Inheritance and Linkage Disequilibrium

Robert Brown

Thank you!

UCLA Computational Medicine

Inheritance

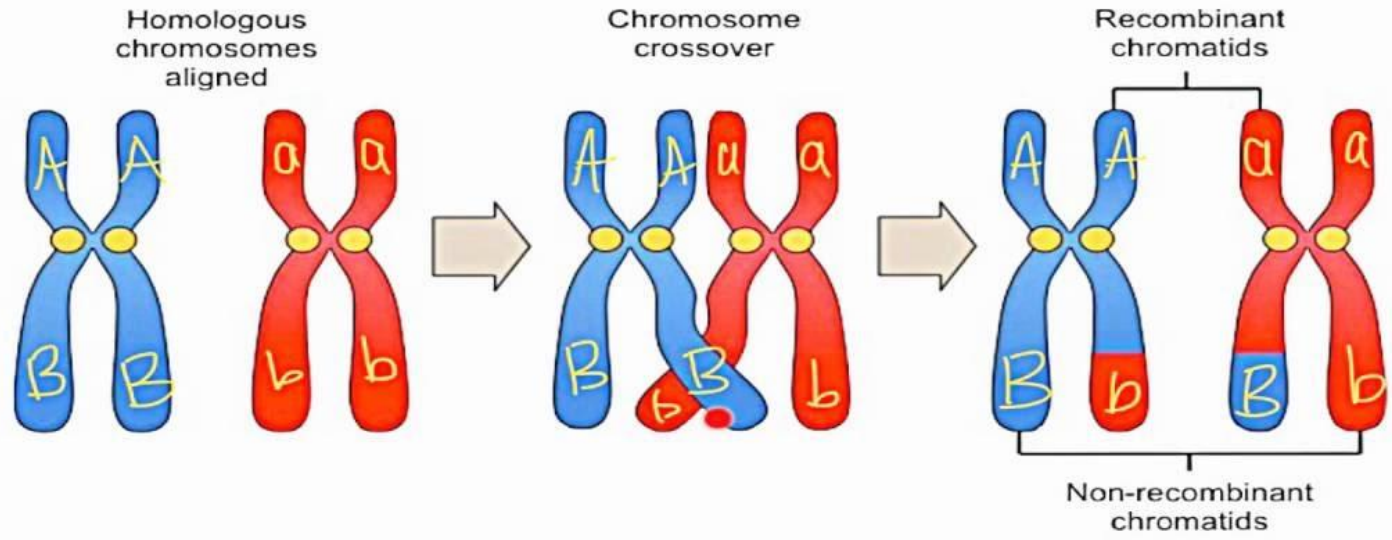
…CTCGTCACTTCAC---TG…
…CACGTCACTTCACGTATG…

…CTCCTCACTTCAC---TG…
…CTCGTCACGTCAC---TG…

…CACGTCACTTCACGTATG…
…CTCCTCACTTCAC---TG…

Recombination

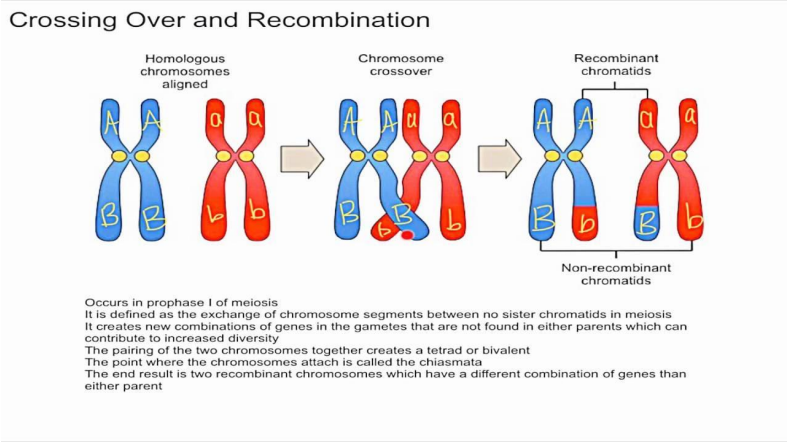
Crossing Over and Recombination



Occurs in prophase I of meiosis
It is defined as the exchange of chromosome segments between no sister chromatids in meiosis
It creates new combinations of genes in the gametes that are not found in either parents which can contribute to increased diversity
The pairing of the two chromosomes together creates a tetrad or bivalent
The point where the chromosomes attach is called the chiasmata
The end result is two recombinant chromosomes which have a different combination of genes than either parent

https://www.youtube.com/watch?v=WcfAeZ0nEc8

Inheritance+Recombination



…CTCGTCACTTCAC---TG…

…CACGTCACTTCACGTATG…

Post Recombination:

