S.O.S ONCOLOGY

Giovedì, 24 ottobre 2024

Sala Biagi, Palazzo Lombardia

Dr. Federica Albanese, PhD
Scientific Officer

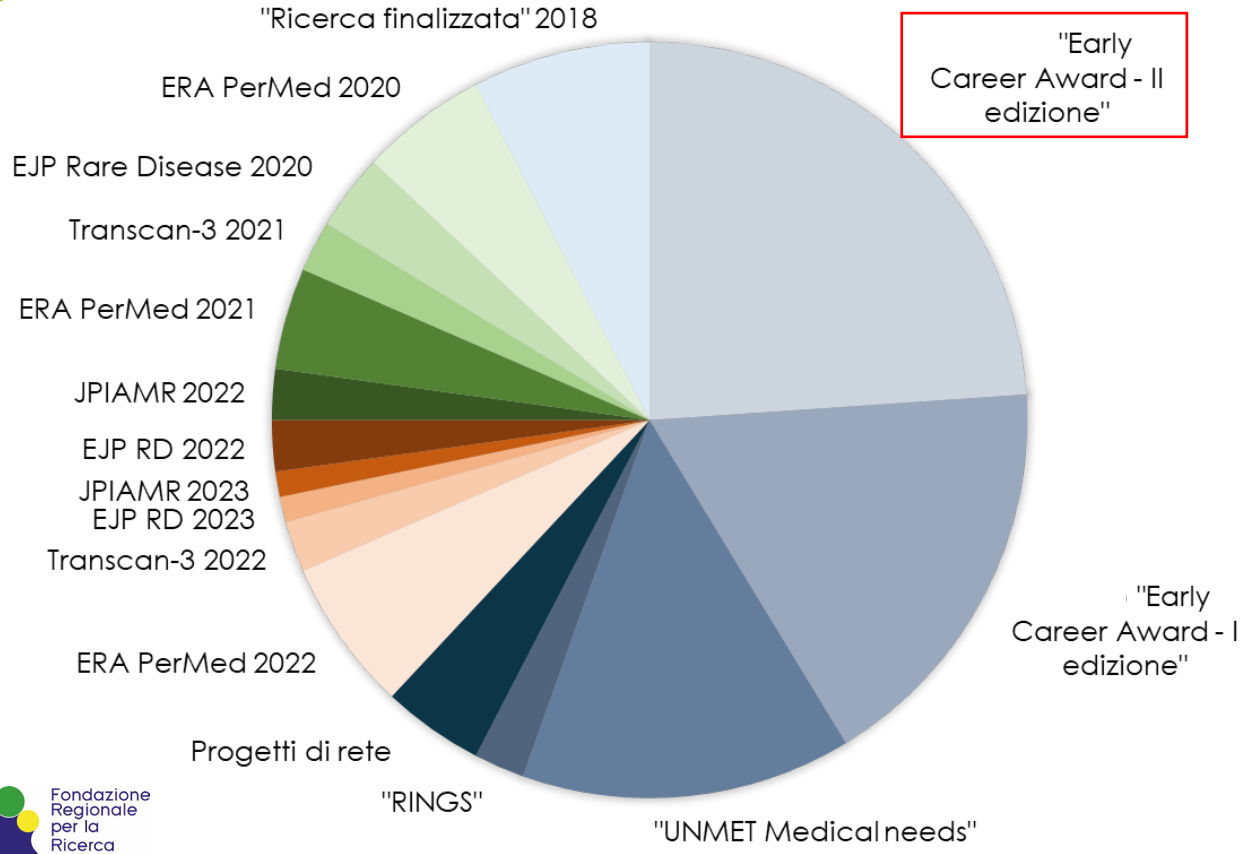
In collaborazione con

Fondazione IRCCS Istituto Nazionale dei Tumori

Sistema Socio Sanitario
Regione Lombardia

Fondazione Regionale per la Ricerca Biomedica

Regional Foundation for Biomedical Research



FRRB is a private law institution established by Lombardy Region in October 2011.

FRRB funds research project proposals at both regional and European level.

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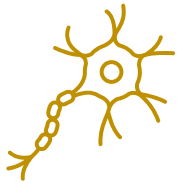
Early Career Award- II edition

Definition of «young researcher» :

- no more than 8 years of experience after PhD degree or medical residency;
- Maximum 40 years old;

Cardiology **Neurology** **Rare diseases** **Oncology**

74

Deadline for project submission

(29th september, 2023)

74

Internal administrative evaluation

(November 2023)

68

Peer-review remote evaluation
72 reviewers
(march to may 2024)

30

Consensus meeting
11 reviewers
(June 20-21, 2024)

22

Final ranking list published
(June 28th, 2024)

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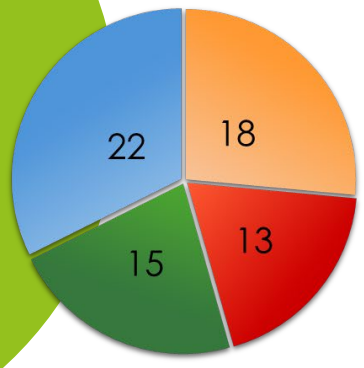
STEP 1



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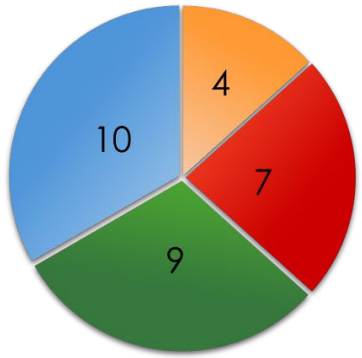
STEP 2



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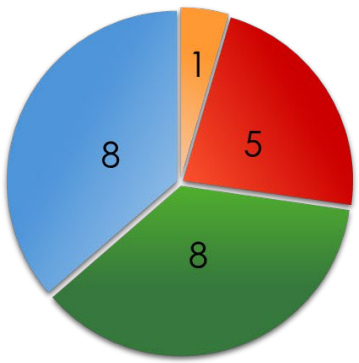
FINAL RANKING LIST



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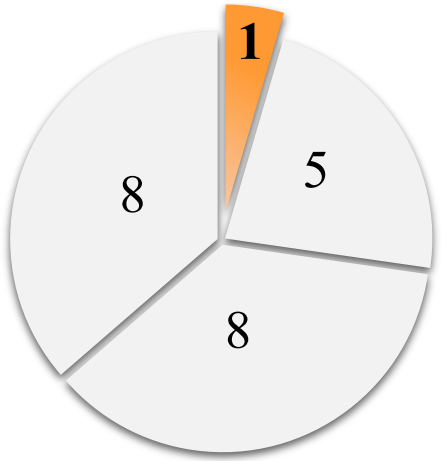
Neurology
Cardiology
Rare diseases
Oncology



Neurology
Cardiology
Rare diseases
Oncology

Success rate thematic area:

- Neurology: 36,4 % (8/22 projects funded)
- Cardiology: 38,5 % (5/13 projects funded)
- Rare disease: 53,3 % (8/15 projects funded)
- **Oncology: 5,6 % (1/18 project funded)**

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Consensus Meeting

Speakers

Prof. Pedro Castelo-Branco, PhD

President of the Algarve Clinical Academic Centre
Portugal

UAlg FMCB
UNIVERSIDADE DO ALGARVE
FACULDADE DE MEDICINA E CIÊNCIAS BIOMÉDICAS

Prof. Triantafyllos (Lakis) Liloglou, PhD

Director of the CardioRespiratory Research Centre
Edge Hill University
UK

Edge Hill University
Medical School

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Writing a successful grant application

