



NSC3 Webinar

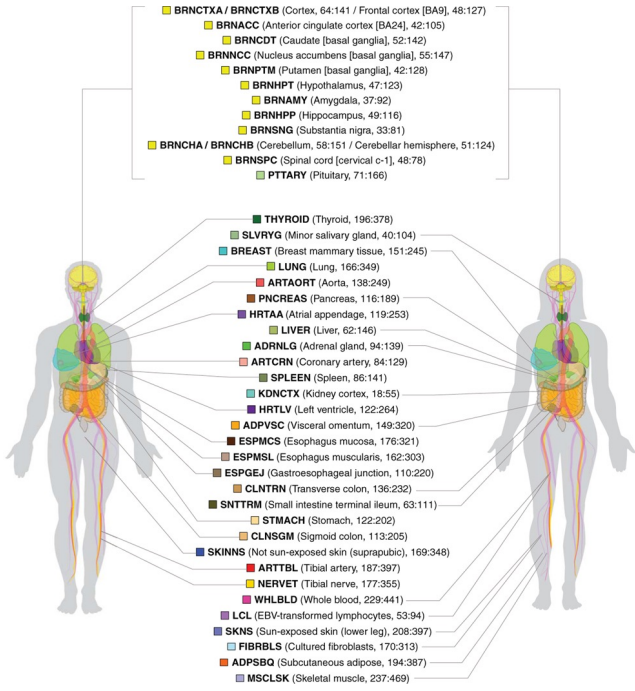
Considerations in the Study of Sex as a Biological Variable in Aging Research: “Omics”

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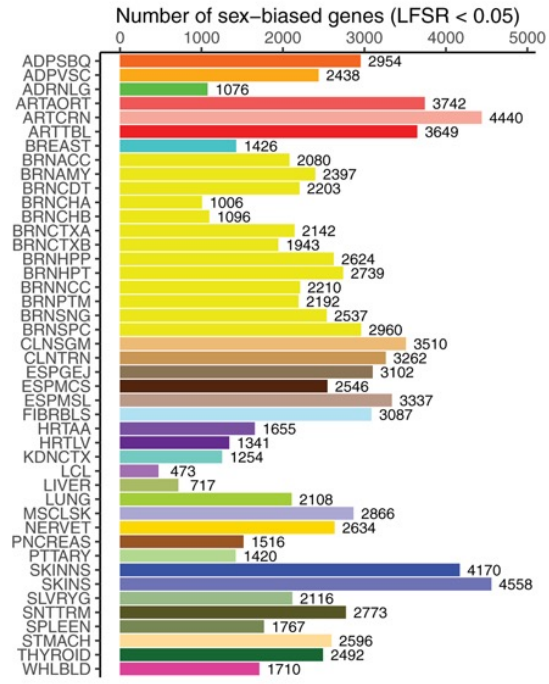
Sex-differences are ubiquitous in “omics” experiments

- Sex-differences permeate gene regulation processes across somatic cells and tissues: *e.g.* GTEx v8

