

The QUEST Replication Call

Background

Science is incremental with new experiments often resting on findings from previous studies. This is particularly true in translational biomedical research where a long chain of interconnected experiments potentially results in a therapeutic breakthrough. Despite many success stories, there are also failures that are detected late in the translational process often at a significant cost. These failures arise particularly when research relies on weak evidence in earlier studies. The challenge is thus to strengthen the evidence along the translation process so that later stages build on a solid basis. One suggestion to approach this challenge are independent replications¹ of important (sometimes called 'keystone' or 'pivotal') findings that are essential for future work. Often, however, limited resources and time constraints affect the feasibility of such replications. With this funding scheme, the QUEST Center aims to foster replication of biomedical research. At the same time, we aim to explore the feasibility and practicability of replications and establish best practices of conducting replications.

Application process

To apply for funding for a replication project, researchers and clinicians at Charité and MDC are encouraged to hand in a short (500 words) informal letter of intent. Guiding questions are:

- What are the previous results and have they been published?
- What are the limitations of previous results?
- What is the keystone finding that needs replication?
- Why is this important in a translational context?
- What evidence will potentially be generated by the replication?

On the grounds of application fit, translational relevance, and feasibility, the QUEST Center, together with a team of international reviewers, will select a subset of proposals. In a second stage, the selected proposals are then invited for a full proposal. Details on this second stage will be communicated to successful applicants.

As this is a first attempt to approach funding of replication projects, we currently do not know how many proposals we will be able to fund. Moreover, funding will be available for 2018 only. That is, our focus is on short-term projects that require little prior investment and administration. This first round will inform us on how prevalent the need for replications is within the BIH and particularly what researchers need for their replications. To give some guidance, we have compiled a non-exhaustive list of vignettes of projects which may qualify for funding below.

¹ For a full account of reproducibility and types of reproducibility we recommend reading: Goodman, Steven N., Daniele Fanelli, and John P. A. Ioannidis. 2016. "What Does Research Reproducibility Mean?" *Science Translational Medicine* 8 (341):341ps12-341ps12. <https://doi.org/10.1126/scitranslmed.aaf5027>.

Vignettes

Vignette 1: Reanalysis of existing data (Preclinical and Clinical)

Researcher A has published an analysis based on a particular analysis method. You collaborate with researcher A and have requested access to the data. You attempt to reproduce the findings from the publication by repeating the analysis. Additionally, you may apply a different analysis method and compare both results.

Vignette 2: Replicate previous results (Preclinical)

You have conducted an experimental study, which indicates a potentially interesting effect to be transferred to the next stage in the scientific process. The observed effect size is large but associated with a large degree of uncertainty indexed, for instance, by a large confidence interval. As the planned next study will require a significant amount of work, you decide that before proceeding, an independent replication of the main finding from the previous study should be conducted. That is, an independent lab (academic or contract research organisation) receives funds to replicate the same experiment.

Vignette 3: Confirmatory study (Preclinical and Clinical)

Researcher A has collected a data set and you have found an interesting, unexpected effect by exploring the data. This effect was not initially hypothesized but is potentially relevant. An academic or contract research organization receives funds to conduct a confirmatory study to investigate the effect in detail by collecting new data (e.g. new study population, new batch of animals or cell lines).

Vignette 4: Multi site matching (Preclinical)

You and researcher A, both in different laboratories, collaborate. You have agreed on a multi site design. After an initial phase, results from one lab do not match the results from the other lab. You and researcher A decide to investigate this problem in detail and agree to exchange lab members to learn the exact protocol of each other's lab to find boundary conditions for the experimental results.

Formal criteria

Co-funding is permitted and encouraged. Teams can also apply.

Independency of the applicant from the original researchers is required (e.g. PhD students are not independent of their supervisor, collaborators in different labs at for example the MDC are independent).

We expect results to be published open access. We also encourage preregistration and open data alongside open analysis or open code if possible.

At least one applicant must be an employee of Charité or Max Delbrück Center.

Employees of QUEST are not eligible for this funding.

Submit letters of intent before **09. March 2018 12 pm (midday)**.

If you have further questions do not hesitate to contact us.

Letters of intent should be sent to quest@bihealth.de.

Questions can be directed at quest@bihealth.de 030 543013

<https://www.bihealth.org/de/forschung/transforming-biomedical-research/news/>