Lakis Liloglou & Pedro Castelo Branco

Fondazione Regionale per la Ricerca Biomedica

Regione Lombardia

Edge Hill University
Medical School

UAlg FMCB
UNIVERSIDADE DO ALGARVE
FACULDADE DE MEDICINA E CIÊNCIAS BIOMÉDICAS

Fondazione Regionale per la Ricerca Biomedica

WELCOME

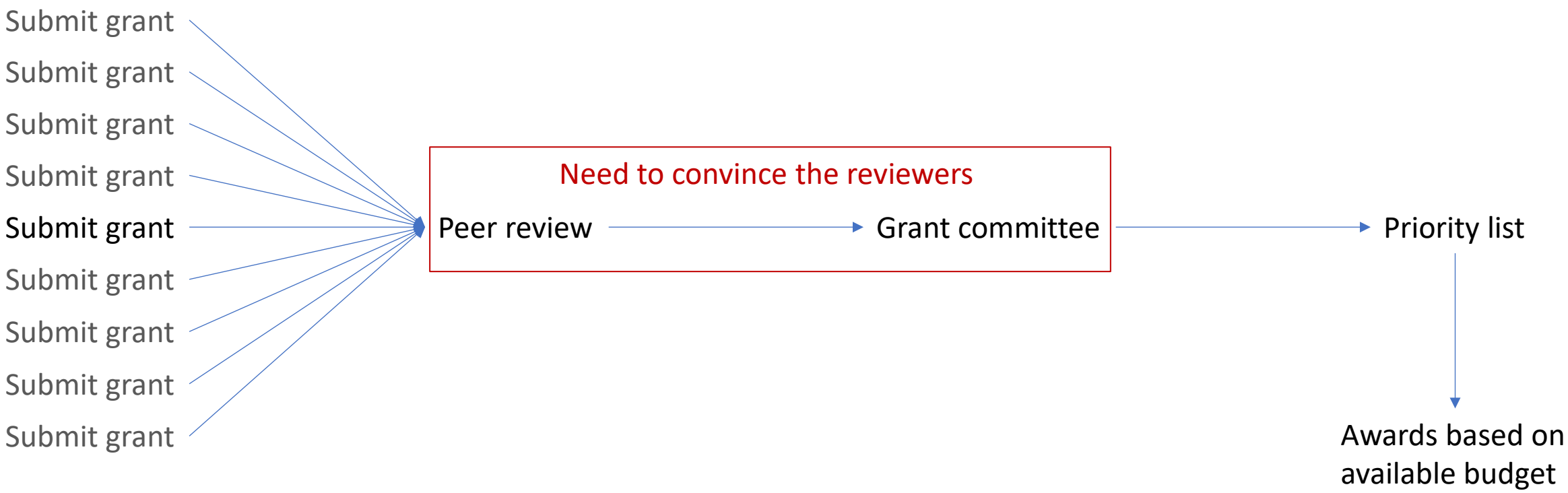
Who are we?

Fondazione Regionale per la Ricerca Biomedica

Today's aim

Assist you in writing grant applications with a higher chance of success

Grant application process



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Convince reviewers about what?

- This is research that is worth doing
- You have a solid research plan in mind
- The research team has the expertise
- The environment can support the project

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This is research that is worth doing

- You have a clear and precise research question / hypothesis
- The focus of research is a significant problem
- For translational research -> addressing a clinical problem
- The phrase is "clinical unmet need"
- There is a knowledge gap that your proposal will fill
- The research output has high chance to benefit healthcare

Translational research

Utilise

- **Patient populations (ex vivo)**
- **Animal models, xenografts etc (in vivo)**
- **Cell culture, organoids etc (in vitro)**
- **Combinations of above**

look for

- **Biomarkers of clinical outcomes**
- **Mechanistic studies**
- **Intervention effect on cells**
- **Genetic/epigenetic impact on intervention response**
- **Combinations of above**

You have a solid research plan in mind

- Study design
- Study size
- Bias reduction

Maximise **internal** and **external validity**

- Research planning and time management

Study design

Your study design can facilitate the Research Question /Hypothesis

Your starting point

Population
Intervention (or exposure)
Control(s) ← **Confounding factors**
Outcome(s) ← **Measurable** **Widely accepted**
(**T**)ime

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Study designs

Observational

Can produce associations ONLY

Descriptive

Hypothesis generating

Analytical

Hypothesis testing

Interventional / Experimental

Can indicate causation

Hypothesis testing

Aims, Objectives, Outcomes & Endpoints

Aim: what do I want to demonstrate

Objectives: How am I going to demonstrate it (break down to components)

Outcomes: The measured variables used to quantify the objective

Endpoints: The point along the outcome measure that defines a significant biological or clinical function (physiological or pathological)

Make these **clear** – potentially bullet points – **do not hide** them in rows of text.

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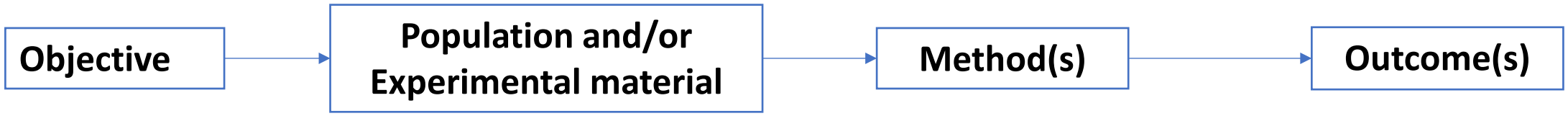
Design and define your “killer experiment” !

Organise research WPs (if applicable)



Sample size calculation

State-of-the-art

Controls

Ensure WP cohesiveness and low inter-dependency

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Study size & statistical power

How many subjects are enough?

Hypothesis testing: Type I / Type II errors

The **null hypothesis (H_0)** is that there is **no difference** between the entities (groups/treatments/etc) compared

The **alternative hypothesis (H_1)** is that **there is a difference** between the entities (groups/treatments/etc) compared

A type I error (alpha) occurs when we reject the null hypothesis incorrectly (i.e., there is no difference between the two groups but we conclude there is difference (false positive conclusion)

A type II error (beta) occurs when we accept the null hypothesis incorrectly (there is a difference between the two groups but we conclude that there is no difference (false negative conclusion).

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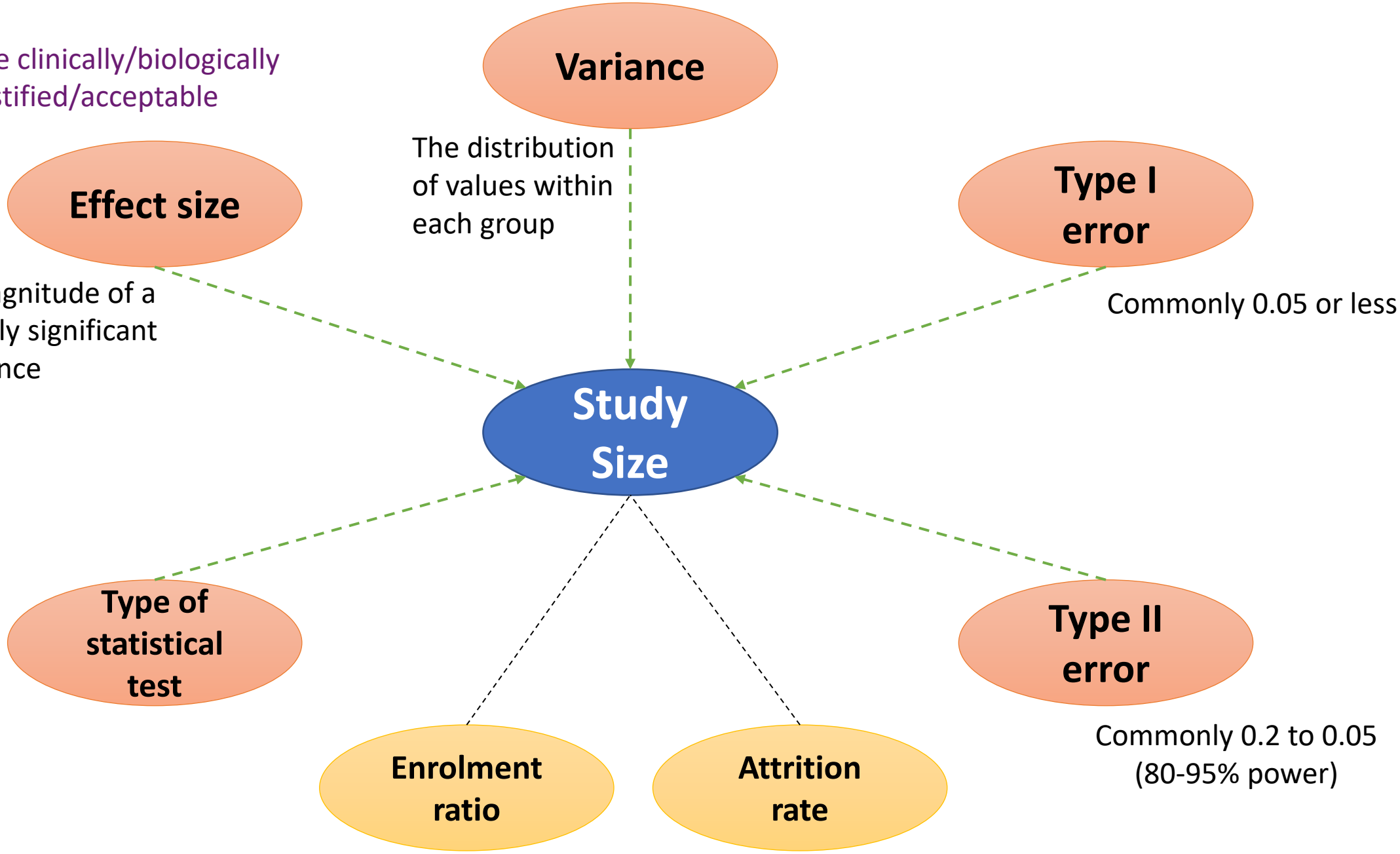
Statistical power

