The Red-Queen model of recombination hot-spot evolution: a theoretical investigation.

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Recombination hot-spot

- Meiotic recombination events are not uniformly distributed.
- Hot-spot typical length 1-2 kb.
- Between 20k and 40k hot spots identified in humans.
- Over 40k hot spots identified in mouse.
- Hot spots are not conserved between humans and chimps.
- Hot spots are not conserved between mouse subspecies.

What is determining hot spot location?

Why are hot spots location not conserved?

Determination of hot spot location

- Specific sequence motifs of approximately 10-20bp.

- PRDM9 protein binds sequence motifs through its ZnFinger domain.

- PRDM9 catalyzes histone H3 Lys4 trimethylation (H3K4me3) at neighboring nucleosomes through its SET domain.

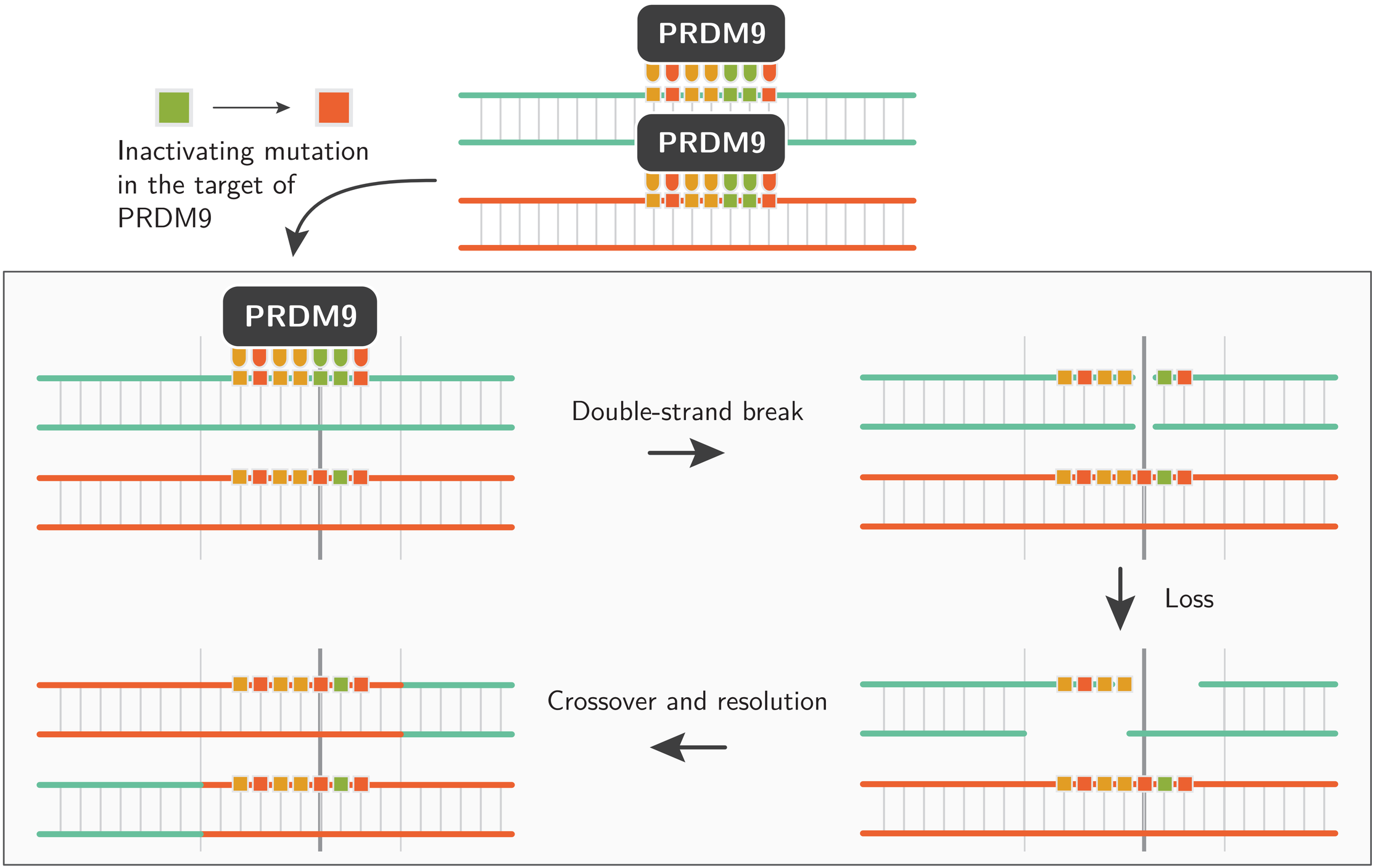
- Leads to recruitment of Spo11, triggering the formation of a double strand break (DSB).

