**ABSTRACT 150 words**

Although meiotic recombination is required for successful gametogenesis in most species that reproduce sexually, the rate of crossing over varies among individuals. Differences in recombination rate between females and males are perhaps the most striking form of this variation. Existing data fail to directly address the extent to which recombination experiences similar evolutionary pressures. To fill this gap, we measured meiotic recombination in both sexes for a panel of house mouse cross three subspecies. Using inbred strains and single cell immunohistochemistry allowed us to place sex-specific observations within the same genetic background and meiotic context. Our results indicate highly discordant evolutionary patterns in the two sexes. Whereas male recombination rates show evidence of rapid evolution over short evolutionary timescales, female recombination rates measured in the same strains are mostly static. These results strongly indicate that house mouse has two genome wide recombination rates which display distinct evolutionary trajectories.

The rapid evolution in male gwRR is significantly predicted/correlated by the number of double strand breaks and spacing of double crossovers.

However the relative spacing of double crossovers in the high recombining group is greater compared to the low recombining group – (that is the relative recombination landscape – is less dense – but has more recombination).

<understanding the pathway>

INTRO

1.(strong **hook** and first sentence)!!

-sex differences in recombination rate, house mouse, closely related species

-Closely related species (there are more gwRR measures), but for both sexes is rare

-why gwRR important

Method

-single cell cytology (co counts) and chromosome morphology

- empirical measures from

-surveyed panel of house mouse inbred strains , spanning 3 subspecies

Summary of results

- but evolutionary patterns for the variation for why sexes differ is not understood.

**1. importance of recombination**

**2.variation in recombination rate**

**3.  The House Mouse is a great model for uncovering evolutionary patterns at a short timescale.**

Commensal with humans -- World-wide distribution – found on every continent – the house mouse is a greater evolutionary biology model.

* The House mouse complex is comprised of (3 main subspecies, molossinus is an ‘artificial’ hybrid (of a combination of musculus and castaneaus).
* The divergence times spanning 0.5 mya (cite / Geraldes et al 2008 and Geraldes et al 2010) – related murid species divergence 3 mya for (x and Z) and 5 mya for caroli
* This short evolutionary time – provides an opportunity to interrogate natural variation (ie there are fewer mutations that would be causing hereitable variation in the genome wide recombination rate).
* Classical lab strains of mice have generated extensive knowledge central to meiosis and outcomes on recombination through extensive studies on the genes involved in the meiotic recombination pathway (cite) and previous crosses for understanding the genetic architecture of recombination rate variation (Dumont, Murdoch, Wang).
* **Same genome**  \*\*Wild derived inbred strains generate the best comparison of females and males, besides the sex chromosomes, the mouse for each genome are almost identical.

Inbred strains enable one of the most direct comparison of both female and male -- versions of meiosis

--enable use to conclude that sex is a primary factor --

Additionally due to their global distribution allows us to compare samples of natural diversity from a broad geographic range. (wild derived inbred strains – will capture genetic diversity not represented in classical lab strains.)

* While there are strains with Robertsonian translocations, in house mouse and related murid species it is possible to assemble sets of strains with identical karyotypes, 20 pairs of acrocentric chromosomes.
* House mouse is well suited for single cell cytology approaches. The single cell level allows integration of data at a closer connection to the molecular pathway and meiotic program. In addition to the quantification of gwRR. This study quantifies precursors to crossovers, double strand breaks (DSBs), and meiotic chromosome morphology across stages of meiosis which would not be accessible to with genetic linkage data and crosses.

The House mouse species complex arose from a recent radiation providing an opportunity to interrogate natural variation at short evolutionary scales, potentially narrowing the mutational space for identifying variants which would cause gwRR variation. Add divergence ranges. divergence spanning 0.5 mya to 5 mya (cite / Geraldes et al 2008 and Geraldes et al 2010).

Classical lab strains of mice have generated extensive knowledge central to meiosis and outcomes on recombination through extensive studies on the genes involved in the meiotic recombination pathway (cite) and previous crosses for understanding the genetic architecture of recombination rate variation @dumont2011house; @murdoch2010; @Wang2017island].

\*\*Wild derived inbred strains generate the best comparison of females and males, besides the sex chromosomes, the mouse for each genome are almost identical\*\*. Inbred strains enable one of the most direct comparison of both female and male -- versions of meiosis --enable use to conclude that sex is a primary factor --

Additionally due to their global distribution allows us to compare samples of natural diversity from a broad geographic range. (wild derived inbred strains – will capture genetic diversity not represented in classical lab strains.)

While there are strains with Robertsonian translocations, in house mouse and related murid species it is possible to assemble sets of strains with identical karyotypes, 20 pairs of acrocentric chromosomes.

House mouse is well suited for single cell cytology approaches (due to large cell sizes). The single cell level allows integration of data at a closer connection to the molecular pathway and meiotic program. In addition to the quantification of gwRR. This study quantifies precursors to crossovers, double strand breaks (DSBs), and meiotic chromosome morphology across stages of meiosis which would not be accessible to with genetic linkage data and crosses.

**3. What we did in this study**

**Main messages: these results are centered/focused on a unique evo comparison**

**Advantages / importance of using multiple strains from and multiple subspecies**

**-importance / advantage of sampling for multiple geographic locations.**

**Importance of multiple gwRR measures – results for the gwRR measures.**

**Importance of chromosome morphology / general recombination landscape**

**-results for general landscape**

For the first time in many of these strains, We report a rare, direct, evolutionary comparison of recombination rate in females and males for this short evolutionary scale.

We use rare strains from a broad range of geographic locations of the species territory.

We choose *Mus musculus* because (of the available strains across subspecies. – our design of using multiple inbred strains within subspecies --- and multiple subspecies across the species -- (can provide information anaglogous to polymorphism within and divergence within subspecies of the house mouse.

Measures from outgroups – are – good for placing in broader evolutionary context.

Our results indicate rapid male specific evolution of gwRR occurred in a subset of house mouse lines. We observed up to a 30% difference (translating into approximately ~7 more crossovers per cell), a surprising amount considering the short evolutionary time scale. (found previously for PWK (forjt) (PWD beth) – but mostly measures from males.

**Brief mouse background and (touch on polymorphism**

-musculus subspecies – have mostly been samples from central Europe – we extend with samples from more eastern extent of the subspecies range in Russia and kazakstan.

-molossinus is endemic to the japan – a hybrid that arose with humans brining musculus and castaneus to the islands.

(AGAIN the divergence between mus musculus subspecies is ~500K – and males and females share the same phylogeny)

OUR results for genome wide recombination rate (variation) we observed highly distinct evolutionary trajectories between males and females. This is due to rapid male specific evolution in the gwRR from two strains in musculus and 1 strain in molossinus. (this pattern of rapid evolution was not observed in females)

The metric of the genome wide recombination rate reflects a non-random process of crossover formation on individual chromosomes // the recombination landscape at the single chromosome level.

The recombination landscape for single chromosome scale can be general summarized by i) spacing of crossovers and ii) the linear area of synapsed homologous chromosomes where crossovers can form.

we quantified the general recombination landscape (because – patterns in the recombination landscape are important to document because they can shed light on constraints and regulation of the processes ( could end up leading to variation in the genome wide recombination rates. )

Our results confirm (well established) previously reported patterns for sex differences in the general recombination landscape – and add by demonstrating that these patterns hold even in the case of genome more crossovers, but general landscape patterns still maintain sex-specific patterns.

Conserved patterns of the recombination landscape of the single chromosome level – reflect constraints At the single chromosome level – (crossover number is conserved – suggesting processes regulating the rec landscape at this scale might face similar constraints