$$\text{Power} = 1-\beta$$

Minimum power acceptable: 0.8 or 80%

MUST be clinically/biologically Justified/acceptable



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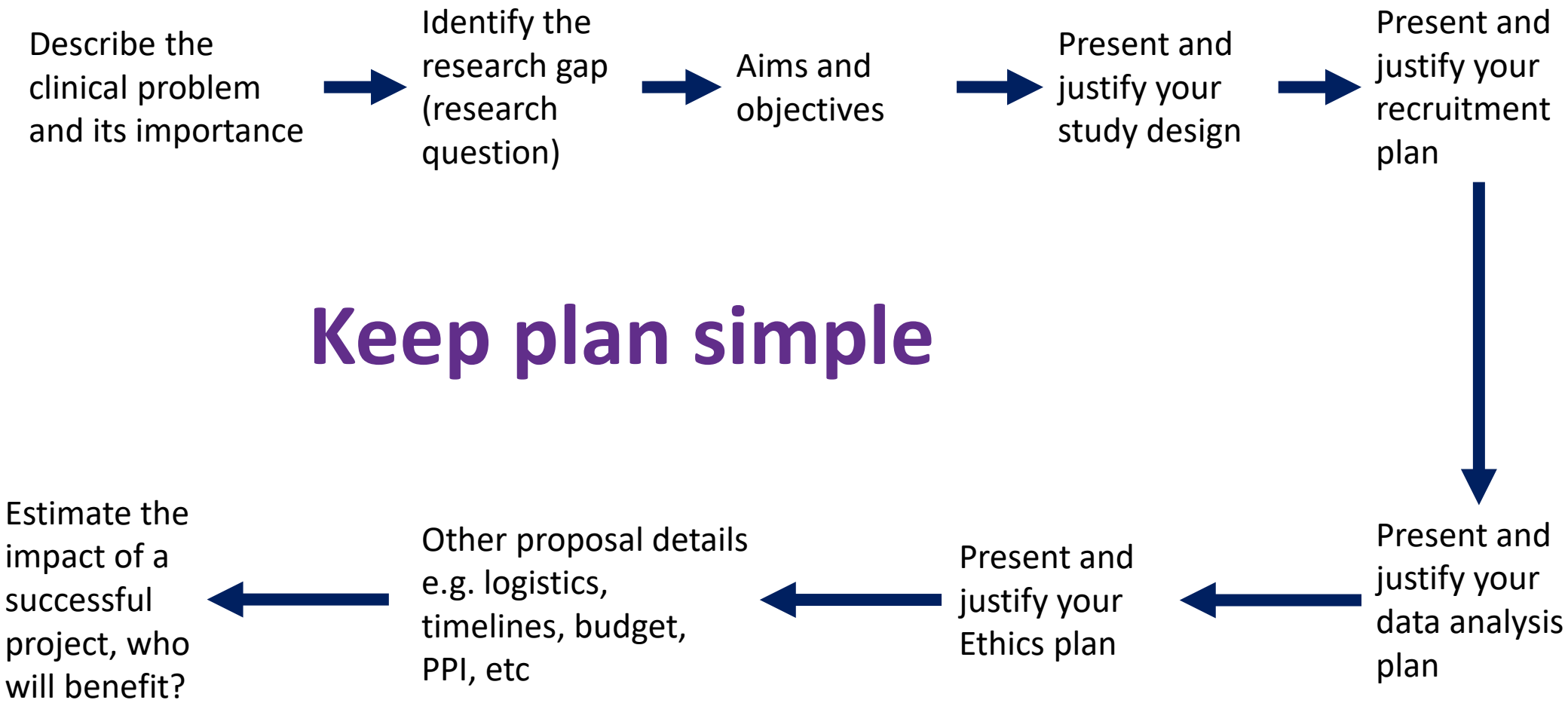
Have a statistician on board at the proposal design

Create a story line: Proposal



Keep plan simple

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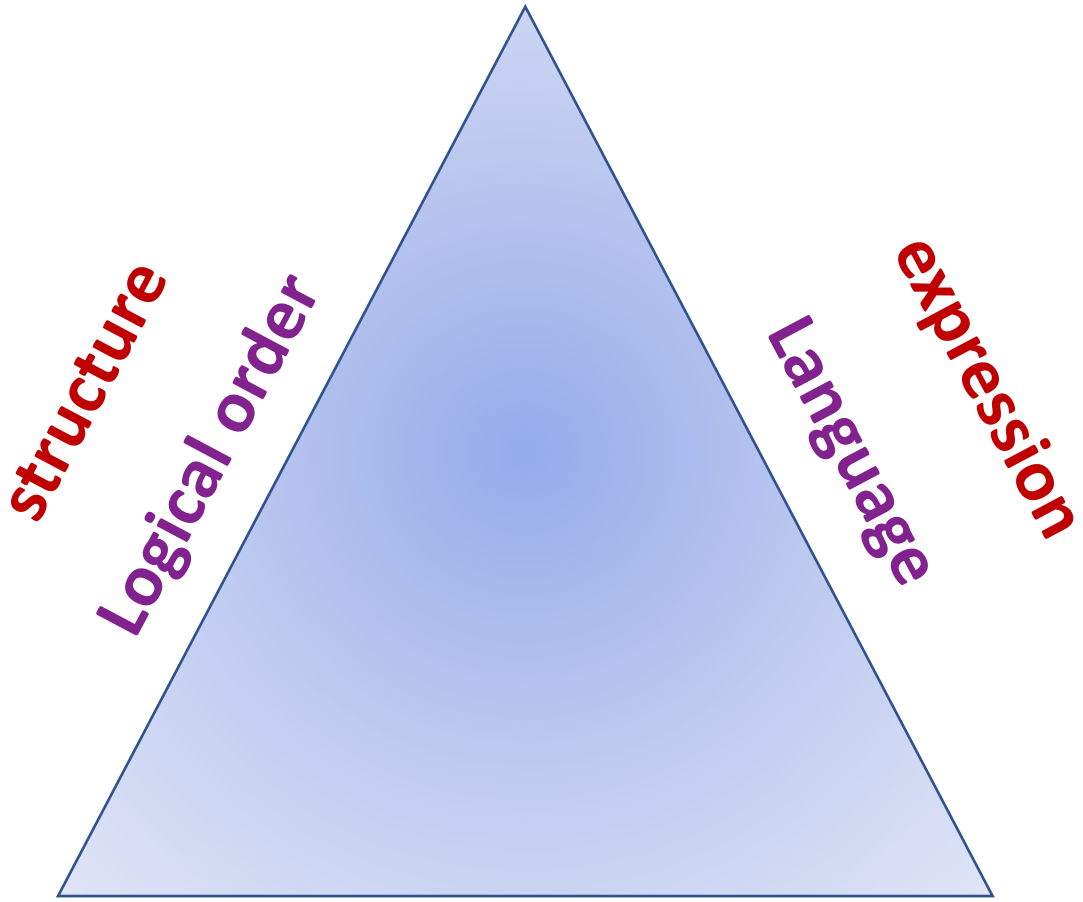
Scientific writing



