GENETICS

BUSY TIMES

8.06.2007

The last 2 weeks have been extremely busy in population genetics – probably more advances than in the 2 decades before with 2 dozens GWAs (genome wide association scans) being published:

Nature Genetics published on
1 Apr prostate cancer: rs1447295/rs6983267 DQ515897
26 Apr type II diabetes: TCF7L2, CDKAL1
1 May Crohns disease: CARD15, IL23R, ATG16L1, PHOX2B, NCF4, 16q24.1 (FAM92B)
13 May obesity: FTO
27 May breast cancer: FGFR2
27 May breast cancer: rs13387042, rs3803662 (TNRC9?)
6 June Crohns disease: IRGM, NKX2-3, PTPN2, 1q, 5p13
6 June type 1 diabetes: 12q24, 12q13, 16p13, 18p11
10 June celiac disease: KIAA1109-TENR-IL2-IL21
1 July type 2 diabetes: WFS1
1 July type 2 diabetes: TCF2
1 July prostate cancer: 17q (TCF2)

Nature published on
26 May bipolar disorder: PALB2, NDUFAB1, DCTN5, KCNC2, GABRB1
dto coronary artery disease: CDKN2A, MTAP, MTHFD1L, ADAMT217
dto Crohn's disease: CARD15, 5q31, IL23R, ATG16L1, ZNF365, IRGM, MST1, NKX2-3, PTPN2, HLA, TFNAIP3, STAT3, CD40LG
dto hypertension: RYR2?, CHRM3?
dto rheumatoid arthritis: PTPN22, CTLA4, IL2RA, TNFAIP2, GZMB, KAZALD1, HLA
dto type 1 diabetes: HLA, PTPN22, IL2RA, CTLA-4, IFIH1, ERBB3?, PTPN11?, CD69?
dto type 2 diabetes: PPARG, KCNJ11, TCF7L2, FTO, CDKAL1, CDKN2A, IGF2BP2
27 May breast cancer: FGFR2, TNRC9, MAP3K1, LSP1
1 July atrial fibrillation: PITX2

Science published on
1 June type II diabetes: CDKN2A, IGF2BP2, HHEX, SLC30A8, GCKR

1 June type II diabetes: CDKAL1, CDKN2A, IGF2BP2, HHEX, SLC30A8
1 June type II diabetes: CDKAL1, CDKN2A, TCF7L2, SLC30A8, HHEX, FTO, PPARG, KCNJ11
8 Jun coronary heart disease: CDKN2A
8 Jun myocardial infarction: CDKN2A

American Journal Human Genetics published on
8 Mar progressive supranuclear palsy: MAPT, DDB2/ ACP2
7 May type II diabetes: TCF7L2

Molecular Psychiatry published earlier on bipolar disease and DGKH, a reminder not to forget the ~10 or so pooling studies, e.g. for RA describing HLA, PTPN22 + MAGI3, for asthma describing ATPAF1 + IL1RAPL2 or for lung cancer describing KLF6.

It will probably take a long time to figure out what this will mean for an individual. I expect genetics to be only useful if it will reveal targets for new drug treatment or if it will help to define subgroups that benefit from a dedicated treatment.

There is clearly a bias towards common results as all these studies relied more or less on the same SNP sets ;-) One of the master questions, however, are there any disease hubs? The Wellcome Trust Case Control Consortium already noticed

> We observed association at many previously identified loci, and found compelling evidence that some loci confer risk for more than one of the diseases studied.

There might still be many artifacts as there are errors in assignment of SNPs as I showed here earlier. Only rheumatoid arthritis had sex specific effects which comes quite unexpected.

There could be also stratification effects introduced by the control population (will come back to that later). And of course, none of the papers showed the genetic architecture of a disease. Like the early expression experiments – these studies show only the top hits. This might be quite irrelevant as I expect mainly combinations of variations to be influential.

BTW, a disappointing situation as that there is virtually no contribution of German science. Yea, yea.

Addendum

15-6-07 The Lancet comments “Big step for science, small step for medicine”. I agree.