Mapping mitonuclear epistasis using a multiparental recombinant population of *Saccharomyces cerevisiae*

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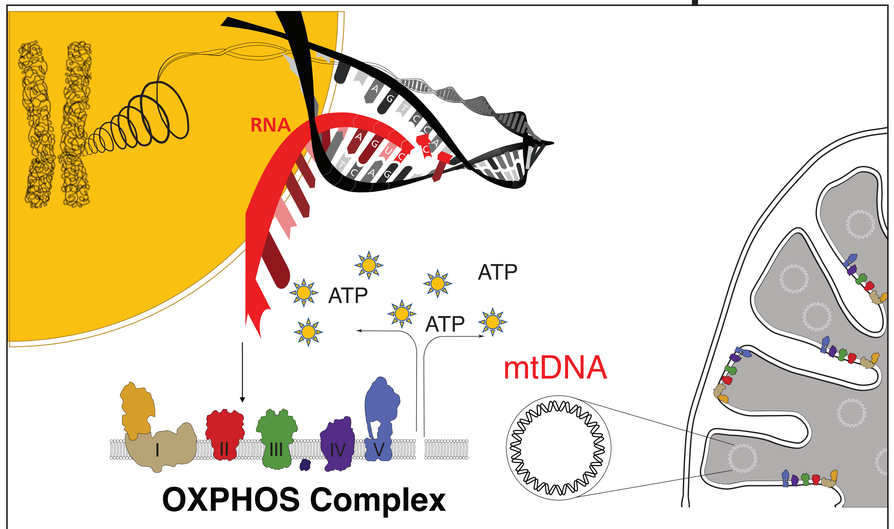
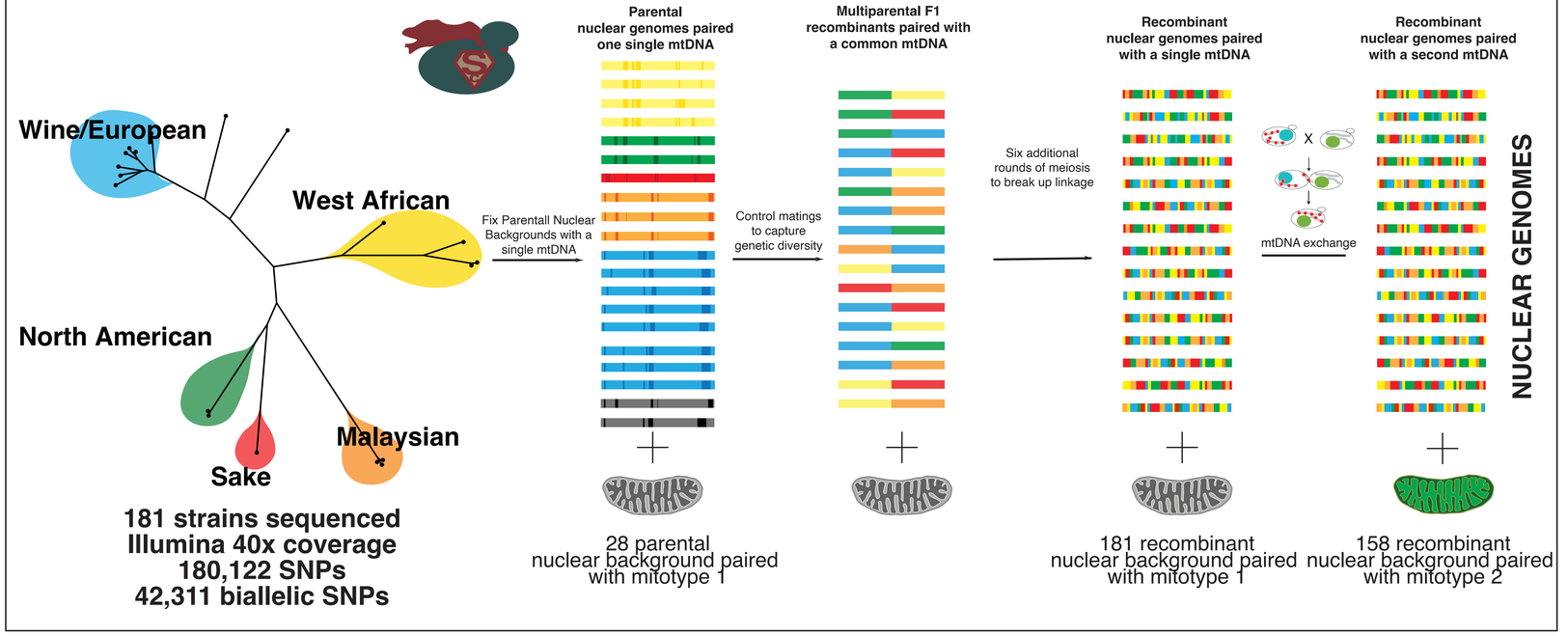
Mitonuclear interactions are important



OXPHOS Complex

Mitonuclear coadaptation is required for mitochondrial functions and cell fitness
Mitonuclear interactions contribute to phenotypic variation
Environmental factors alter the efficiency of mitonuclear interactions
Mitonuclear interactions are a component of “missing heritability” making mapping mitonuclear interacting alleles difficult