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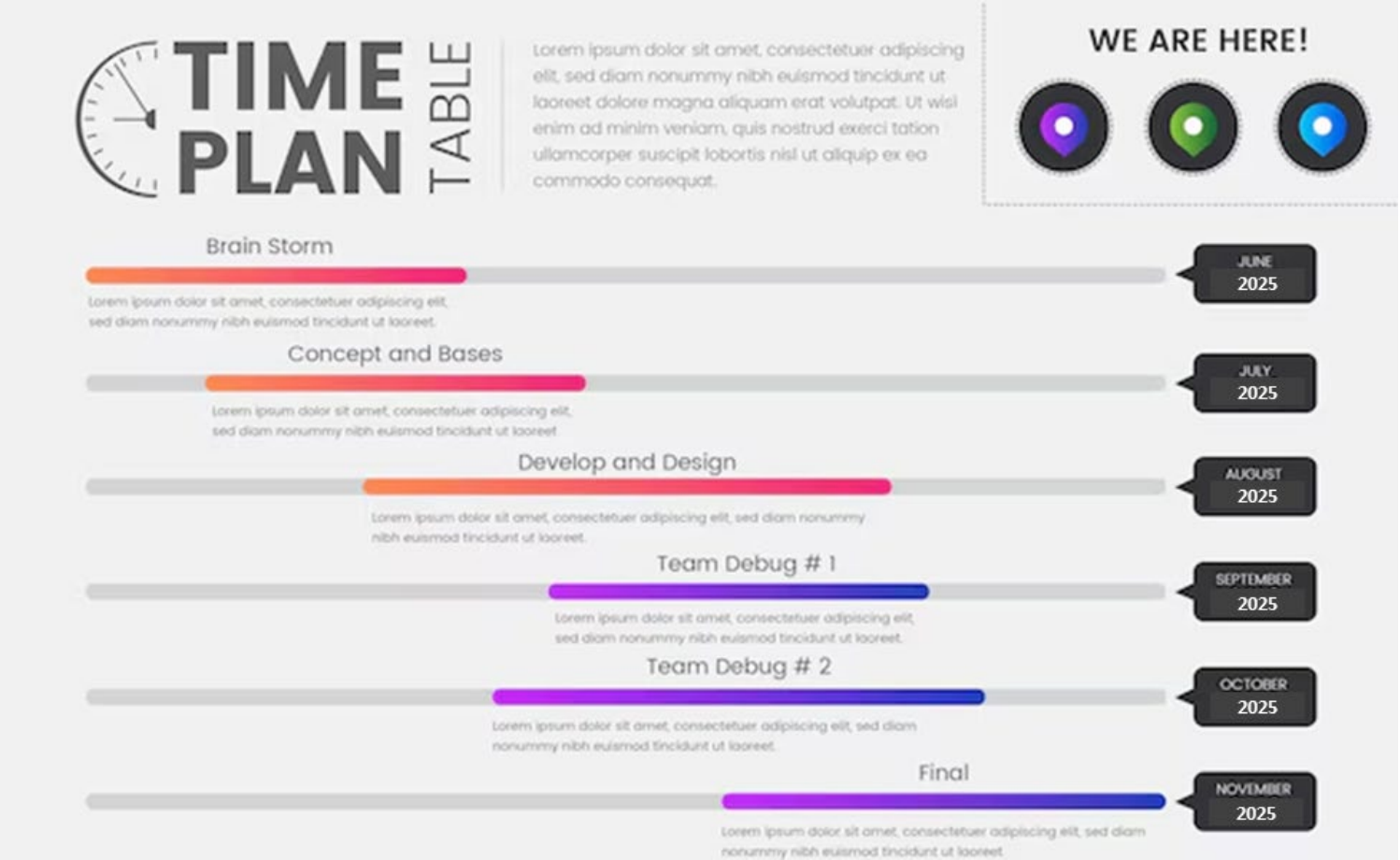
Have a realistic time plan to write it



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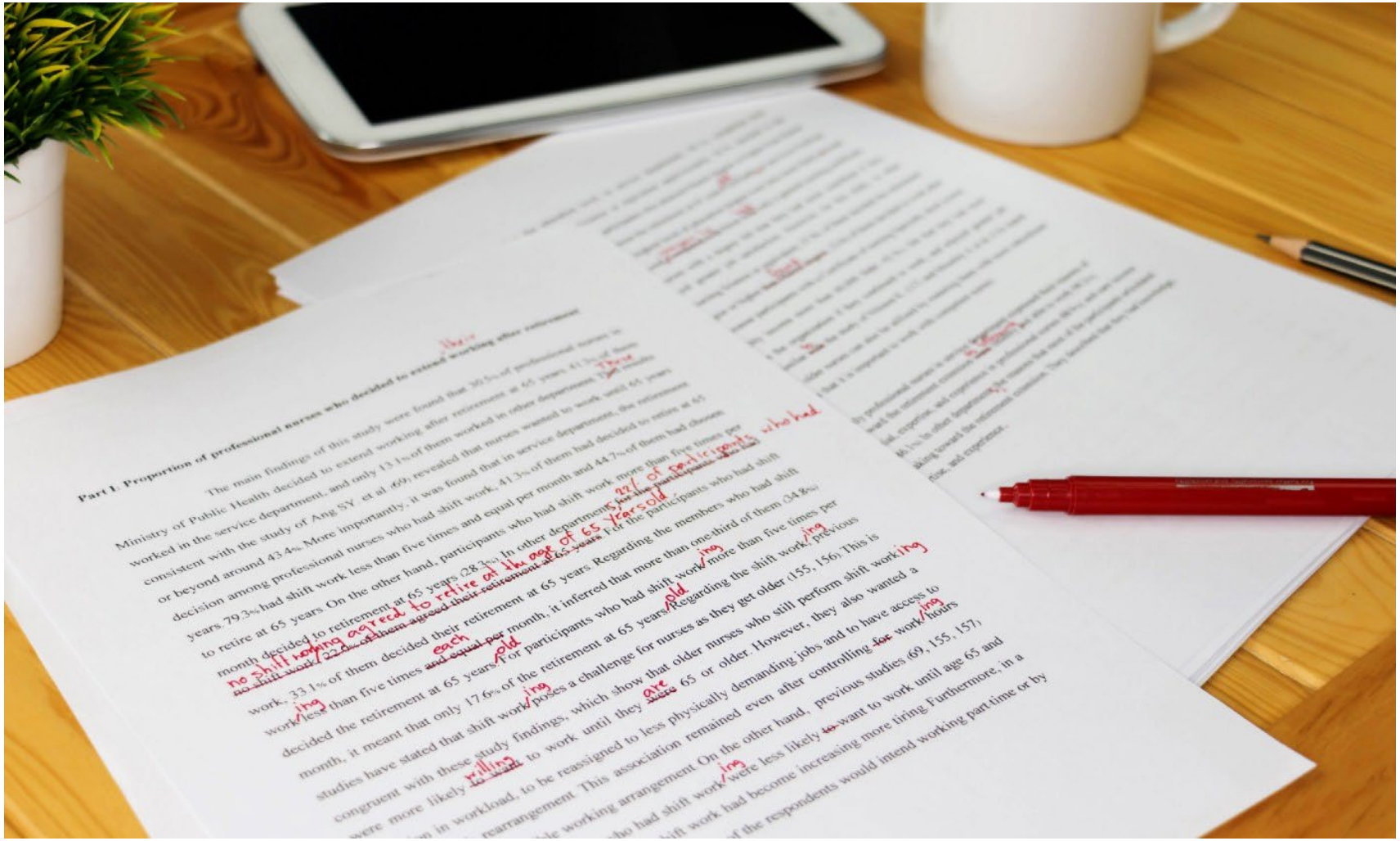
Be prepared for A FEW drafts



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Interact with your mentor(s)

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…and your peers

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So, you have an idea for research

What is the first thing to do?