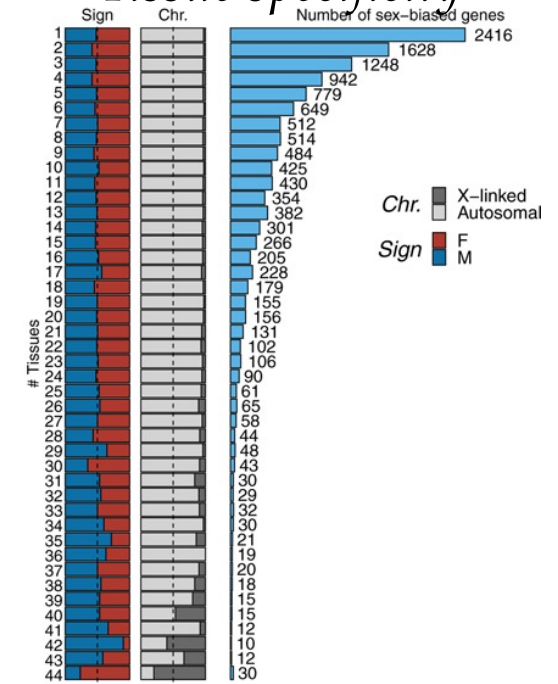
44 tissue types



SexDim genes



Genomic location/
Tissue specificity



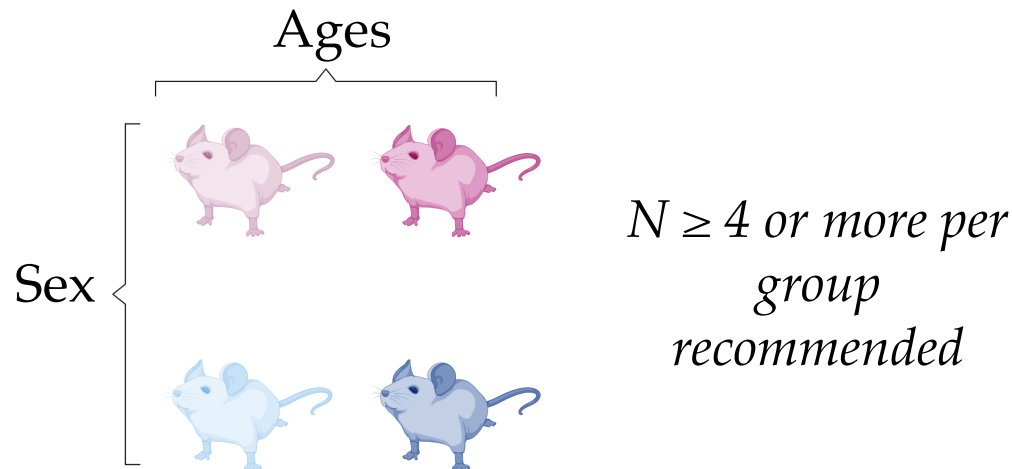
Olivia et al, *Science*, 2021



- Sex-differences in « omics » across cells / tissues exist whether or not you care about them!

Sex-differences are ubiquitous in “omics” experiments: general considerations

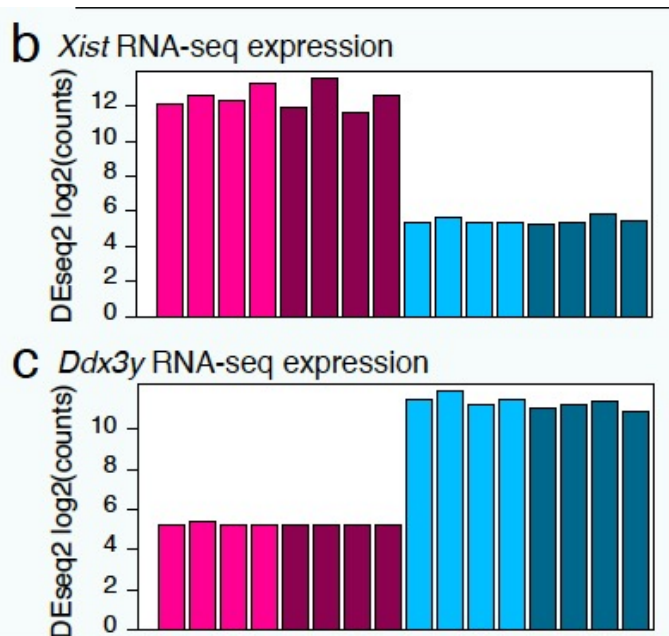
- Ideally, to account for sex, aging « omics » experimental design should :
 - Include **females** and **males** in all groups ;
 - Include animals of **the same reproductive status** across age groups;
 - **Avoid** mixed-sex pooled samples;
 - Be sufficiently powered to study **females** and **males** separately (if needed);



Important QC steps for sex-inclusive omics

Am I recovering X and Y linked gene signal as expected?

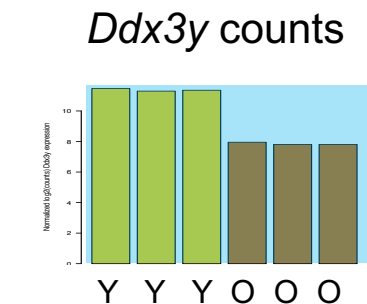
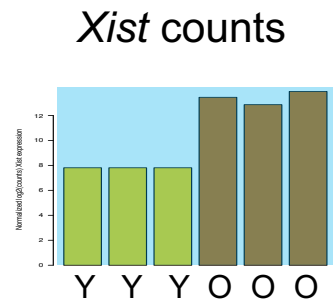
Example 1:



