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Embracing variation to improve reproducibility and translation

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Reproducibility in animal research is alarmingly low. Various potential causes of poor reproducibility have been identified, including poor scientific rigor, low statistical power, analytical flexibility, and publication bias. However, the reproducibility of a result is also a function of its external validity. Unless results are robust against common sources of variation between independent replicate studies, they will not be reproducible. In animal research, effects of experimental treatments usually vary depending on the phenotype of the animals. Because the phenotype depends also on the environment of the animals, small differences in the environment between replicate studies can produce conflicting results. Therefore, systematic variation (heterogenization) rather than more rigorous standardization is needed to improve reproducibility. Based on a theoretical analysis of phenotypic plasticity, simulations with existing preclinical animal data, and experimental results, I will show how heterogenization of study populations can improve robustness and reproducibility of results without a need for larger sample sizes. Using more representative study samples will be crucial to avoid wasting animals for inconclusive research.