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Search the existing literature

Basic elements of my Research Question/Hypothesis

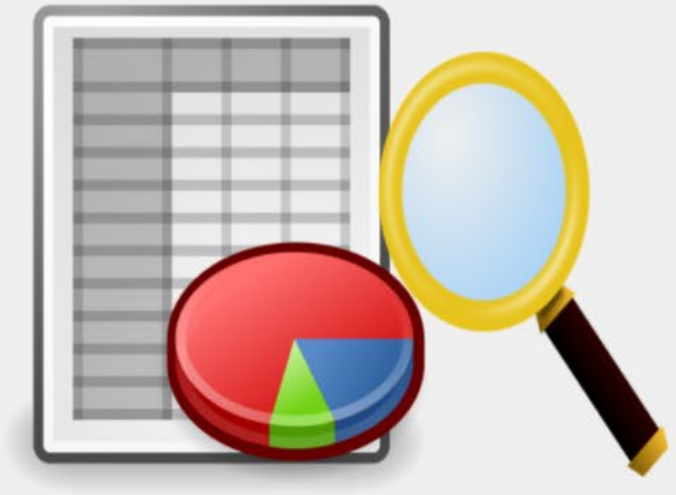
P Population (patients, animals, cell lines, POs, PDXs, etc)

I (E) Epidemiological or Molecular Factors (exposures, demographics etc)

C ontrol Intervention(s)

O Outcomes (functional, clinical, quality of life, etc)

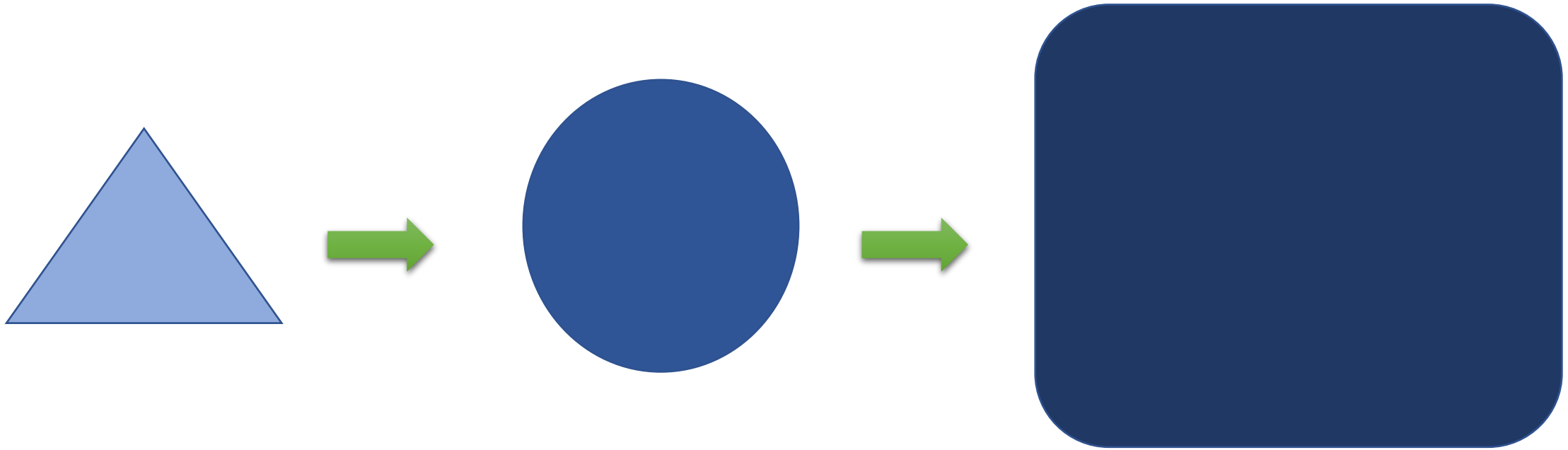
VS



Qualitative research

Quantitative research

Research Study levels



Feasibility study **Pilot study** **Main study**

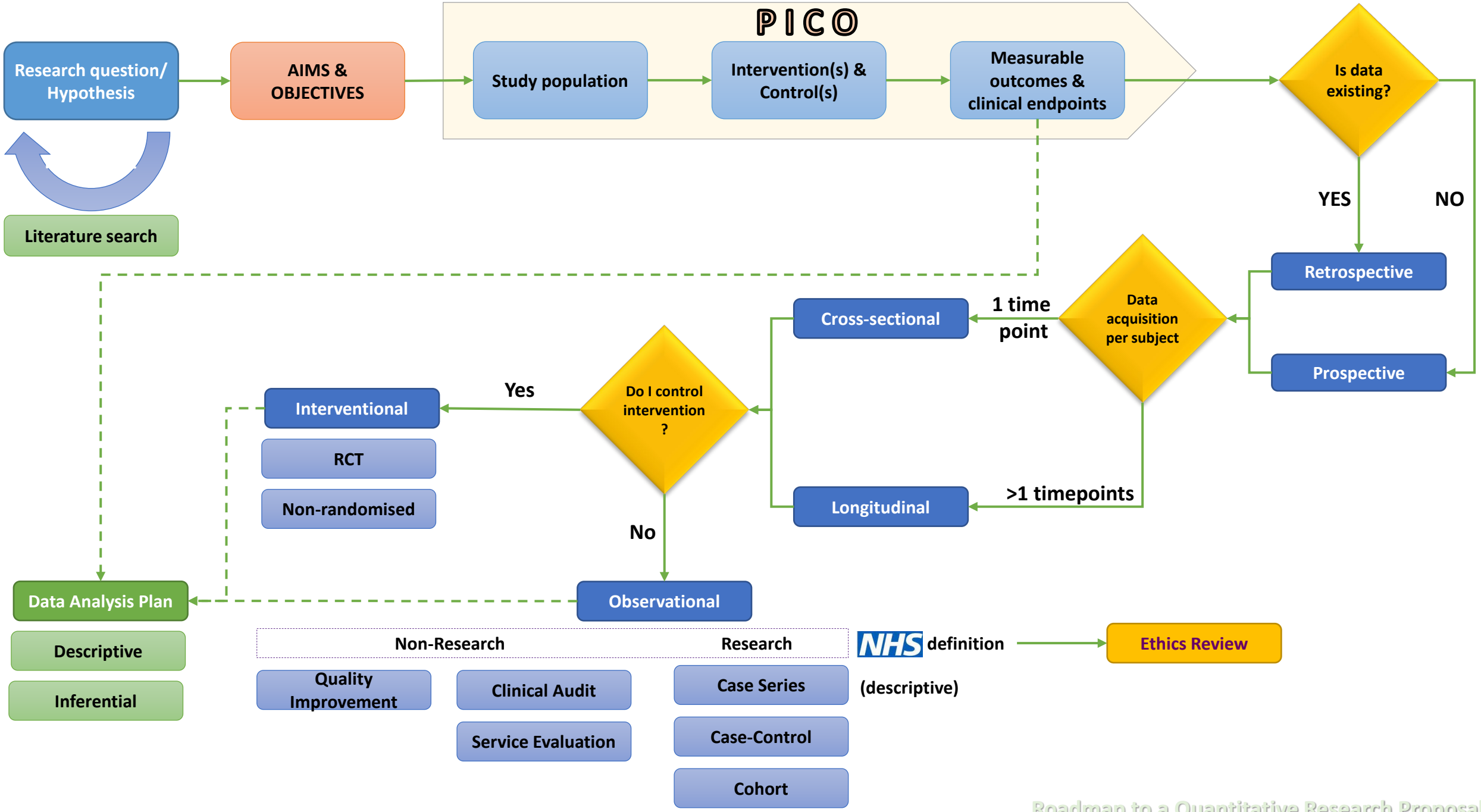
Proof-of-concept study

Study Design

- **Epidemiological Studies**
  - **Observational**
    - **Population-based**
      - **Descriptive**
        - Health surveys
      - **Analytical**
        - Ecological studies
    - **Individual-based**
      - **Descriptive**
        - Case studies
        - Case series
      - **Analytical**
        - Case control studies
        - Cohort studies
  - **Interventional / Experimental**
    - **Randomised**
      - **Randomised Controlled Trial (RCT)**
        - Phase I, II, III
        - Unblinded, Single/double/triple blinded
        - Crossover Adaptive
        - Cluster
    - **Non-randomised**
      - **Quasi-experimental**
      - **Field trial**
      - **Community trial**

