GENETICS

AN UTTER REFUTATION

4.12.2006

I am slow in commenting on a paper that has already been published earlier this year – Joe Terwillingers vivid refutation of the fundamental theorem of the hapmap proponents that

> if a marker is in tight LD with a polymorphism that directly impacts disease risk, as measured by the metric r^2, then one would be able to detect an association between the marker and disease with sample size that was increased by a factor of 1/r^2 over that needed to detect the effect of the functional variant directly

I cannot comment on the statistical proof but fear from my recent experience with Crohn and asthma tags that he may be right with his assumption: Even marker in high LD with the functional variant may not show any association at all. These may be bad news for all those currently running large screening programs with hapmap based variants believing that P(A|BC)=P(A|Bc)=P(A|B), yea, yea.

Addendum

Tag SNPs also do not work with CNVs