Searching for IgA Nephropathy Candidate Genes: Genetic Studies Combined with High Throughput Innovative Investigations

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Abstract

Idiopathic IgA Nephropathy (IgAN) is the most common biopsy-proven glomerulonephritis worldwide. All races with the exception of Blacks and Indians are involved. Families with two or more relatives affected by IgAN may be observed in 15–20% of pedigrees of IgAN patients. Genome wide linkage study has been considered the most promising approach to identify IgAN susceptibility genes. Therefore, some European investigators constituted the European IgAN Consortium which was initially funded by the European Union. Data from linkage analysis studies, family association studies and case-control association studies are reported. To date, the Consortium has identified two loci (located on chromosomes 4q26–31 and 17q12–22), in addition to the previous study which described the first IgAN locus on chromosome 6q22–23. The functional mapping of genes involved in the disease proceeds from the identification of susceptibility loci identified by linkage analysis (step 1) to the isolation of candidate genes within gene disease-susceptibility loci, after obtaining information by microarray analysis carried out on peripheral leukocytes and renal tissue samples (step 2). Then, the process will proceed from the design of RNA interference-agents against selected genes (step 3) to the application of systematically tested effect of RNA agents on functional cellular assay (step 4). The above combined high-throughput technologies will give information on the pathogenic mechanisms of IgAN. In addition, these data may indicate potential targets for screening, prevention and early diagnosis of the disease and more appropriate and effective treatment.