Sex-specific evolution in genome wide recombination rates

For distinguishing results and method

## Intro outline

-definition of HetC

-“Here we define heterochiasmy as sexual dimorphism in recombination rates in dioecious species where both sexes recombine.”

- HetC is a ‘made-up’ metric from sex specific measures. Here we define it as the ratio of average female to male mean genome-wide rec rate.

-caveats and how they will be addressed

-Heterochiasmy definition should encompase correlated traits to gwRR (SC axis length, NCO:CO, DSB number)

-The common pattern of heterochiasmy are: (overall magnitude and position of COs)

1. female higher rec levels compared to male (female-biased)

2. females more uniform CO positions across chromosomes

(3. females have longer SC/Axis, (exceptions in some fish and bird species)

-Theories for evol of heterochiasmy have focused on indirect selection

Summarize Trivers, Lenormand, BrandvainCoop, SardellKirkpatrick

- Fewer models focus on direct selection driving evolution of heterochiasmy. (segregation of chromosomes; euploidy or efficient homolog pairing)

- some gametogenesis patterns that are universally sexually dimorphic

-asymetrical vs symmetrical cell division results in big size differences in gametes

- anastral vs astral microtubule organization / acentrosomic vs centrosomic

-differences in gametogenesis could result in sexual dimorphism in meiotic recombination rates

## Result outline

1. **MLH1 results (Main\_Report\_Results.rmd)**

Rapid male specific evolution in PWD and MSM, two subspecies

-Distribution of gwRR across mouse subspecies and outgroups,

-female very constant across strains, large error (se), strain specific evo

-male dom, very similar, male musc and molf rapid evolution in two strains

- POLYMORPHISM in musc, not in dom

Should the next two sections be focused on the female-male comparison?

### A.1 **Mean** MLH1 per cell

1.figure of means … histograms

2.Mixed models and testing coefficients / hypotheses

Test of Subsps coefficient

Mostly NS

Test of sex

Interaction coefficient

More sig?

Test of random strain effects

(which tests are used?)

Mixed model (Sup Table 1)

-No significant (and consistent) effects of subspecies or sex for mean CO

Post hoc investigation for strain effects (PWD and MSM)

GLM (all fixed effects) for strains … G, PWD and MSM have strain effects

Sex-specific evolution (nuanced female patterns…)

### A.2 **Variance** in MLH1 per cell

1. histograms of within mouse variance

2.Mixed models and testing coefficients / hypotheses

(Figure X of mouse level variance)

Test of subsp

Mostly NS

Test of sex

Most sig

Test of interaction

Some sig (for cv and Var)

Test of random effects

(when quality is accounted for…)?

## Rapid male evolution (Fig2)

* 1. **(post hoc tests (just males?)**
  2. **Chrm proportions**
     1. More 2COs : 1COs in high rec strains
  3. **Total SC length**
     1. High rec males have more total
  4. **Relative positions (pool all cells for a group)**
     1. (can’t detect differences in relative position
     2. THERE is a difference in interfocal distance
  5. **DMC1** **results**

Figure 3. (DMC1 distribution)

1) ANOVA, strain effect across mice holds for L but not Z cells.

2) post-hoc – t-tests between high and low groups

t-test between the ‘High’ and ‘Low’ MLH1.group is significant for L cells, but not Z

## Nuanced female pattern (Fig3)

* 1. More 0CO / errors –
  2. More variance at multiple levels
  3. Fewer COs than expected given the sc length
  4. Less dense CO land scapes
  5. Uniform placement
  6. More poly / morphism – mouse effects?
  7. Subsampling?

## D. Heterochiasmy patterns incorporating total SC, IFD, and relative CO placement (fig4)

Conserved and evolving patterns of sexual dimorphism in meiotic traits. Longer total SC length and telomere position are conserved sexually dimorphic meiotic features.

Definition of heterochiasmy (HetC plot with female CO rates X adjusted)

Difference in Proportions of 1CO: 2CO evolves?

Conserved

-SC length

-telomere biased position

Evolving

-higher COs in females

(How do High recombining strains differ from low, How do the sexes differ from each other)

(Figure 4 (HetC plot)?

Figure 5 chromosome class proportion plot

Figure X total SC scatter plot, relative CO position plot, and IFD scatter plot

Review caveats with heterochiasmy definitions

Heterochiasmy values adjusted for female XX bivalent

**D. Predictions of selection on bivalent structure**

*Purifying selection for bivalent structures to converge on metaphase spindle in spermatocytes*

*(For males, in high recombining strains the REC landscape is evolving to increase sister-cohesion-tension area and low recombining strains REC is evolving to minimize that area)*

1. There should be less variance (within mouse and strain) in relative CO positions and raw SC length in males relative to females.
2. Given that high recombining strains have ~1:1 proportions of 1CO and 2CO bivalents, the relative position of 1CO foci will be less telomeric. (1COs in high recombining strains will be distinct from 1CO in low recombining strains).
3. The interfocal distances for 3COs in males should be less symmetrical than in females. The distances between foci will maximize or minimize the amount of sister cohesion tension area.

## Mat and methods

-setup data output file

explain all the plots that are printed out

\*don't print out tables that are really big\*

\*add mouse ages to the table (make sure the ages are correctly added

(add\_age)

-save the final .RData file.

-Permutation scripts/files

### Mixed model framework

**1.Mixed Model – the model was made which the following logic,**

Mean\_co\_mouse ~ subsp \* sex + random(strain \* sex)

Main goal of the chosen variables is to test for effects of

1. Subspecies (Divergence)
2. Sex
3. Interaction term
4. *Random effects* of strain background (Polymorphism)

### Error rate estimates

Human (repeatability was calculated X)

### Total SC

Used RW’s python script – (outliers removes – segmentation visually confirmed for subset)

AP – analysis script, src/totalSC.R

### Biv features

Used DNACrossover (ref)

Mixed hand measures and bivmeasures when needed.

-how some mice and cells were choosen or excluded

Interfoci distance (IFD) / interference (raw and normalized)

-t.tests

(glms for accounting for SC length and effects…

-within cell SC ranking ….(only a subset)

-XX adjustment for females

-characterize how reliable chrm compaction(ranking) is from human data?

## Discussion

Table X, Current models and their predictions for the evolution of heterochiasmy

Table X, results from proposed predictions

(Figure X, cartoon of difference in bivalent on spindle for 1CO and 2COs)

1. Review main patterns
   1. Male specific polymorphism for gwRR in musculus and molossisnus, may not be a species wide optimum for gwRR
   2. More variance in females for meiotic features, resulting in greater variation in gwRR
   3. Rapid male specific evolution upstream of CO repair stage
2. SACE predictions and bivalent selection models are not mutually exclusive,
3. Importance of broad scale patterns for recombination

(centromere effects for mis-segregation rates) - (high rate of robertsonian translocation in Dom, and absent in Musc – maybe something about centromeres (encourages transloactions + suppresses 2CO (rec near centromere) in DOM

(that has changed in Musc, REC near centromere suppresses rates of robertsonian translocation)