…CTCGTCACTTCACGTATG…

…CACGTCACTTCAC---TG…

…CTCGTCACTTCAC---TG…

…CACGTCACTTCACGTATG…

…CACGTCACTTCAC---TG…

…CTCGTCACTTCACGTATG…

Recombinations occur on average 50-60 million, basepairs apart. There are “hot spots” where recombinations occure more often than expected

Inheritance+Recombination

…CTCGTCACTTCAC---TG…
…CACGTCACTTCACGTATG…

…CTCCTCACTTCAC---TG…
…CTCGTCACGTCAC---TG…

Post Recombination

…CTCGTCACTTCACGTATG…
…CACGTCACTTCAC---TG…

…CTCCTCACTTCAC---TG…
…CTCGTCACGTCAC---TG…

…CTCGTCACTTCACGTATG…
…CTCCTCACTTCAC---TG…

Linkage Disequilibrium (LD)

No linkage (No LD)

25% …CTCGTCACTTCA…
25% …CACGTCACTTCA…
25% …CACGTCACCTCA…
25% …CTCGTCACCTCA…

Linkage (Linked)

10% …CTCGTCACTTCA…
40% …CACGTCACTTCA…
10% …CACGTCACCTCA…
40% …CTCGTCACCTCA…

…CACGTCAC?TCA…

Perfect LD

0% …CTCGTCACTTCA…
50% …CACGTCACTTCA…
0% …CACGTCACCTCA…
50% …CTCGTCACCTCA…

Linkage Disequilibrium (LD)

Perfect LD or No LD?

25% ...C**A**CGTCAC**T**TCA...

25% ...CTCGTCACCTCA...

25% ...C**A**C**C**TCAC**T**TCA...

25% ...CTC**C**TCACCTCA...

Pos2-Pos4?

Pos2-Pos9?

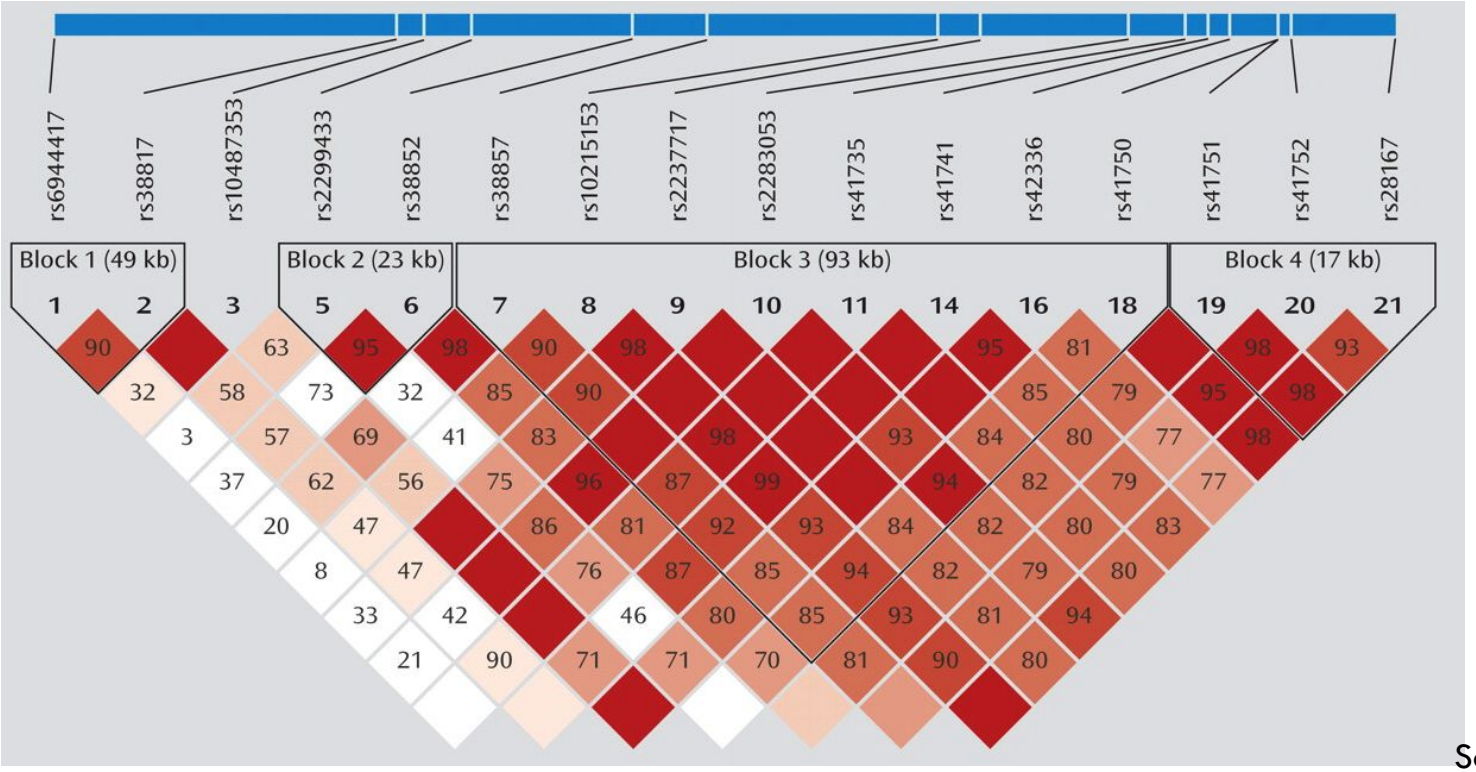
Pos4-Pos9?

