Development of Therapeutic Cancer Vaccine through Cancer Genomics Approach: Construction of Clinical Research Network in Japan

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cDNA microarray technologies have enabled us to obtain comprehensive data for gene expression profiles of human cancers. To isolate novel molecular targets for diagnosis (predictive biomarker for the efficacy of treatment as well as tumor marker) and for treatment of cancer (molecular-targeting drug, cancer vaccine, antibody, small molecular compound, siRNA, and functional peptide), we constructed expression profile database of cancer cells originated from various organs with their corresponding non-cancerous tissues using a cDNA microarray that consists of more than 30,000 genes. These experiments disclosed a number of genes that appeared to be involved in development and/or progression of cancers in those tissues. We also constructed expression profile database for 30 normal human tissues/organs. So far, we have analyzed approximately 1,400 clinical cancer samples of the liver, pancreas, stomach, colon, esophagus, bile duct, uterus, lung, ovary, kidney, urinary bladder, testis, prostate, breast, and soft tissues as well as acute and chronic myeloid leukemias. We have selected hundreds of candidate genes by the following criteria; (1) gene expressions were transactivated in a large proportion of cancer tissues in comparison with their corresponding normal tissues and (2) expression was not observed or hardly detectable in any of important vital organs. The further functional analysis of these molecules identified dozens of genes that are likely to function as oncogenes in various cancers. The suppression of expression of such genes with siRNA induced cell cycle arrest, apoptosis, or suppression of anchoring-dependent cell growth. We screened 9- or 10-amino-acid peptides corresponding to a part of such oncoantigens that induce cytotoxic T lymphocytes that would specifically kill cancer cells in an HLA-A restricted manner. We have already isolated nearly 60 peptides (HLA-A02 or HLA-A24 restricted) derived from about 50 oncoantigens and started translational research using some of them in August 2006. We have organized a group that performs translational research and now consists of more than 40 hospitals (Cancer Peptide Vaccine Translational Research Network = Captivation Network). We are now running more than 30 different protocols and more than 700 cancer patients have been enrolled by the end of August, 2009. The promising clinical data of our translational research will be introduced in the meeting. These results indicated that systematic expression analysis should be a very effective approach for identification of molecules that are potential targets for development of novel therapeutic drugs.