Cross-sectional vs Longitudinal

Retrospective vs Prospective


PICO
Research question/ Hypothesis
AIMS & OBJECTIVES
Study population
Intervention(s) & Control(s)
Measurable outcomes & clinical endpoints
Is data existing?
YES
NO
Literature search
Retrospective
Prospective
Data acquisition per subject
1 time point
Cross-sectional
Longitudinal
>1 timepoints
Do I control intervention ?
Yes
No
Interventional
RCT
Non-randomised
Observational
Data Analysis Plan
Descriptive
Inferential
Non-Research
Research
NHS definition
Ethics Review
Quality Improvement
Clinical Audit
Service Evaluation
Case Series
(descriptive)
Case-Control
Cohort
Roadmap to a Quantitative Research Proposal

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Work on examples

Please share research questions to discuss

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Thank you

Questions

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Project evaluation

REFLEXION !!!!

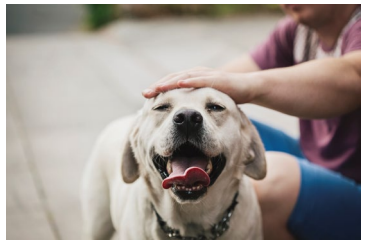
Category: PRINCIPAL INVESTIGATOR (PI) – TRACK RECORD	Maximum score: **20**
Ability of the PI in conducting research projects in a creative and independent manner, as demonstrated by previous experiences	0-10
Scientific skills of the PI necessary to successfully implement the proposed project	0-10
Category: EXCELLENCE OF THE PROJECT PROPOSAL	Maximum score: **20**
Clarity and relevance of the proposed objectives	0-10
Soundness of the hypothesis and of the preliminary data, credibility of the proposed methodology, ethical aspects included	0-10
Category: IMPACT OF THE PROJECT PROPOSAL	Maximum score: **20**
Possibility of the project to contribute to the advancement of scientific knowledge, beyond the state of the art, in the related research area	0-10
Quality of the proposal in terms of: – Dissemination to and sharing of results with the scientific community	0-10
– Dissemination of results to the lay public – Description of Responsible Research and Innovation principles (RRI)	
Category: QUALITY AND EFFICIENCY OF THE PROJECT PROPOSAL	Maximum score: **20**
Quality and efficiency of the workplan, adequacy of the budget and of the resources allocated to each work package in line with the project objectives	0-10
Appropriateness of the technical infrastructures and of the management of the project	0-10

Project evaluation

Category: PRINCIPAL INVESTIGATOR (PI) – TRACK RECORD	Maximum score: **20**
Ability of the PI in conducting research projects in a creative and independent manner, as demonstrated by previous experiences	0-10
Scientific skills of the PI necessary to successfully implement the proposed project	0-10

- Funded projects; Masters and PhD Students projects
- Publications (1st, last and/or corresponding authorship)

THIS IS ABOUT WHO YOU ARE SO PET YOUR CV !!!!



Project evaluation

Category: EXCELLENCE OF THE PROJECT PROPOSAL	Maximum score: **20**
Clarity and relevance of the proposed objectives	0-10
Soundness of the hypothesis and of the preliminary data, credibility of the proposed methodology, ethical aspects included	0-10

- If needed number your objectives (clarity). Relevance comes from your line of study.

- Make the hypothesis very very clear.
  - Ex…based on the presented case **WE HYPOTHESIZE** that…
  - Priliminary data supporting the project, show it, do not only list published papers…
  - Link the methods with the technologies to be used.
  - Please do not forget ethics. If ethical considerations are not an issue, state it!!!

Project evaluation

Category: IMPACT OF THE PROJECT PROPOSAL	Maximum score: **20**
Possibility of the project to contribute to the advancement of scientific knowledge, beyond the state of the art, in the related research area	0-10
Quality of the proposal in terms of: – Dissemination to and sharing of results with the scientific community – Dissemination of results to the lay public – Description of Responsible Research Innovation (RRI) principles	0-10

THIS HAS TO BE A 10!!!

- Advancement of the scientific Knowledge – it comes from your hypothesis and objectives that will lead to the expected impact.

Project evaluation

Category: QUALITY AND EFFICIENCY OF THE PROJECT PROPOSAL	Maximum score: **20**
Quality and efficiency of the workplan, adequacy of the budget and of the resources allocated to each work package in line with the project objectives	0-10
Appropriateness of the technical infrastructures and of the management of the project	0-10

THIS HAS TO BE A 10!!!

- Workplan: link the work packages with the people in the team
- Budget: link it with the work packages and objectives

- Add a work chart

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Common mistakes

Project title

Ex: The role of PTB binding to Shc and IRS-1 in a phosphotyrosine-dependent fashion to peptides that form a b turn.

WHAT IS WRONG?

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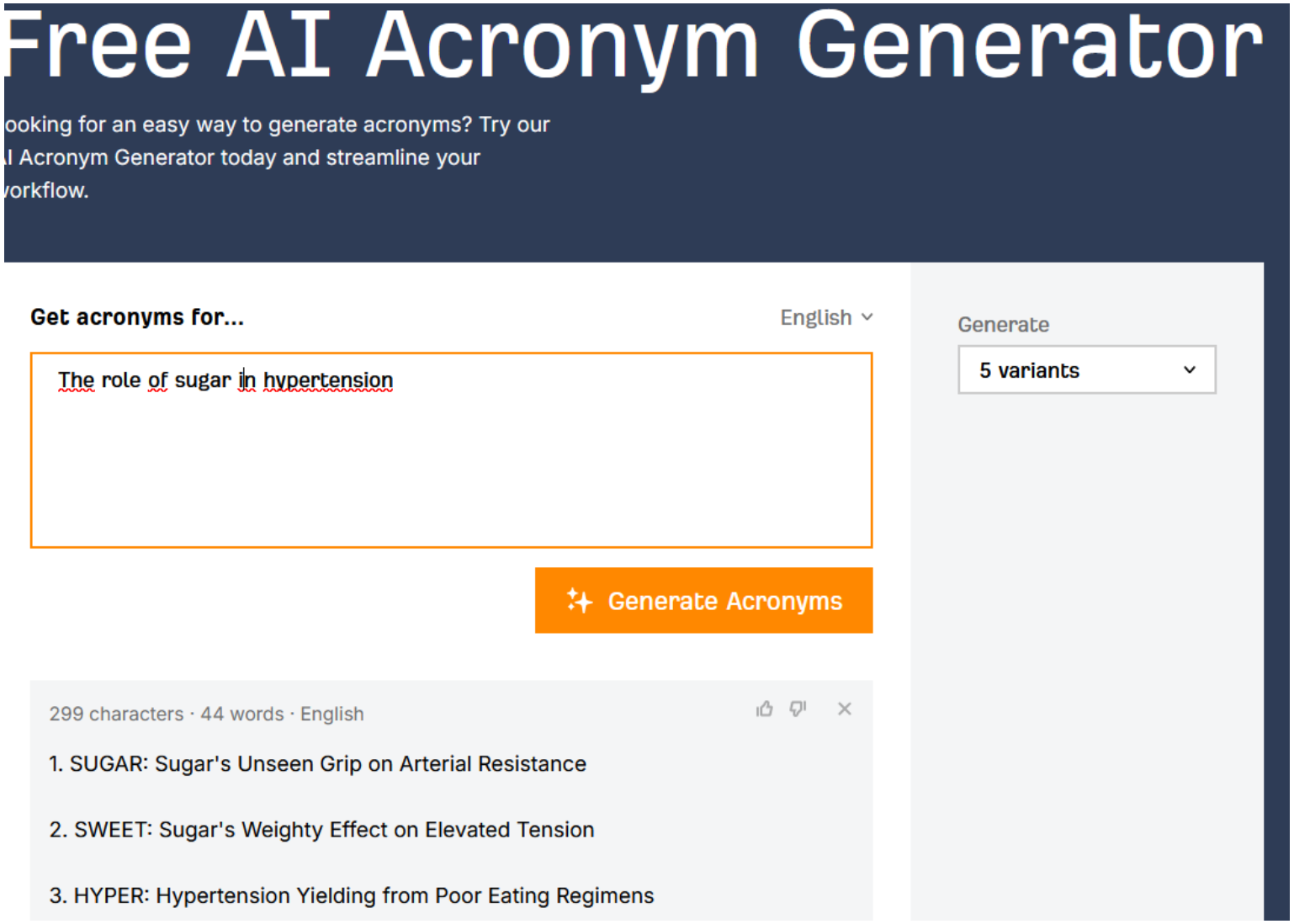
Common mistakes

Project acronym

Ex EPI-PTB-NUC

WHAT IS WRONG?



