

# Recombination—the Making of New Allele Combinations

The best combinations in the future will depend on a broad selection of cow and sire lines from our breed

Part of the excitement of the holiday season is the thrill of unwrapping a beautiful present from under the Christmas tree. Often a gift will be packaged with fancy paper and a beautiful bow—and inside it'll contain something wonderful. Well, in dairy cattle breeding, we also need to think about how the genetics of our elite animals is presented to the next generation. The genetic merit of the animal, i.e., the sum of all of the alleles that the animal possesses, is the content of the package. The packaging of these alleles is done with chromosomes.

Each of our Holsteins has two sets of genes, which are arranged on 30 pairs of chromosomes. One chromosome from each pair will be transmitted to each of its offspring. The alleles that are linked together on the same chromosome tend to be transmitted together. However, even for these linked genes, Mother Nature has provided us with a way for new combinations to occur. This process is called crossing over, or recombination, of chromosomes.

In the creation of eggs and sperm, the pairs of chromosomes come together, duplicate, and then divide. The outside chromosomes are identical to the original parental pair. But, the two inside chromosomes often become intertwined, break, and exchange pieces. This exchange of chromosome segments creates new combinations of alleles, or “recombinants.”

One pair of chromosomes is involved in determining the sex of the animal (X and Y chromosomes). The other 29 pairs of chromosomes are referred to as autosomes. The naming of these 29 autosomes is done based upon their size. The largest, Chromosome 1, is three times longer than the shortest, Chromosome 29.

The number of crossover events per chromosome, i.e. the number of new combinations of alleles, differs according to the length of the chromosome. For example, Chromosome 3 will, on average, have 1.2 crossovers, while Chromosome 21 will average only 0.7. More than one crossover event can occur

per pair of chromosomes. For example, with Chromosome 3, 41 percent of the time there will be one crossover between the inner pair of chromosomes; 27 percent of the time there will be 2 crossovers, and 9 percent of the time there will be 3 or more.

What’s particularly fascinating about this repackaging of our genetic material is

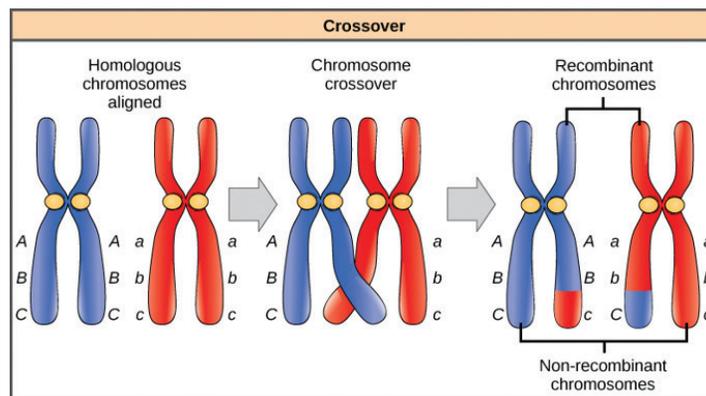


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that the rate of exchange of genetic material between pairs of chromosomes differs between species and amongst individuals within a species. In cattle, bulls have a 10 percent higher rate of producing new recombinants than cows. In humans, it’s the opposite: the eggs of our mothers will have a higher number of recombinants than the sperm of our fathers.

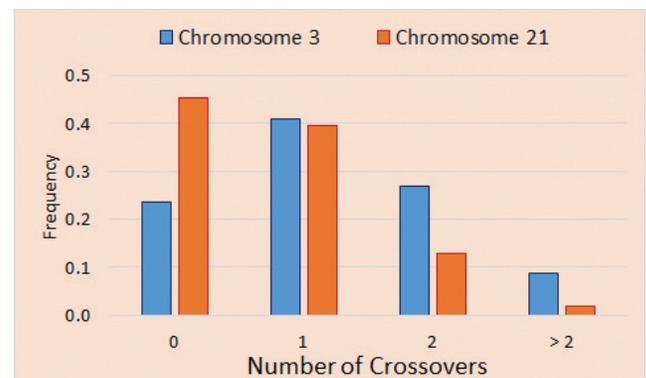
One possible explanation for why recombinants occur more often in women may

be due to the repair mechanism involved with the breaking and recombining (repairing) of chromosomes. Occasionally, at the time of cell division, an extra chromosome or a missing chromosome can be transmitted. Eggs with more repaired chromosomes (recombinants) have fewer errors than eggs with more nonrecombinant chromosomes. This is especially important for older women, because their eggs are more



Source: OpenStax College, Concepts of Biology. OpenStax CNX, Nov. 7, 2014

## Researchers identified over 8.5 million maternal and paternal recombination events.



susceptible to errors. An extra Chromosome 21 in people is responsible for Down syndrome, while having an extra one of the larger chromosomes will often lead to a nonviable embryo. The leading cause of pregnancy loss is abnormalities in chromosome number. In women, having more recombination is advantageous. If the natural selection of more viable embryos results in higher recombination in women, could we be driving up the recombination rate in bulls by selecting for better and better allele combinations? Is that a good thing?

