Genetic backgrounds of myocardial infarction

Toshihiro Tanaka

RIKEN Center for Genomic Medicine

Myocardial infarction (MI) is a disease of vessels that feed cardiac muscle, called coronary artery. Immediately after the occlusion of the vessel by complex causes including inflammation, necrosis of myocardium occurs, resulting in cardiac dysfunction with various degrees. Since cardiovascular diseases including MI represent more than 15% of the cause of death in Japanese population and more than 20% of total medical expenses in Japan, it is socially important to reveal mechanism of this disorder. To reveal genetic backgrounds of MI, we analyzed approximately 3,000 cases and 3,000 general populations. By a large scale SNP association analysis, we found two SNPs in *LTA* were associated with the risk of MI. One of the significant SNPs increased expression level of LTA protein, and the other modified functions of this protein. Since two SNPs were in complete linkage disequilibrium, we concluded increased expression level of functionally modified LTA protein leads to risk of MI. Next, we identified a protein, galectin-2, as a binding partner of LTA protein. Genetic investigation into the gene encoding galectin-2, *LGALS2*, revealed one SNP in this gene confers risk of MI. This SNP influenced the degree of inflammation by regulating extracellular amount of LTA protein. This result indicated the importance of LTA cascade in the pathogenesis of MI. In total, we have so far identified six genes that were associated with MI. Although each variation carried modest odds ratio (~1.4), their combination increased odds ratio up to nine, indicating that multiple genetic factors in combination contribute greatly to its pathogenesis.