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REPORT ON THE SECOND INTERNATIONAL MEETING, Cambridge, UK, 1–3 April 2000

Genetic Epidemiology of Complex Traits

When you work in a field such as genetic epidemiology, which is simultaneously specialised but also broad ranging, how do you keep abreast of the latest thinking? The Second International Meeting on the Genetic Epidemiology of Complex Traits took place in Cambridge, UK, 1–3 April 2000 with the aim of assembling leading researchers all under one roof. Over 150 people attended the conference, 29 posters were displayed and 27 talks were given. Attendees came from the USA, Australia, Europe and Asia, representing academia and industry.

In response to suggestions from the first meeting, the three-day conference was divided into an introductory day and the main conference.

Day 1 provided an introductory overview to the essentials of genetic epidemiology to bring everyone up to scratch and to clarify terminology, whilst days 2 and 3 covered twin and family studies, QTL analysis, advances in TDT and, after all the theory, an afternoon of clinical research examples, debate and question time.

Some of the highlights of the weekend included John Blangero on anticipated future methods such as functional genomics for handling sequence data through the statistical identification of functional polymorphisms; Lon Cardon on the identification of QTLs using combined linkage and association tests, and a humorous debate between Robert Elston and Pak Sham on the need for formal guidelines to significance testing in genetic studies.

A recurring theme at the conference reflected a basic point that a strong association between alleles at two loci (loosely referred to as 'linkage disequilibrium' or LD) does not necessarily mean they are in close proximity to one another on a chromosome. For example, Andy Collins presented a study of combined single nucleotide polymorphism (SNP) and other marker data sets to investigate the relationship between LD and physical map distance. This powerfully illustrated how heterogeneous this relationship can be across different sections of the genome, with the Southampton group finding LD extending far further (263–526 Kb) than Kruglyak's influential simulation study originally suggested (about 3 Kb). This is likely to be good news for the implied reduction in the total number of markers required for genome-wide scans, but raises a major problem for the accurate positional cloning of disease loci. John Blangero vividly posed this problem with a simulated example, whereby tests for association between loci detected a larger genetic signal for a QTL with a heritability of only 10% but in high LD with a marker, compared with that of a QTL in low LD but with an 80% heritability.

These issues have refocused interest on the value of the combined tests of linkage and association, which interestingly was the original rationale for developing the transmission/disequilibrium test (TDT). Cathryn Lewis (Guy's, London) and Norman Kaplan (Research Triangle Park, North Carolina) provided both expert overview and detailed insight into just how far the TDT has been extended since the test based upon a triad of affected child and both parents, first proposed by Spielman and Ewens in 1993. A promising new development outlined by Kaplan is the PDT – pedigree disequilibrium test, treating the family rather than individuals as the independent sampling unit. Lon Cardon (Oxford University) presented a regression-based method that identifies to what extent observed phenotype–genotype association for continuous traits is due to linkage, by studying the relationship between linkage and LD parameters. Applied to angiotensin-converting enzyme (ACE) levels and genetic data, this new approach provided promising evidence for advances in positional fine mapping.

Clinical research examples were presented on Type II diabetes (Mark McCarthy, St Mary's Hospital, London), osteoporosis (Alex MacGregor, St Thomas' Hospital, London) and cardiovascular disease (Harold Snieder). The conference was brought to a close with a question and answer session chaired by Tim Spector with an expert panel of Chris Amos, John Blangero, David Clayton, Robert Elston, Norman Kaplan and Pak Sham.

Details will be found at www.blacksci.co.uk.

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