

PubMed

Display Settings: Abstract[BMC Med Genomics](#). 2008 Oct 10;1:49.

The molecular basis of genistein-induced mitotic arrest and exit of self-renewal in embryonal carcinoma and primary cancer cell lines.

Regenbrecht CR, Jung M, Lehrach H, Adjaye J.

Max Planck Institute for Molecular Genetics, Department for Vertebrate Genomics, Ihnestr, 73, D-14195 Berlin, Germany. regenbre@molgen.mpg.de

Abstract

BACKGROUND: Genistein is an isoflavonoid present in soybeans that exhibits anti-carcinogenic properties. The issue of genistein as a potential anti-cancer drug has been addressed in some papers, but comprehensive genomic analysis to elucidate the molecular mechanisms underlying the effect elicited by genistein on cancer cells have not been performed on primary cancer cells, but rather on transformed cell lines. In the present study, we treated primary glioblastoma, rhabdomyosarcoma, hepatocellular carcinoma and human embryonic carcinoma cells (NCCIT) with mu-molar concentrations of genistein and assessed mitotic index, cell morphology, global gene expression, and specific cell-cycle regulating genes. We compared the expression profiles of NCCIT cells with that of the cancer cell lines in order to identify common genistein-dependent transcriptional changes and accompanying signaling cascades.

METHODS: We treated primary cancer cells and NCCIT cells with 50 muM genistein for 48 h. Thereafter, we compared the mitotic index of treated versus untreated cells and investigated the protein expression of key regulatory self renewal factors as OCT4, SOX2 and NANOG. We then used gene expression arrays (Illumina) for genome-wide expression analysis and validated the results for genes of interest by means of Real-Time PCR. Functional annotations were then performed using the DAVID and KEGG online tools.

RESULTS: We found that cancer cells treated with genistein undergo cell-cycle arrest at different checkpoints. This arrest was associated with a decrease in the mRNA levels of core regulatory genes, PBK, BUB1, and CDC20 as determined by microarray-analysis and verified by Real-Time PCR. In contrast, human NCCIT cells showed over-expression of GADD45 A and G (growth arrest- and DNA-damage-inducible proteins 45A and G), as well as down-regulation of OCT4, and NANOG protein. Furthermore, genistein induced the expression of apoptotic and anti-migratory proteins p53 and p38 in all cell lines. Genistein also up-regulated steady-state levels of both CYCLIN A and B.

CONCLUSION: The results of the present study, together with the results of earlier studies show that genistein targets genes involved in the progression of the M-phase of the cell cycle. In this respect it is of particular interest that this conclusion cannot be drawn from comparison of the individual genes found differentially regulated in the datasets, but by the rather global view of the pathways influenced by genistein treatment.

PMID: [18847459](#) [PubMed] PMCID: [PMC2577110](#) [Free PMC Article](#)[+ LinkOut - more resources](#)