Abstract of Presentation

Note: This paper should be typed in "Times New Roman" of 12pt.

<u>Presentation Title(Should be no more than 20 words):</u>

Pharmacogenomics for rheumatic diseases

<u>Abstract :</u>

In Institute of Rheumatology, Tokyo Women's Medical University, we have been performing, for 7 years, a large cohort study of rheumatoid arthritis patients called IORRA in which about 5,000 patients have been enrolled. We have analyzed genomic variations in part of the patients, and tried to associate SNPs with the drug responses. The largest problem was under which conditions we can use genetic data in clinical practice. About two year ago, we started the project in which the drug use is based on patients' genetic variations. This was because the following 3 criteria necessary to translate the genomic evidence into clinical practice were fulfilled in 4 items. The 3 criteria were (a) Result of the test of the association between a genomic variation and a phenotype (for example adverse events to a drug) proves to be significant by a valid statistical method. (b) The conclusion of (a) is replicated using independent samples, and the result of the replicated study proves to be essentially the same as the previous result. (c) Algorithm for the application of the genomic evidence to the medical intervention can be constructed, and the application is expected to give beneficial outcome to the patients. The 4 items were (1) Prediction of the adverse events of sulfasalazine (2) Prediction of the adverse events of methotrexate (3) Prediction of the efficacy of methotrexate (4) Prediction of the complication of amyloidosis. Each of the 4 items has fulfilled the 3 criteria as listed above. So far, about 240 rheumatoid arthritis patients have been enrolled. In all the 4 items, replication studies have been published and most of the reports supported our findings. Although it is too early to examine the benefit of our personalized drug delivery system, the following data strongly suggest that it is beneficial to the patients. Thus, after the start of the project, 4 patients have been hospitalized because of the severe adverse events by sulfasalazine, and, in 4 of them, the occurrence of the severe adverse events would have been avoided if they were enrolled in the personalized drug delivery project. From none of the patients who have been enrolled in the project, severe adverse events have occurred. The data thus far suggest that the drug administration based on genomic data is beneficial to the patients if it is performed in accordance with the valid road map.