

Spring '07 Seminar Series

Detecting imprinted genes in the human genome using genotyping microarrays

Katharine Pollard

Department of Statistics, UC Davis

Date : April 13 (Friday)

Time : 11 am - 12 noon

Abstract

Genomic imprinting is an epigenetic process in which the copy of a gene inherited from one parent (maternal or paternal) is consistently silenced or expressed at a significantly lower level than the copy from the other parent. In an effort to begin a systematic genome-wide screen for imprinted genes, we analyzed differential allelic expression at 4000 bi-allelic protein coding sites in the human genome. We used the presence of both over- and under-expression of the reference allele compared to the alternate allele to identify candidate imprinted genes. After stringent quality control filtering, we found 61 genes with at least two-fold differential allelic expression plus “flipping” of which allele was more highly expressed among different heterozygous samples. Twenty flipping genes were genotyped and assayed for differential allelic expression in an independent data set of lymphoblastoid cell lines from two CEPH pedigrees. We confirmed that PEG10 is imprinted (paternal expression) and identified two genes for which classical imprinting is the most likely explanation for the observed patterns of differential allelic expression across the pedigrees: ZNF331 (paternal expression) and TBC1D4 (maternal expression). Data for an additional six genes are consistent with imprinting, but other potential causes for differential allelic expression have yet to be eliminated by empirical tests. With samples of mRNA from appropriate tissues, this technology could identify an exhaustive catalog of genes that undergo genomic imprinting. The major statistical challenge is to develop an actual test for “flipping” of differential allelic expression to be used in place of the ad hoc fold-change threshold described above. The prototypical flipping gene expression pattern will be described and a few preliminary ideas presented.