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Common mistakes

Total requested budget (MAXIMUM 1,000,000 EUROS)

Ex: 1,000,000 Euros

Ex: 999973 Euros

WHAT IS WRONG?

EX: 900,000 Euros for Human Resources is requested…

WHAT IS WRONG?

Your buggest should be balanced…

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Common mistakes

Preliminary data

- **Show only what is direclty relevant for the proposal.**
- **Published work that supports your project is ok to be mentioned in the text.**
- **There is a difference between preliminar data and previous data…**

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Common mistakes

Figures and tables

Very often figures and tables are shown with poor quality and overly crowded. Reason might be the conversion of files. Test this in advance!!!

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Common mistakes

- In agnostic approaches, have **no** independent **discovery (training)** and **validation (test)** groups

- For outcome prediction, not to calculate **PPV** and **NPV**, but stick with sensitivity and specificity

- Put all the weight in p-values and miss the **effect size**

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Common mistakes in data analysis

- Use means and parametric tests for continuous variables that do not fit normal distribution
- Use p-value in correlation tests (Pearson's / Spearman's) as an indication of significant correlation

Common mistakes

Research hypothesis and specific aims

Describe here how the proposal fits the scope of the call,

the personalized medicine dimension of the proposed work,

the rational,

specific objectives and the overall strategy of the proposed research,

highlighting the novelty and feasibility,

and the potential impact of the project results on health care.

Max 2.000 characters including spaces.

- **Often part of what is asked is not addressed.**

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Common mistakes

Experimental plan (work packages)

Report, for each work package (WP): (a) the WP number and title (**max. 5 WPs**),
(b) its objective(s),
(c) tasks, and related activities,
(d) methodology used,
(e) milestones1 (**max. 2 milestones for each WP**),
(f) expected results and deliverables2 (**max. 2 deliverables for each WP**),
and (g) a contingency plan to mitigate any pitfalls and caveats. After each WP describe feasibility and contingency

In case of clinical studies/trials a scheme of the study design must be provided (max. 1 page).
… for projects involving clinical trials, enrolment of patients and/or healthy subjects
and/or the collection of human material and/or data, approval(s) by the Competent Regulatory Authority.
are due before the project start. Therefore, the achievement of such approval(s) cannot be a milestone or a deliverable.
Note: A translational oncology project has to have some of these materials. Show the status of ETHICAL APPROVALS.

- **Often part of what is asked is not addressed.**

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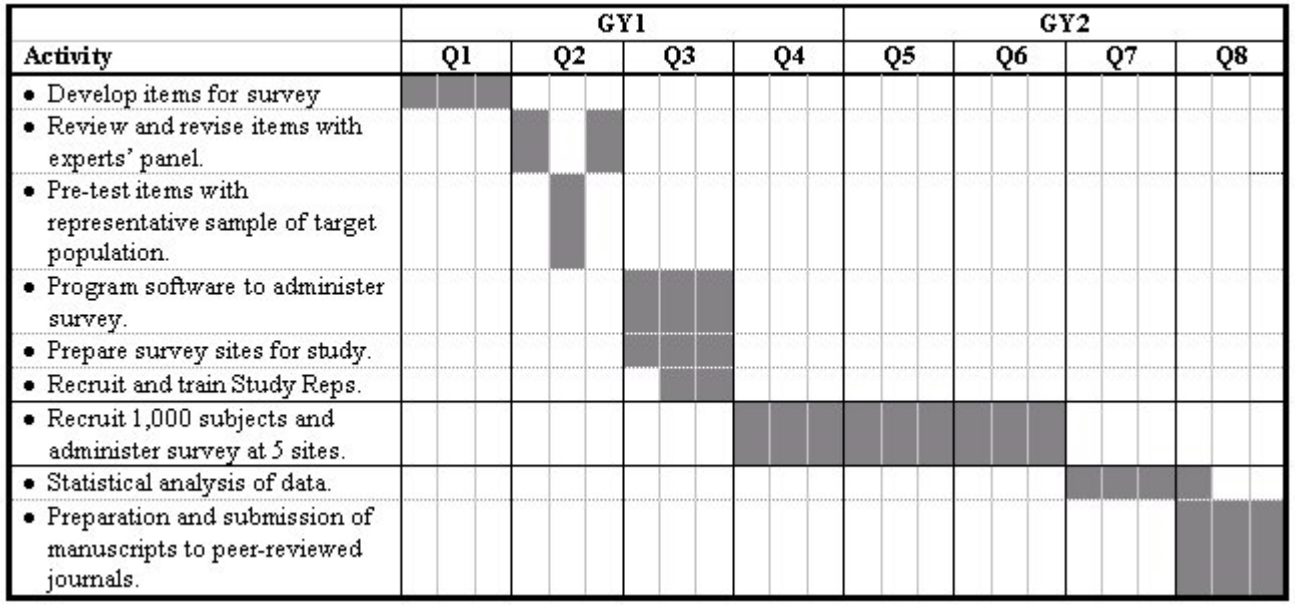
Common mistakes

Gantt chart

Insert here the Gantt chart. The Gantt must report the WPs as described in section X, their duration (in months), the milestones described in section Y and the deliverables described in section Z.



Activity	GY1 Q1	Q2	Q3	Q4	GY2 Q5	Q6	Q7	Q8
• Develop items for survey								
• Review and revise items with experts' panel.								
• Pre-test items with representative sample of target population.								
• Program software to administer survey.								
• Prepare survey sites for study.								
• Recruit and train Study Reps.								
• Recruit 1,000 subjects and administer survey at 5 sites.								
• Statistical analysis of data.								
• Preparation and submission of manuscripts to peer-reviewed journals.								

WHAT IS WRONG?

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Common mistakes

- **Potential impact of expected project results on the regional healthcare system, patient wellbeing and personalized medicine advancement.**
  - **Needs to be very clear. If your project is not really translational you will have a hard time writing this up. Outcomes need to have impact in the “near future”. Therefore combining basic scientists with clinicians is fundamental.**

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Common mistakes

- **Dissemination and communication plan/activities**

  - **To the scientific community**
  - **To the society in general**
  - **Educational programs**

  ➢ **Often part of what should be addressed is not.**

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Common mistakes

- **Implementation of Responsible Research and Innovation (RRI) principles**

  - **PUBLIC ENGAGEMENT**
  - **GENDER EQUALITY**
  - **SCIENCE EDUCATION**
  - **ETHICS**
  - **OPEN SCIENCE**
  - **GOVERNANCE**

- **READ THE DOCUMENT!!!!**
- **ADRESS EACH ISSUE SEPERATLY IF POSSIBLE!!**

Common mistakes

- **Project management and infrastructures**

- *Describe how the project will be managed,*
- *the scientific environment in which the research will be done*
- *… and any institutional facilities,*
- *resources and equipment available to the PI and the research team.*

- **MANY TIMES THE MANAGEMENT STRUCTURE IS MISSING OR NOT CLEAR…**
- **STATING THAT YOU WORK AT A WIDELY ACCLAIMED CENTER IS NOT ENOUGH!**
- **MATCHING FACILITIES AND EQUIPMENT WITH THE TEAM MEMBERS IS A GOOD IDEA…**

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What reviewers like

- **Any issues or limitations in your study? If yes what is your contingency plan?**
- **No mistakes!**
- **Final statment: Why is your proposal very importante?**
  - How will you improve the knowledge?
  - Are you opening a new way of dealing with the problem?
  - Who will you help and how?
  - Any economical considerations?

