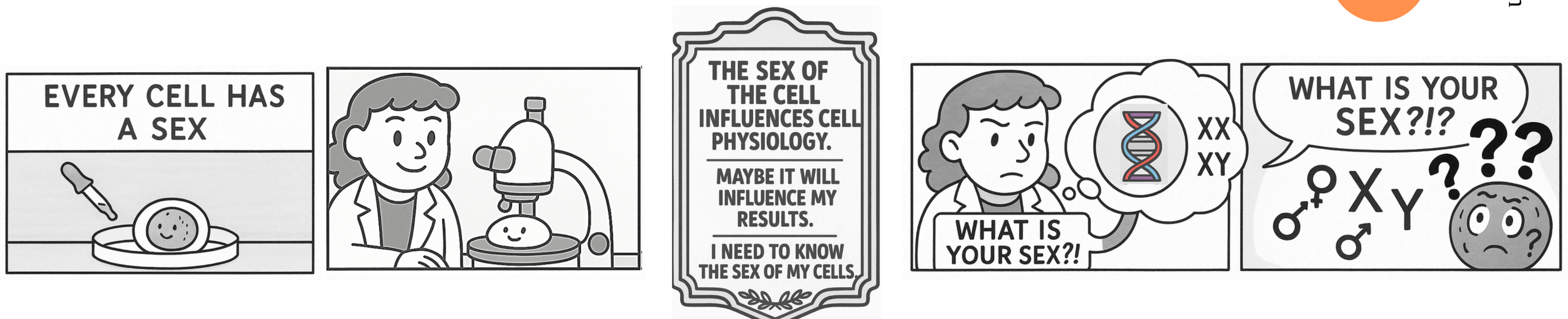


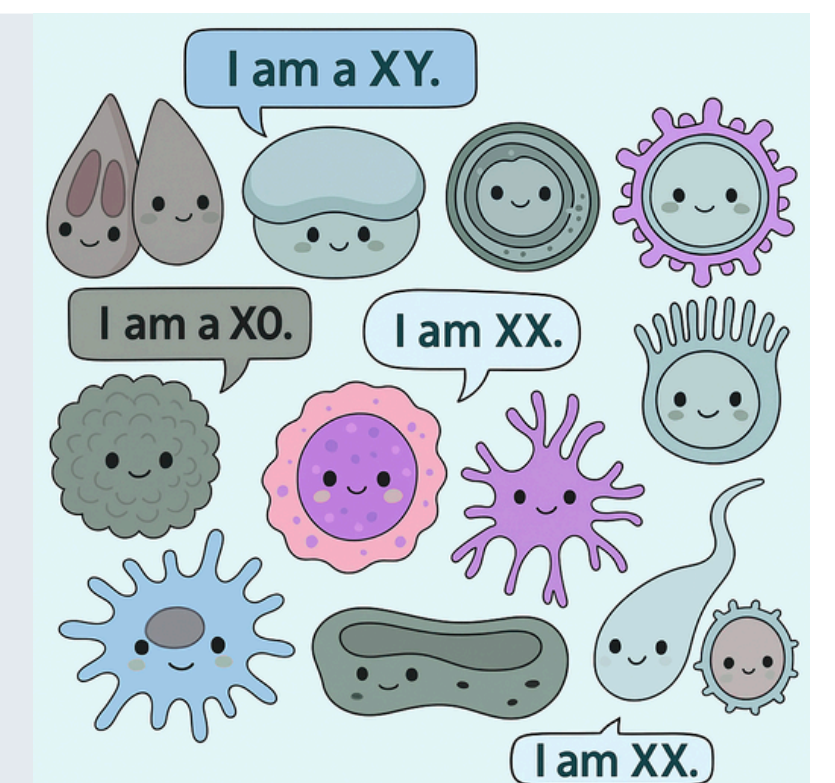
Sex in the Petri Dish: Integrating Biological Sex in Cellular and Tissue Research

„Every cell has a sex“ (1)

In every experiment with tissues or cells, sex might play a role.



Most researchers do not know the sex of their cells or tissues (2). However, not only sex-specific tissues and cell-lines from reproductive tissues and organs have a sex. Sex-chromosomes potentially influence cell physiology and biochemical pathways of the experiment. Studies show influences of sex diversity of gene expression in the brain and CNS, kidney, lymphatic cells, heart, liver, and many more (3).



Collect and Analyze Data

Collect



- Match your sample.
- Cell media: The used cell media might influence the expression of genes or cell behavior.