Female samples have high Xist, male samples have high Ddx3y

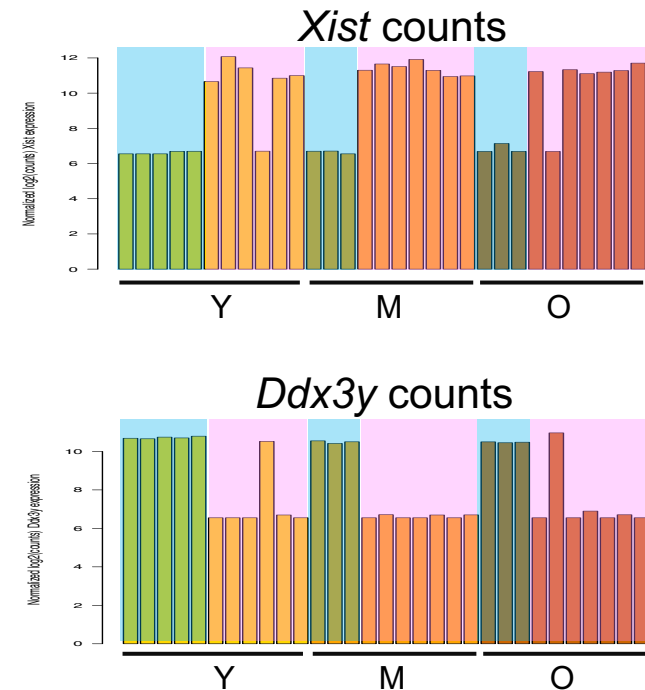
Lu et al, *Nat aging*, 2021

Example 2: (male only label)



Xist/Ddx3y confounded with age

Example 3: (both sexes label)



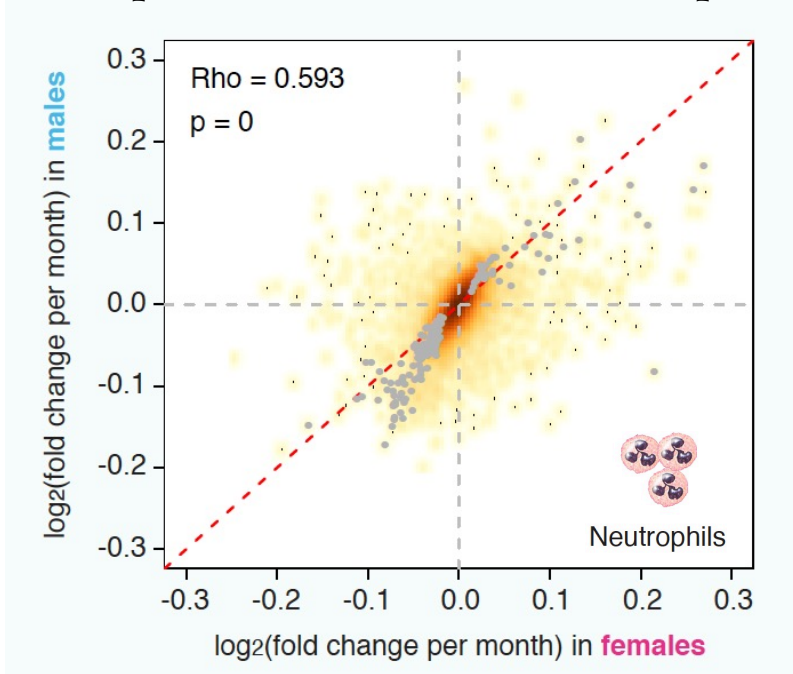
Xist/Ddx3y consistent with mislabeling

Published datasets – Anonymized

Key analytical considerations for sex-inclusive omics

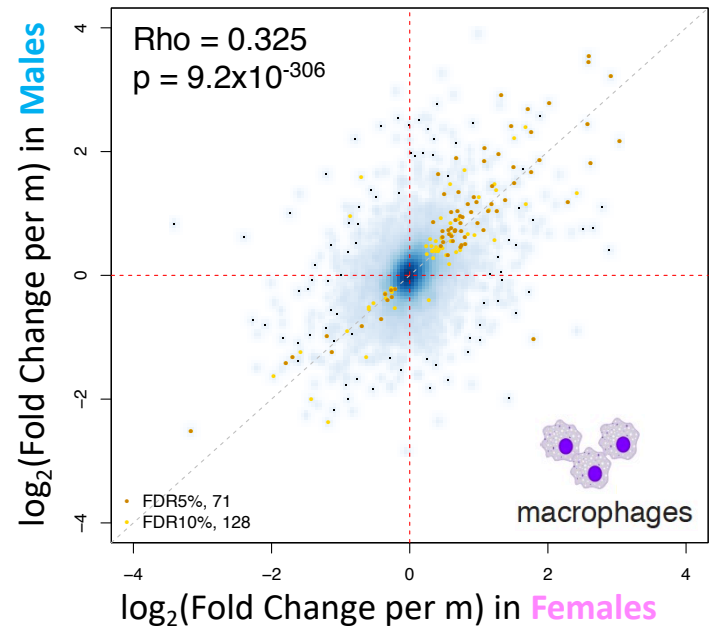
Does aging impact my system in a linear/additive way to biological sex ?