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What reviewers like

- **Preliminary Data in Support for the Current Proposal: Clinicopathologic characteristics**

Characteristics	Number of patients N = 35	Percentage (%)
Age	66 (42–82)	
Sex		
Male	23	66
Female	12	34
Tumor location		
Ventral	9	26
Dorsal	5	14
Laterally to the right	12	34
Laterally to the left	9	26
Characteristics of the procedure		
Low anterior resection	28	80
Coloanal resection	2	5.5
Hartmann's operation	3	8.5
Rectal amputation	1	3
Intersphincteric resection	1	3
Type of procedure		
Laparoscopic	27	77
Classic	3	8.1
Conversion	3	8.5
Robotic-assisted	2	6
Stage (y)pT		
T0	2	6
T1	8	23
T2	19	54
T3	6	17
T4	0	0
Stage (y)pN		
0	29	83
1	6	17
2	0	0
Angioinvasion of blood vessels	0	0
Lymphoangioinvasion	5	14
Perineural propagation	1	3
pCRM[a]		
Negative > 1 mm	32	91.5
Positive ≤ 1 mm	3	8.5
Cannot assess (ypT0, Dworak 4)	0	0
Mesorectal excision quality		
1	17	48.5
2	10	28.5
3	8	23
Extent of mesorectal excision		
TME	26	74
PME	9	26

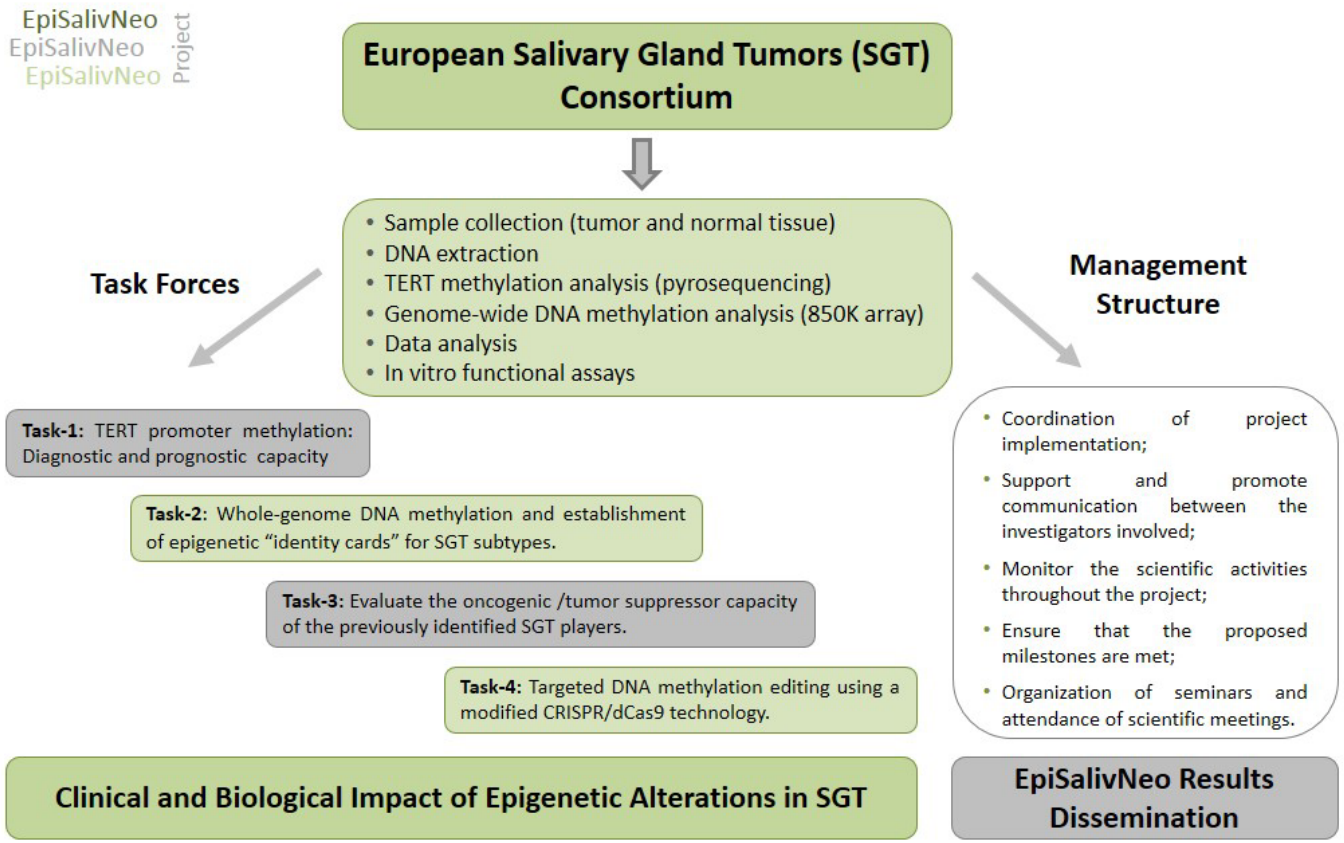
[a] pCRM = circumferential resection margin assessed by the pathologist.

Variable	Mean±SD	Median (25–75% IQR)	No of patients (%)
Age (years)	63±13	66 (57–73)	105
Male gender			67 (64)
NYHA class III/IV			51 (49)
BMI (kg/m^2)	24±4	23 (21–27)	105
Systolic BP (mm Hg)	130±25	130 (112–145)	105
Diastolic BP (mm Hg)	75±17	72 (63–84)	105
Heart rate (beats/min)	73±14	70 (61–81)	105
Haemoglobin (g/dl)	13.1±2.0	13.2 (12.0–14.7)	105
Serum creatinine (mg/dl)	0.97±0.28	0.93 (0.76–1.13)	105
eGFR (ml/min/1.73 m^2)	60±16	59 (48–71)	105
Corrected calcium (mg/dl)	9.4±0.4	9.4 (9.2–9.7)	105
Inorganic phosphorus (mg/dl)	3.6±0.5	3.7 (3.3–3.9)	105
Magnesium (mg/dl)	2.1±0.2	2.1 (1.9–2.2)	105
Haemoglobin A1c (%)	6.2±1.1	6.0 (5.5–6.6)	105
Uric acid (mg/dl)	7.2±2.4	7.2 (5.3–8.4)	105
PTH (pg/ml)	46±25	40 (31–56)	105
BNP (pg/ml)	403±479	203 (59–613)	105
ACE inhibitors/ARB			81 (77)
β Blockers			35 (33)
Calcium channel blockers			26 (25)
Loop diuretics			59 (56)
Aldosterone blockers			31 (30)

ARB, angiotension receptor blockers; BMI, body mass index; BNP, B-type natriuretic peptide; BP, blood pressure; eGFR, estimated glomerular filtration rate; NYHA, New York Heart Association; PTH, intact parathyroid hormone.

What reviewers like

- **Project overview**



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What reviewers don´t like

- **Preliminary data (non-published) is different from previous data (published).**

- **Don´t state that your idea is new if it is not!!! If your idea is based on something already known, state what is different.**

- **Can´t find a figure reference in the text…**

- **Figures that are so dense that one can´t read it. Figures, like in papers need to be self explanatory and visualy acceptable.**

- **To presente a different Grant structure to that in the call.**

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General Recommendations

- Aim 1 should be almost done (supported by preliminar data)
- Optional material is not an option
- Some people use **bold** in the text. Nice idea but use it with care!!!

- Translation goes beyond cell line work (2D alone not very sexy at the moment)
- Imagine your reviewer as somone very busy, so you need to capture his/her attention all the time.
- You should not right a translational oncology project without an Oncology clinician in the team.
- You should not right a translational oncology project without a basic scientist in the team.

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Thank you

Questions