

Increasing the knowledge gain per animal used

According to the prevailing view, the reproducibility crisis in pre-clinical animal research is caused by a lack of scientific rigor, low statistical power, and publication bias. However, ignorance of biological variation that we will encounter whenever conducting an experiment with living animals might be a major reason for irreproducibility of research findings. Biological variation is the sum of genetic variation, environmentally induced variation, and gene-by-environment interactions. Ignoring the implications of biological variation is likely to lead to spurious results that are idiosyncratic to the specific standardized laboratory conditions, thereby causing poor reproducibility. Irreproducible results generate the need for follow-up studies requiring further animals, or might—in the worst case—lead researchers into scientific dead ends, wasting even more animals for studies that cannot provide any benefits in terms of knowledge gains. Implementing experimental designs that embrace biological variation can increase the external validity and the reproducibility of animal experiments and can, therefore, increase the knowledge gain accrued per animal used.