Requirements for the clinical application of human genome variation data

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Genotype data are now available for 500 thousands – 1 million SNPs for each subject. In addition the technologies to obtain omics information are in progress. Researches are aiming at increasing the efficacy of new drug development and optimal individual drug therapy using such information. However, there is some warning that the information about human individual variation should be applied to the clinical practice with caution. Although the aim of the development of new drugs and the treatment by use of them is the maximum safety and the maximum efficacy, 100% safety and efficacy cannot be achieved. We therefore should aim at the maximization of the safety and efficacy since humans vary between subjects. To achieve that aim, statistical analyses in which biases and confounders are excluded as much as possible are inevitable. We should keep in mind that false-positive association results are more likely when we have large amount of information. We have proposed, as the requirements for the application of genetic variation data to clinical practice, that both (a) clinical validity and (b) clinical utility are necessary. To achieve (a), confirmation of the result of the first association study by replication using independent sample is necessary. To achieve (b), the construction of the algorithms for the use of genetic variation to clinical practice followed by the estimation of the efficacy of the algorithm is required. Based on the criteria as stated above, we have performed individualized medicine for more than 400 patients with rheumatoid arthritis concerning either effects or adverse events with methotrexate and sulfasalazine using genotype or haplotype data of MTHFR and NAT2 genes.