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CANCER GENOMICS FOR TARGETED THERAPEUTICS

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In recent years, as exemplified by Gleevec, Herceptin, Avastin, and others, targeted therapeutics is revolutionizing cancer therapy. Systematic and comprehensive characterizations of genome-wide expression patterns might reveal new critical molecular factors that can be used in the targeted cancer therapeutics. We have constructed an extensive database containing genome expression profiles of surgical specimens from cancer patients using Affymetrix GeneChip system. Mining of the database allowed us to identify many novel genes that are differentially expressed in cancerous tissues, and subsequent experimental validation processes of the genes revealed new cancer-associated factors with therapeutic potentials. As an example, we identified a novel gene encoding a secreted protein that was dramatically upregulated in several human cancer types including pancreatic adenocarcinoma. Over-expression of the gene enhances cell proliferation, motility and invasiveness *in vitro* through specific intracellular signaling pathways and promotes tumor growth *in vivo*. Treatment of cancer cells with the protein promotes cell motility and invasiveness, whereas treatment with antibodies diminishes those abilities. Another utilization of the database is to identify potential diagnostic markers by examining cancer-specific expression of soluble proteins. To this end, we have built an expression profile database that enables us to compare both differential expression and absolute expression of a protein in a family across many human cancer types and, therefore, to easily identify potential marker genes for a specific cancer type.

Key Words: Cancer, Expression profiling, Novel target, Therapeutic antibody, Biomarker