- DSB results in crossover or a non-crossover recombination event.

- Biased gene conversion (dBGC): sequence motif is resected from the chromosome and is repaired using the homologous chromosome as a template (300 to 1k bp).

Why are hot spots location not conserved?

dBGC leads to the loss of current hot spots



Hot spots are self-destructive

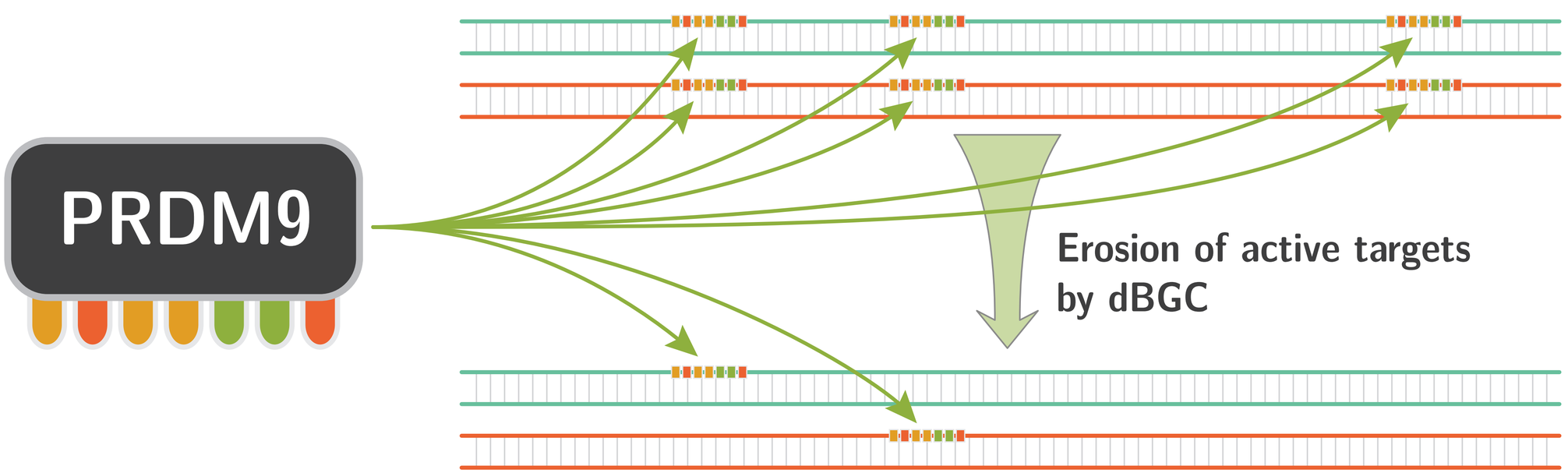
- Active sequence motifs are converted by their inactive homologue.

- At the population level, dBGC results in accumulation of inactive sequence motifs.

- Activity of hot spots decreases genome-wide.

How are hot spots even maintained in population ?

Hot spots are self-destructive genome-wide



How are hot spots maintained ?

- Recombination is required for the proper segregation of chromosomes

- Prdm9 knockout mice are sterile

- PRDM9 is the most rapidly evolving gene in primates and rodents

The Red Queen of recombination

- dBGC results in accumulation of inactive hot spots.

- Mutation and positive selection at the PRDM9 locus leads to recruitment of new hot spots.