Creation of a Mitonuclear Mapping Population



181 strains sequenced
Illumina 40x coverage
180,122 SNPs
42,311 biallelic SNPs

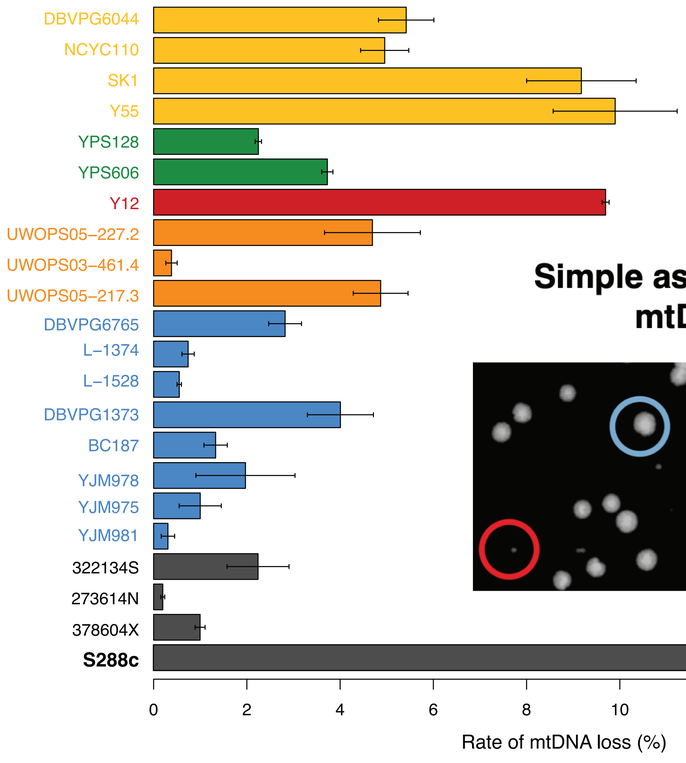
28 parental nuclear background paired with mitotype 1

181 recombinant nuclear background paired with mitotype 1

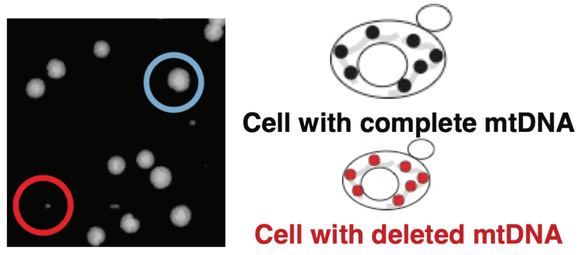
158 recombinant nuclear background paired with mitotype 2

The mitonuclear population can be used to uncover the interacting loci underlying mtDNA instabilty in natural yeasts

mtDNA instability is a variable trait in wild yeast population



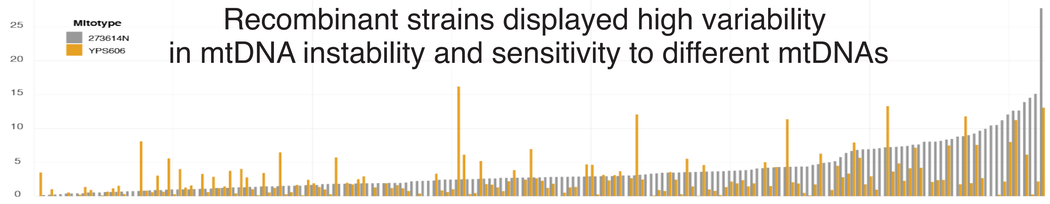
Simple assay for monitoring mtDNA stability



Cell with complete mtDNA

Cell with deleted mtDNA

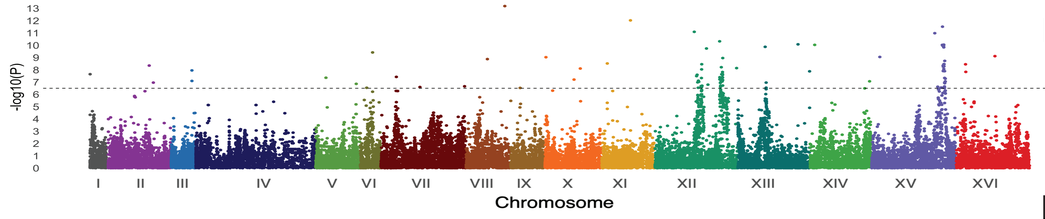
Recombinant strains displayed high variability in mtDNA instability and sensitivity to different mtDNAs



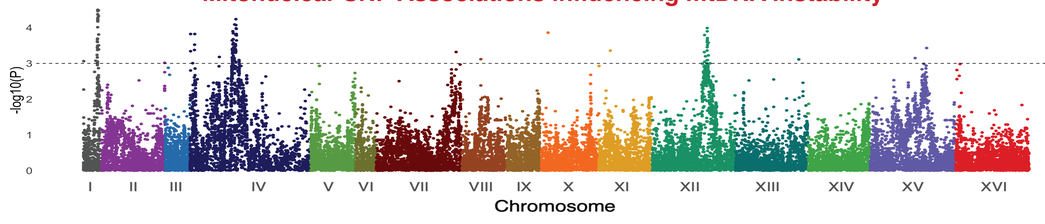
Generalized inear model for GWAS:
cbind(#Petite, #Grande) ~ SNP + mtDNA + SNP*mtDNA + covariates

- **Nuclear SNP unaffected by mtDNAs**
- **Mitonuclear SNP**
- To account for residual population structure: covariates include 20 PCAs + auxotrophies

Nuclear SNPs unaffected by mitotype underlying mtDNA instability



Mitonuclear SNP Associations influencing mtDNA instability



ongoing works:

Idemtify associated SNPs

Annotate SNPs to determine upstream, downstream, synonymous, and non-synonymous SNPs

↓

Retain SNPs within coding sequence + within 500bp upstream

↓

Determine significant SNPs Bonferonni significant or -log10(P) >3

↓

Candidate SNPs