Selection of the COMMON SNPs on the iCOGS Array

Selection of Common SNPs

Published GWAS hits were taken from the NHGRI GWAS catalogue (May 2010), including SNPs at $P<10^{-7}$ with any trait. The most strongly associated SNPs from GWAS for four other cancer types and other related phenotypes were also included (see table 1). The common SNPs also include a set of tagging SNPs covering 111 DNA repair genes, SNPs associated with allelic imbalance, ancestry informative markers (AIMs) and SNPs on MT and Y covering the major haplogroups.

Fine-mapping SNPs

For the common allocation, four regions (8q24, ESR1, CDKN2A and TERT) were included, aiming to cover the loci associated with any cancer type.

For each locus, we defined intervals around the most strongly associated SNP (or SNPs, if there was evidence of more than one signal). We defined intervals based on Hapmap (CEU), such as to include all SNPs with $r^2>0.1$ with the target SNPs. We then identified polymorphisms in each interval from the 1000 genomes dataset (CEU) available in April 2010, together with Hapmap phase III. We identified all variants for which the minor allele was called at least twice, and for which the Illumina Design score was >0.8. From the resulting set of typeable SNPs, we selected all SNPs with $r^2>0.1$ with any of the target SNPs, together with a set of SNPs that tagged all the remaining SNPs at $r^2>0.9$.

Table 1. Summary of SNPs available in the COMMON allocation

Category	List	Supplied by	SNPs on iCOGS
PopStructure	AIM	Jonathan Tyrer	735
PopStructure	Y	Jim Wilson	82
PopStructure	MT	Jim Wilson	50
Fine-mapping	Fine-mapping	Maya Ghoussaini/Alison Dunning	3608
GWAS	Published_cancer	DE/Diether Lambrechts	136
GWAS	Published_other	DE/Diether Lambrechts	375
GWAS	Lung cancer	Richard Houlston	687
GWAS	Endometrial cancer	Mandy Spurdle	1547
GWAS	Melanoma/naevi	Tim Bishop	1227
GWAS	Melanoma/naevi	Stuart MacGregor	498
GWAS	Testis cancer	Clare Turnbull	742
GWAS	Age at menarche	Cathy Elks	2271
GWAS	Age at menopause	Cathy Elks	2552
GWAS	Telomere length	Karen Pooley	1614
GWAS	Mammographic Breast Density	Rulla Tamini/MODE	1829
GWAS	Mammographic Breast Density	John Hopper	459
GWAS	Serum oestradiol level	Deborah Thompson	1235
GWAS	Serum testosterone level	Deborah Thompson	1257
GWAS	Serum SHBG level	Deborah Thompson	1218
GWAS	Other hormone level	Deborah Thompson	259
GWAS	Endometriosis	Georgia Chenevix-Trench	30
Candidate	DNA Repair	Zsofia Kote-Jarai	2343
Candidate	Allelic Imbalance	Jacques Simard	465
Candidate	Cancer SNP Panel		1168
Candidate	Rare Variants	Mandy Spurdle (ENIGMA), Melissa Southey, Zsofia Kote-Jarai	107

Table 2. Fine-mapping regions (COMMON)

Region	Chromosome	Interval	Target SNP(s)	SNPs on iCOGS
CDKN2A	9	21,600,000-22,200,000	rs7023329, rs101970, rs11515, rs7023329 rs10757278 rs10757257 rs2218220 rs4636294	686
ESR1	6	151,600,000-152,650,000	rs2046210 rs3757318 rs3020314	933
8q24	8	127,630,906-129,184,370	rs13281615 rs13262406 rs1562430 rs12543663 rs10086908 rs1016343 rs13252298 rs6983561 rs620861 rs6983267 rs10090154 rs16901979 rs13254738 rs7000448	1870
TERT	5	1,280,000-1,415,000	rs401681 rs2736109 rs3816659 rs33964002 rs2853669 rs2736100	119