Transcriptional signature induced by a metastasis-promoting c-Src mutant in a human breast cell line.

Abstract:

Deletions at the C-terminus of the proto-oncogene protein c-Src kinase are found in the viral oncogene protein v-Src as well as in some advanced human colon cancers. They are associated with increased kinase activity and cellular invasiveness. Here, we analyzed the mRNA expression signature of a constitutively active C-terminal mutant of c-Src, c-Src(mt), in comparison with its wild-type protein, c-Src(wt), in the human non-transformed breast epithelial cell line MCF-10A. We demonstrated previously that the mutant altered migratory and metastatic properties. Genome-wide transcriptome analysis revealed that c-Src(mt) de-regulated the expression levels of approximately 430 mRNAs whose gene products are mainly involved in the cellular processes of migration and adhesion, apoptosis and protein synthesis. 82.9% of these genes have previously been linked to cellular migration, while the others play roles in RNA transport and splicing processes, for instance. Consistent with the transcriptome data, cells expressing c-Src(mt), but not those expressing c-Src(wt), showed the capacity to metastasize into the lungs of mice in vivo. The mRNA expression profile of c-Src(mt)-expressing cells shows significant overlap with that of various primary human tumor samples,
possibly reflecting elevated Src activity in some cancerous cells. Expression of c-Src(mt) led to elevated migratory potential. We used this model system to analyze the transcriptional changes associated with an invasive cellular phenotype. These genes and pathways de-regulated by c-Src(mt) may provide suitable biomarkers or targets of therapeutic approaches for metastatic cells. This project was submitted to the National Center for Biotechnology Information BioProject under ID PRJNA288540. The Illumina RNA-Seq reads are available in the National Center for Biotechnology Information Sequence Read Archive under study ID SRP060008 with accession numbers SRS977414 for MCF-10A cells, SRS977717 for mock cells, SRS978053 for c-Src(wt) cells and SRS978046 for c-Src(mt) cells.