

Who appropriated the PARK loci, and where were the geneticists?

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Despite, or perhaps because of technological advances in genotyping, sequencing and computational biology, some of the basic theoretical concepts in human genetics, such as linkage and association between pedigree and population mapping, are being blurred. In parallel, classical linkage mapping for monogenic disease has been overtaken by higher-resolution genome-wide association. Thousands of loci have been nominated but a paucity of functional gene variants, with a defined attributable risk (personal or population-specific), now challenges the fundamental thesis (CVCD) on which these studies were based. Ironically, several companies sell prediction of individual disease risk based on SNP variants that have no utility to predict it. However, for a database to be more than a list of genomic variants, proof of pathogenicity, risk and penetrance must be defined for all genetic variation. The nomenclature for pathogenic mutations in monogenetic disease once embodied these concepts and provides a framework. As next-generation technologies come on-line the challenge is to help steer curation, discovery and its application i.e. to predict risk, assign diagnosis and guide translational neuroscience/therapeutic development. In Parkinson's disease, data from next-generation sequencing, GWAS, population and pedigree genetics, used to assess the pathogenicity of variants in disease, will highlight some of the pitfalls.