# A look at pedigree analysis and the closest common ancestor

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When studying breed-related hereditary conditions, a common practice for breeders and medical experts alike is to compare pedigrees of affected or carrier dogs. In doing so, there is a tendency to trace back to common ancestors and blame these individuals as carriers or progenitors of a defective gene.

This, however, is a false and misleading practice. This type of analysis cannot identify ancestral carriers of defective genes. Carriers of a defective recessive gene can only be identified if: a) they have produced an affected offspring; b) are an offspring of an affected individual; or c) test as a carrier with a reliable genetic test.

The only value of a closest common ancestor analysis is to determine the minimum age of a defective gene in the population - and therefore its possible genetic spread. This allows breeders to determine the minimum breadth of the gene pool that is liable for carrying the defective gene, and that requires genetic counseling.

Why do you want to do this? Simply stated, knowing the minimum age of the gene in the population gives you an idea as to how hard it will be to manage the gene in the breed pool. If all affected dogs trace back within one to two generations to a common ancestor, the mutation could be a recent one and management may be attainable. If the closest common ancestor traces far back in a pedigree, or is an imported or foundation animal for the breed, then the gene is widespread and management will be difficult.

**A Different Approach**

With an autosomal recessive gene, the closest common ancestor is the ancestor or ancestors that trace back from all *parents* of affected individuals. All parents of affected individuals are carriers and must carry one copy of the defective gene. With autosomal dominant genes, the closest common ancestor must trace back from each affected individual. Although we would expect the parent that carries the defective dominant gene to be affected, some dominant genes show incomplete penetrance. If it cannot be identified which parent passed on the defective dominant gene, the one that is closest in relationship to other affected individuals, indicates the minimum age of the gene in the population.

The closest common ancestor for an x-linked recessive gene is the common ancestor of mothers of affected males, and both parents of affected females.

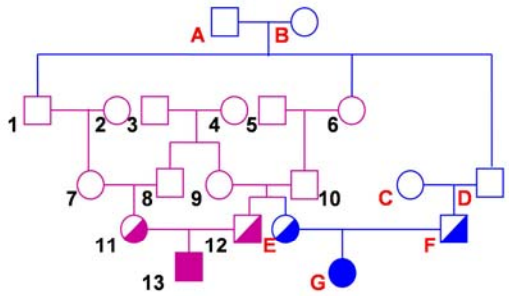
Two separate mutations producing a defective gene could possibly explain the appearance of two distantly related affected individuals, but it is improbable that the same spontaneous mutation would occur twice in the same breed within a short time span. Therefore, tracing the common ancestors of all confirmed affected dogs is valid.

The closest common ancestor analysis usually identifies a prolific male, or a prolific breeding pair. This is because prolific individuals will become the central convergence points for bringing families together in ancestral pedigree analysis. Some common ancestors will be identified due to their being bred to carriers, or being a "pedigree shortcut" (the shortest generational connection) between true ancestral carriers and affected individuals.

**Going Way Back**

Additional affected individuals may change the closest common ancestor to one further back in the population, thus increasing the minimum age of the defective gene. The addition of each confirmed affected case can dynamically alter the closest common ancestor and pedigree maps so that the prior ancestors may not even be included in the new pathway (see diagram on right). Therefore, the identification and publication of closest common ancestors may be more detrimental than helpful. Unfounded accusations of carrier status from such an analysis can result in quality breeding animals being spayed and neutered, and in negative influences on breeders and the breed.

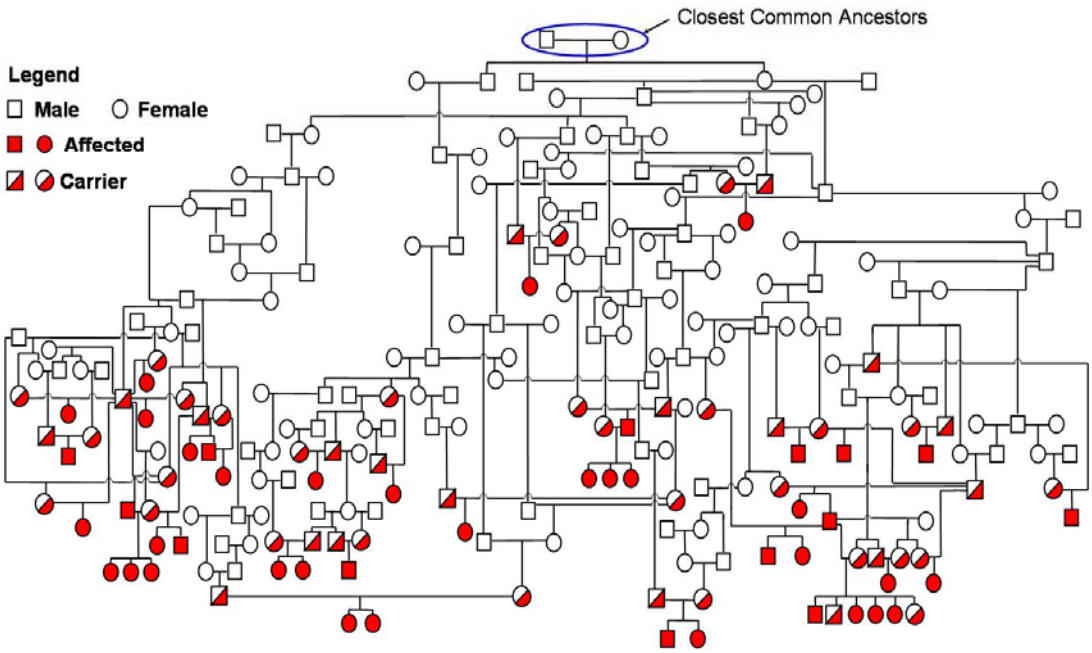
A breed is not served by focusing on ancestors, who may or may not be carriers, and are usually so far back in pedigrees that their influence on the breed cannot be modified. The focus in managing genetic diseases must be on today's breeding dogs. Genetic testing, or relative-risk analysis based on open health registries (such as CHIC, found at www.caninehealthinfo.org), provides selective pressure against defective genes.




The following is a simple example of why you should not try to predict that the closest common ancestor is a carrier.

Male 8 and Female 9 are full-siblings. Their parents, 3 & 4, are the closest common ancestors who could pass down a recessive gene through 11 and 12 to double up on affected male 13. Now let's say another affected individual comes along, and for the sake of clarity, we will label her and her (additional) ancestors with letters.

Female E is a full-sib to 12, and can therefore still bring the gene down from 3 or 4. However, Male F doesn't share common ancestors 3 or 4 with the other obligate carriers. Instead, the closest common ancestor to all obligate carriers is now either A or B, through the full-sibs 1, 6, and D. As you can see, neither 3 nor 4 is needed to explain the affected status of 13 and G. Therefore, they are not the progenitors for the gene, and likely not carriers (although this cannot be proven from the information provided). Likewise, littermates 8 & 9 are not suspect (at this time) of being carriers. Additional affected dogs could shift the closest common ancestor in another direction.




This is a pedigree of a breed-related autosomal recessive genetic disorder. Mating lines connect the male and female symbols from the sides, and offspring have lines that connect to the top of the symbol. Affected dogs always have carrier (or affected) parents, and all offspring are carriers. The closest common ancestors for this gene show that the gene is old, and widespread in the population.