Phenol red

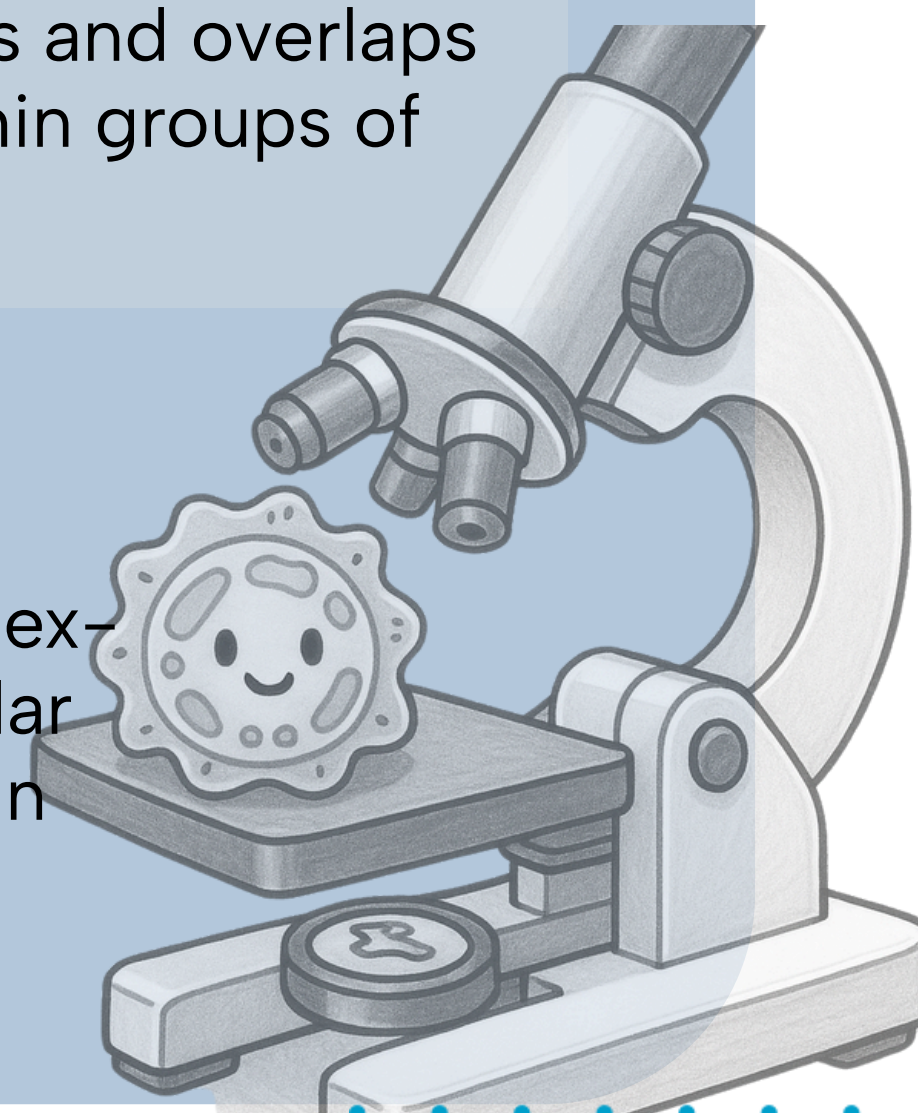


(pH indicator used in cell culture) is estrogenic and should be avoided when studying parameters potentially influenced by estrogens (4).

Analyze

- Analyze sex as a covariate, confounder or explanatory variable.
- Analyze variations and overlaps between and within groups of different sexes.

A recent study (5) using single-cell transcriptomics from over 2.3 million mouse cells across 17 tissues revealed how androgens drive sex-specific gene expression at cellular resolution. Androgens modulated immune cell composition and transcriptional programs, contributing to sex-biased disease risk, including for example autoimmune disorders and metabolic or cardiovascular conditions. These findings highlight the importance of considering Sex as a Biological Variable in preclinical research and suggest androgen signaling as a potential therapeutic target.



Reporting Sex as a Biological Variable (SABV)

- Report the sex of your cells and tissues in every research, even if the experiment did not analyze sex-differences or was a single-sex experiment.
- If sex was used as a variable, report all findings: positive, negative, and indecisive.
- If different sexes were analyzed, report data sex-disaggregated.
- Discuss potential implications of sex on the findings.
- If findings were sex-specific or the experiment was designed as single-sex, discuss potential generalization of findings to all sexes.

References

1. Wizemann TM, Pardue M-L, editors. Exploring the Biological Contributions to Human Health: Does Sex Matter? Washington (DC); 2001.
2. Shah K, McCormack CE, Bradbury NA. Do you know the sex of your cells? Am J Physiol Cell Physiol. 2014;306:C3-18. doi:10.1152/ajpcell.00281.2013.
3. Mauvais-Jarvis F, Arnold AP, Reue K. A Guide for the Design of Pre-clinical Studies on Sex Differences in Metabolism. Cell Metab. 2017;25:1216-30. doi:10.1016/j.cmet.2017.04.033.
4. Souza Santos R de, Frank AP, Palmer BF, Clegg DJ. Sex and media: Considerations for cell culture studies. ALTEX. 2018;35:435-40. doi:10.14573/altex.1806151.
5. Li F, Xing X, Jin Q, Wang X-M, Dai P, Han M, et al. Sex differences orchestrated by androgens at single-cell resolution. Nature. 2024;629:193-200. doi:10.1038/s41586-024-07291-6.