Chr	Pos	Ref	Alt	Ind1-H1	Ind1-H2	Ind2-H1	Ind2-H2
12	2,147,839	C	T	0	0	1	0
12	2,147,913	T	A	1	0	0	1
12	2,152,882	G	A	1	1	1	1

Linkage is often measured as squared correlations (r^2)

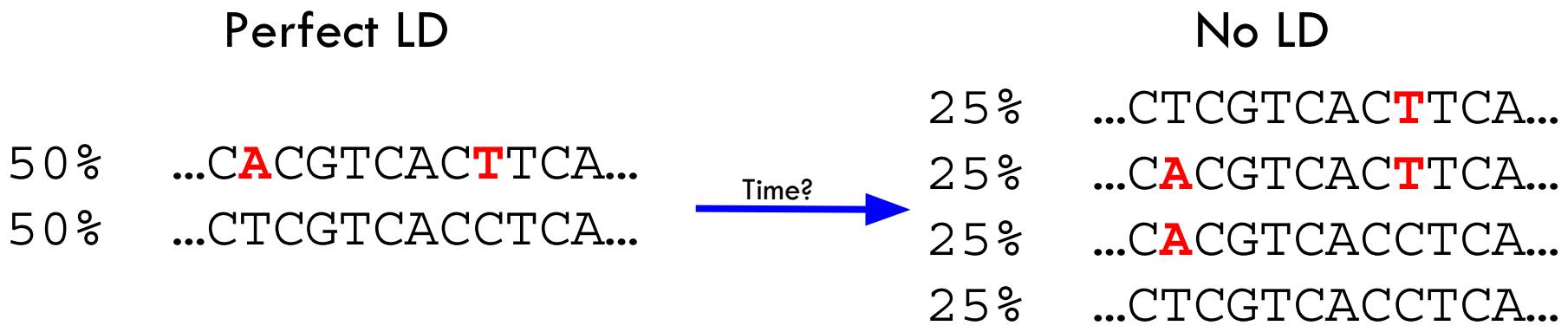
LD-blocks

Chr	Pos	Ref	Alt	Ind1-H1	Ind1-H2	Ind2-H1	Ind2-H2
12	2,147,839	C	T	0	0	1	0
12	2,147,913	T	A	1	0	0	1
12	2,152,882	G	A	1	1	1	1



Source unknown

Linkage Disequilibrium + ?????



Linkage Disequilibrium + Recombination