Recombination leads to more genetic variation available for selection. In 2014, at the World Congress on Genetics Applied to Livestock Production, researchers from the United Kingdom presented the novel idea to include recombination rate as part of a selection index, or use genome editing to modify the recombination rate of all of the top bulls.

Heritability within each group of animals	
Bulls – HIGH rate of recombination	32
Average Bull	30
Average Cow	29
Bulls – LOW rate of recombination	27

At first blush, this seems like a desirable plan. When one takes recombination rates into account, we see that a higher rate of recombination leads to a higher heritability. Obtaining a higher heritability value suggests that increasing recombination rates should lead to faster genetic

progress. But does it really work in practice? Our industry is spending millions of dollars on ET and IVF, looking for just the right combination of alleles. So, if there is any type of advantage of higher recombination rates then we should see it in Holsteins.

A recent article published in the November 2015 PLOS Genetics (10.1371/journal.pgen.1005387) by researchers at the University of Maryland and the USDA's Animal Genomics and Improvement Laboratory is shedding new light on this question. Their analysis of the genomic testing program in Holsteins represents the largest study of recombination rates in cattle ever reported. They identified over 8.5 million maternal and paternal recombination events.

The average number of crossovers or new recombination of alleles per gamete averaged 25.5 in the bulls (sperm cells) and 23.2 in the oocytes of the cows. The figure to the right shows the range amongst all of the bulls recorded. The variation that exists amongst them is quite large, going from only 18 to over 32. And the trend is increasing!

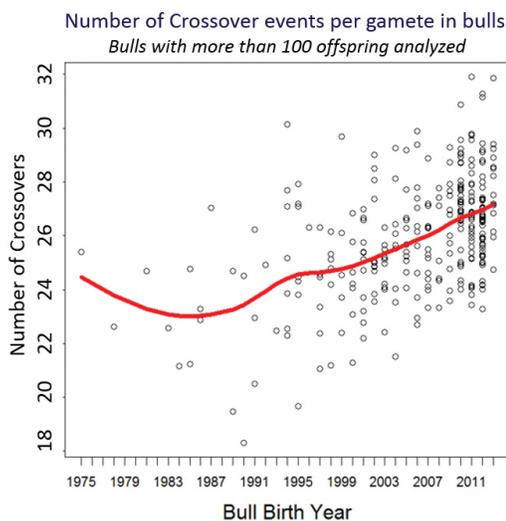


Table 1. lists the average number of crossovers for some of our popular bulls with over 2,000 sperm analyzed. In each of these categories, there are some very impressive bulls. The interpretation here may be that for some bulls the allele

**Table 1**

Bulls	Crossovers per gamete	Category
BALISTO, O-STYLE, SUPERSIRE, KINGBOY, LITHIUM	28	High
MCCUTCHEN, MOGUL, FREDDIE, SHAMROCK, SUPERSTITION, PLANET	25	Medium
SHOTTLE, BOLTON, G W ATWOOD, TANGO, GOLDWYN	22	Low

combination is already favorable and you are better off to keep the good combination of alleles together. Meanwhile for other bulls the highly favorable alleles are more widely dispersed. In this case uncoupling the linked alleles and looking for more favorable combinations to piece back together may be the way to go. Having a different breeding strategy for different animals is not a shocking conclusion to many of our old-time breeders. They've been honing this skill for years.

Our knowledge level on recombination rates still needs to increase before we can provide specific breeding recommendations. However, science is gaining ground. Another important finding by the researchers is that crossover events are much more likely to occur at some locations than at others. These high recombination areas are known as hotspots. Twenty five percent of all crossovers occurred at only 3 percent of the genome. To further complicate things, many hotspots were unique to each sex. For bulls, alleles located at the END of the chromosome are MORE likely to recombine than alleles at the beginning or middle of the chromosome.

This may be important for an undesirable genetic condition such as with the gene APOB which is responsible for Cholesterol Deficiency. Its location is about 70 percent down the length of chromosome 11, closer to the middle than it is to the end of the chromosome. If there are favorable alleles which are closely linked to the defective APOB allele, it'll take a little longer than usual for them to escape their linkage with the Cholesterol Deficiency allele and allow us to select a new combination of all desirable alleles.

Breeding elite Holsteins is still a combination of a skilled eye and a firm grasp of the science behind it. As we go forward and continue to search for better and better combinations of alleles, we need to ensure that we have as many cow families and sire lines represented as possible. Only then can we seek to put together the best combination of alleles, and guarantee that we have obtained the rare alleles from within a wide sector of our breed rather than limit ourselves to only those allele combinations coming from a few predominant individuals. 🐮