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Reproducibility and reporting negative data

The first question that needs to be addressed is 'What is a negative study'? In a well-designed study to test a hypothesis, one can confirm or discard the hypothesis. For starters, the power of the study should be sufficient to come to an actual 'positive' result, i.e. confirm the hypothesis, or 'negative' result, i.e. discard the hypothesis. Depending on the result of a well-powered study, one could speak of positive or negative, but both confirming or discarding a hypothesis is a positive result, which advances science in the particular field of research. Thus, positive and negative results are rather the perception of the investigators and scientific field, who apparently only like to collect and receive results that confirm a hypothesis. So, how to deal with this rather peculiar view on advances in science. In my opinion, supervisors should train their students that any research project starts with a hypothesis, and specific objectives to test the hypothesis. A proper power calculation may be a challenge in relatively new research areas, such as stem cell research, where the number of studies that are required to test hypotheses is still under debate and open to new insights. In a recent consensus document of European Society of Cardiology working groups, recommendations were done to increase applicability of stem cell-derived systems for cardiovascular studies, including a minimum repetition of experiments in three batches from three lines [1]. To stimulate publication of negative results, and minimizing publication bias towards positive results, the registration of clinical studies has been common practice for a long time. More recently, platforms have been introduced to also register animal studies, e.g. https://preclinicaltrials.eu/. Notably, the number of registered animal studies is still low and awareness should increase. Registration of a study in the preclinicaltrials.eu platform is free of charge, anonymous, and protocols can be protected by an embargo, and blinding of specific information. Moreover, while researchers may think it will cost them a lot of time, entering a study is straightforward and fast, and the platform can be easily adjusted based on their requests.

In addition to an accurate design of studies, reproducibility is a crucial part of advances in science, and a challenge for all researchers. While all scientists agree that a study should be reproducible on the basis of the information provided in a manuscript, who is responsible for reproducing a data set? Funding agencies do not support studies which are 'merely' incremental to previously obtained knowledge, but request novel and preferably innovative research ideas. Reproducibility of data highly depends on the quality of tissues used for research. Joint efforts to establish biobanks with human induced pluripotent stem cells (hiPSC) and human tissues and blood using well-defined protocols guarantee quality of specimens for scientific research [2]. In combination with clinical datasets, biobanks thereby represent a solid basis for collaborations using the same cell lines and tissues in different laboratories worldwide. Attempts to obtain results in different institutes within one project using slightly different approaches have been made, and represent an elegant way to test if studies in certain cell lines provide similar results. In such manner, drug responses in hiPSC-derived models may be compared using different set-ups [3], or physiologic parameters can be defined in the same human tissue samples using complementary methodologies to define e.g. sarcomere changes in cardiac disease [4]. Thus, funding of international team efforts is warranted to not only advance science, but also to guarantee reproducibility of findings.

Finally, we need to train the future and junior scientists and make them aware of the urgent need of transparency and reproducibility. The competition in science may be fierce, and may thereby prevent sharing of protocols and ideas, but a sustainable research line can only be built on solid and reproducible data which can only be obtained with team efforts. I urge funding agencies to sponsor next generation consortia that focus on data reproducibility to reduce publication bias by increasing publications of negative data, and advance science in a positive way.

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