Example 1: bone marrow neutrophils



Strong correlation of fold-changes – suggests strong linear/additive effect

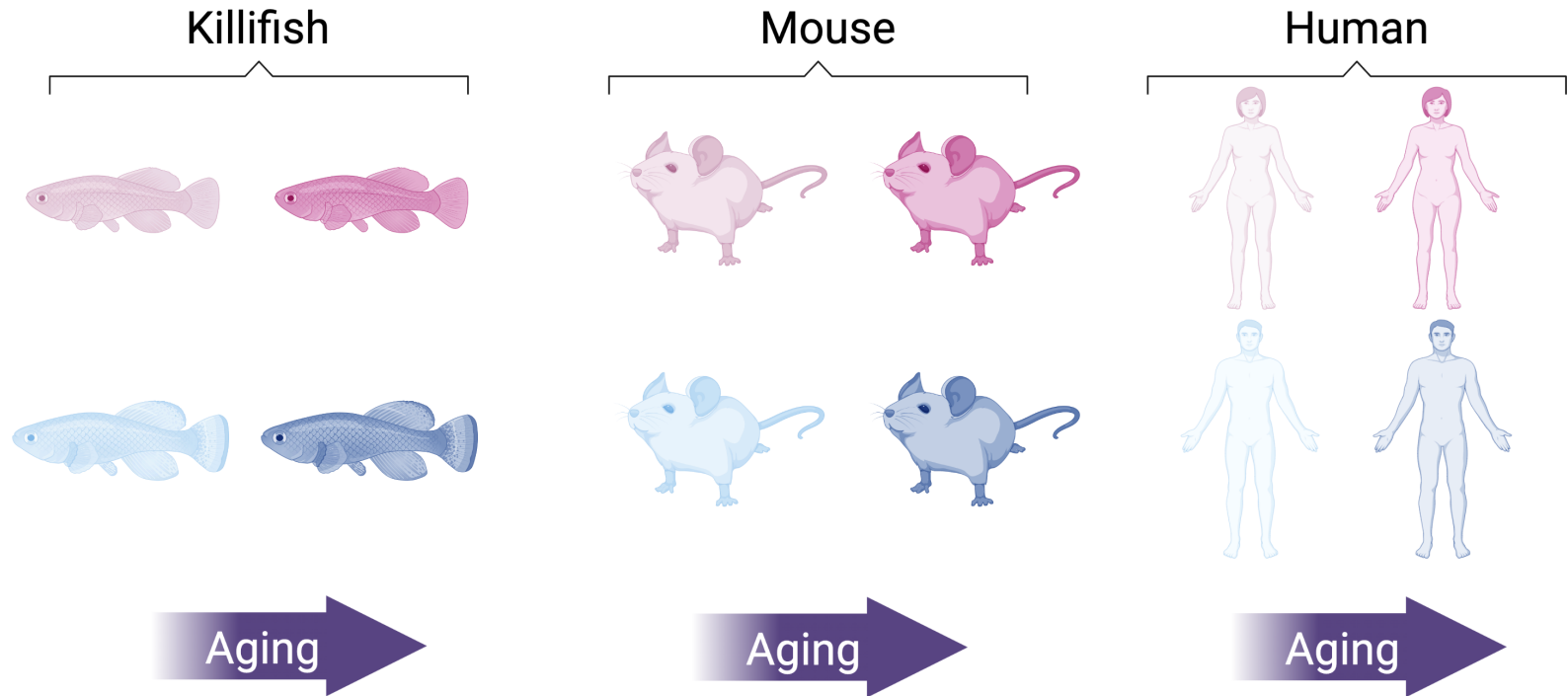
Example 2: peritoneal macrophages



Weaker correlation of fold-changes – most effects are likely not to be linear/additive

Lu et al, *Nat aging*, 2021 and unpublished

Sex: the final “omics” frontier



- Sex-differences in genomic regulation can be very strong:
 - Always account for sex (*even if only to identify commonalities*);
 - Verify that sex metadata matches data;
 - Analyze your data in a sex-aware fashion;

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Generous gift from Ms. Kathleen Gilmore