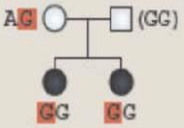
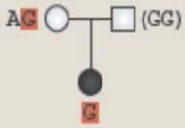
Linkage Analysis vs Association Analysis

Linkage studies are used when you have pedigrees of related individuals. Meanwhile the traits (phenotype) perform in some but not all of the family members. Thus, all the members including parents and children, no matter that wether they do or do not perform the phenotype, they have the same alleles. Linkage studies are always used for penetrant phenotypes. (If you have the allele, you have a strong probability of performing the phenotype.) They can identify rare alleles that are present in small numbers of families, usually due to a founder mutation.Linkage is how we find a mutation associated with a trait(disease). Association studies are used when pedigrees are not available(Not necessarily); Statistical test is a logistic regression or a related test to determine the trends. It is always used when the phenotype is less penetrate. Association studies are how we find common, low penetrance alleles (mutation) that increase susceptibility of a disease.





Property of mapping approach	Linkage analysis	Association analysis
Data type studied	Relatives	Unrelated or related individuals
Relevant parameter	Recombination fraction	Association statistic
Range of effect detected (linkage or association)	Long (≤5 Mb)	Short (≤100 kb)
Number of markers required for genome-wide coverage	Moderate (500–1,000)	Large (>100,000)
Statistics used	Cumbersome (requires tailor-made likelihood methods)	Elegant; can use the range of classical statistical tools
Dealing with correlated markers	Pose problems in presence of ungenotyped individuals	Can be handled efficiently
Biological basis of approach	Observe (or infer) recombination in pedigree data	Exploit unobserved recombination events in past generations
Dealing with allelic heterogeneity	Not a problem	Reduces power
Detecting genotyping errors	Potentially detected as Mendelian inconsistencies	Potentially detected only in family data, but not in case–control data
Most suitable application	Rare, dominant traits	Common traits

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"Linkage is actually looking at physical segments of the genome that are associated with given traits. Association studies go from the other direction, saying, ‘given different pieces of the genome, can we then look for different traits that are associated with those

different segments of genome?’ So we know that individuals don’t have the same genetic makeup. They have the same DNA, but the DNA has different sequences or is expressed differently, and that’s what causes differences among different individuals. So the question is that if we have a trait, particularly a disease trait, can we find and associate that with differences among individuals in the population? So a linkage study is just saying, ‘can we say that there is an association between pieces of the DNA and a trait of interest?’ Association studies are saying, ‘what are the differences we see?' in order to find differences in the traits, particularly disease traits, among different individuals." —Professor Allen Moore