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Statistical genetics, human metagenome, and drug discovery

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Statistical genetics is a research field that evaluates causality of human genetic variations on diseases, using statistical and bioinformatics approaches. Recent development of high-throughput genome sequencing and genotyping technologies, such as whole genome sequencing by next generation sequencers, has provided human disease genome data of hundreds of thousands of the subjects. Large scale disease risk association analyses successfully identified comprehensive catalogues of genetic susceptible loci that are linked to human diseases. However, little is known regarding how to develop methodology to integrate large-scale human genetic study results with diverse biological resources, to which statistical genetics should contribute. Especially, how to interpret and integrate human meta-genome data is becoming an important research topic.

We have developed such methods and applied to a pioneering example of large-scale genetic association studies on a variety of human complex traits. Application of linkage-disequilibrium score regression (LDSC) method to the genome-wide association study (GWAS) results of 58 hematological and biochemical traits of >160,000 Japanese population successfully achieved integration of genetic and epigenetic data (e.g., causal inference of human regulatory T cells on autoimmune thyroiditis)(*1*, *2*). Integration of human genetic and epigenetic data with drug resources could point potentially drug seeds for repositioning (e.g., CDK4/6 inhibitors for rheumatoid arthritis)(*3*, *4*). We would like to introduce our ongoing approaches to visualize, integrate, and interpret the human microbiome data with human genome recourse.

【References】

(*1*) Kanai M, *et al.* Genetic analysis of quantitative traits in the Japanese population links cell types to complex human diseases. Nat Genet In Press.
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(*3*) Okada Y, *et al.* 2014. Genetics of rheumatoid arthritis contributes to biology and drug discovery. Nature 506, 376–381.
(*4*) Rainer M, *et al.* Multi-ancestry genome-wide association study of 520,000 subjects identifies 32 loci associated with stroke and stroke subtypes. Nat Genet In Press.