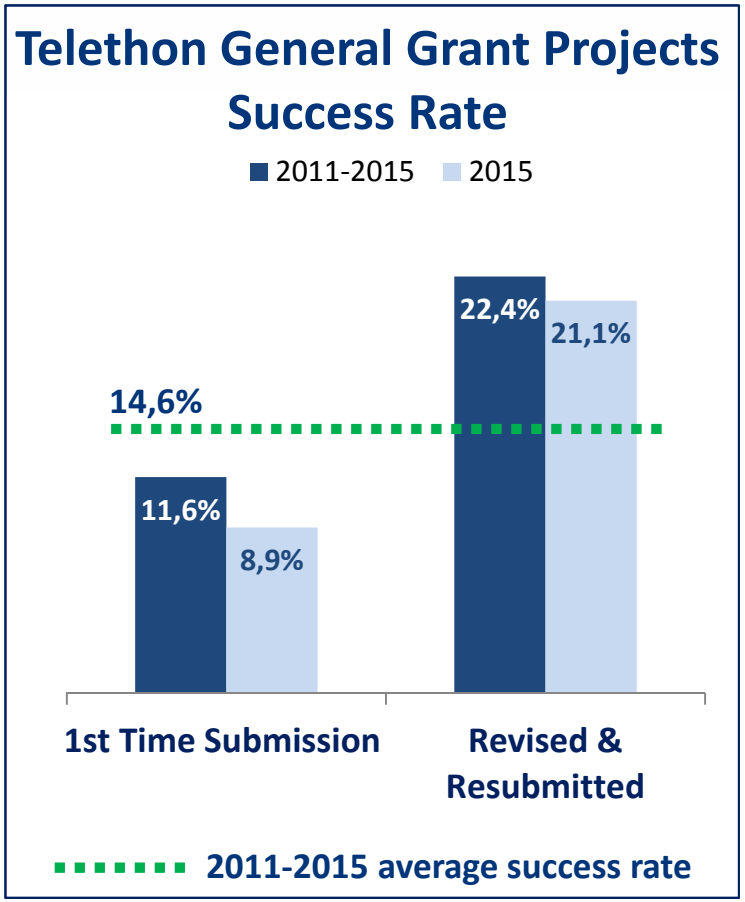
- **All 30+ Reviewers of the review panel** - not only those who evaluated the Application - **will likely read Abstract, Significance, Overall Objectives** and will vote. Keep these parts simple and **don't be too technical**. They all need to grasp your ideas and "fall in love" with your project!

If you are not funded …

- **Don’t get discouraged: You are not the only one!**

- **Listen to your Reviewers**
  - **Read the Telethon Review Report carefully.** It is meant to provide you with suggestions to improve your grant application. Are the issues identified fixable?
  - If Reviewers did not understand your work, perhaps **you did not make it clear and proved it to be feasible**
  - You should **learn from comments** to re-write a more appealing grant the next year
  - Try to **understand and solve all the pitfalls**

- **Seek advice**
  - **Trust your peers and ask for suggestions**
  - Maybe you need **collaborators** with specific expertise, especially if your application is rejected more than one time



The Application in Tetra – *live*

Aldo Borrè

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Links and Contacts

- **CALL** for Applications 2019 & **GUIDELINES** for preparing and submitting the Application online

  http://www.telethon.it/la-ricerca/per-i-ricercatori/bandi

- **The Application** is on **TETRA** - Telethon Projects Managements system portal https://projects.telethon.it

- **CONTACTS** for support and/or inquiries:
  - soffice@telethon.it
  - Send a message from your account in Tetra

Thank you for your attention!

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