PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

Simplifying genetic disorders

ArticleInfo		
ArticleID	:	3787
ArticleDOI	:	10.1186/gb-spotlight-20001005-02
ArticleCitationID	:	spotlight-20001005-02
ArticleSequenceNumber	:	224
ArticleCategory	:	Research news
ArticleFirstPage	:	1
ArticleLastPage	:	3
ArticleHistory	:	RegistrationDate : 2000–10–05 OnlineDate : 2000–10–05
ArticleCopyright	:	BioMed Central Ltd2000
ArticleGrants	:	
ArticleContext	:	130591111

David Bradley

Simple genetic diseases, such as cystic fibrosis and thalassaemia are just that - simple. A single gene underlies them. Finding it is like climbing a steep hill - hard work but straightforward. Complex disorders, such as asthma and type 2 diabetes, by contrast, have many components, which makes finding a cause more like scaling Everest - far harder, requiring more specialist equipment and the strong possibility of failure.

In work published in the October issue of Nature Genetics, University of Chicago researchers have cleared a path to studying the genetic foundation of type 2, or non-insulin-dependent diabetes mellitus (NIDDM). In a study of a Mexican-American population and two white populations (Finns and Germans) they have found that small genetic variations, called single-nucleotide polymorphisms (SNPs), in a particular gene tend to occur more often in diabetics than in healthy relatives. Although finding a common genetic variation in family groups affected by simple genetic disorders is implicit, a gene implicated in a population with a complex disease could provide a potential new target for gene therapy. "Variation in this gene is associated with a threefold increased risk in the groups studied," explains lead researcher Graeme Bell.

Bell and colleagues have used clever detective work coupled with brute force to positionally clone this gene, which seems to affect susceptibility to type 2 diabetes. They point the accusing finger at a gene encoding calpain-10, a ubiquitous cysteine protease, and demonstrate that specific combinations of polymorphisms in this gene are associated with disease risk. "These findings propose a fundamentally new hypothesis for diabetes research," says Leonid Kruglyak of the Fred Hutchison Cancer Center, Seattle, writing in an accompanying News and Views article. Superficially, the enzyme has no apparent connection with the disease but Bell's colleagues, led by Leslie Baier, have reported that variation in calpain-10 is associated with insulin resistance, so there are already clues as to a possible underlying mechanism.

Some observers are cautious of proclaiming triumphs at this stage, suggesting that a new style genetics is needed to understand complex 21st century problems. "How well [Bell's results] will stand up to future tests and extrapolation remains to be seen," explains Kenneth Weiss of Penn State University. "We need to see if it is confirmed in biological as well as epidemiological contexts," he adds, "there are lots of genes we don't know about and perhaps our ideas about diabetes physiology are wrong." Bell counters that "although we don't have information on every population in the world yet, such studies are in progress ... This is just the first step."

The research does represent a shift in the landscape of genetic diseases. "Studies are not going to be easy," says Bell "but they are not impossible and each locus will present its own challenges." Kruglyak feels the path is clearer, if only because of the 'psychological factor' of showing it can succeed. How important it will be in the overall problem of diabetes, or how often this kind of success will occur in other diseases, will emerge in time.

References

1. *Nature Genetics*, [http://www.genetics.nature.com]