

Treating Chemoresistance in Chronic Myelogenous Leukemia



DESCRIPTION

Epigenetic disruptions of gene expression such as by DNA methylation and histone modifications are profoundly involved in tumorigenesis. The gene Hypermethylated In Cancer 1 ("HIC1") is frequently inactivated in many human cancers. HIC1 is unique in leukemia because hypermethylation of the gene's promoter region occurs progressively towards the late phases of hematologic malignancies such as chronic myelogenous leukemia (CML) and relapsed acute lymphocytic leukemias following chemotherapy. A key mechanism by which HIC1 suppresses tumorigenesis is through its regulation of the stress and DNA damage

responsive gene, SIRT1. City of Hope investigators have discovered inhibitors of SIRT1 that can be used in the treatment of BCR-ABL drug resistance in chronic myelogenous leukemia (CML).

KEY ASPECTS

- SIRT1 inhibitors include: sirtinol, a sirtinol analogue, splitomicin, a splitomicin analogue, naphthol, a naphthol derivative, an indole, an indole derivative, siRNA, short-hairpin-RNA and antisense RNA.

PUBLISHED DATA

- Yuan H, Wang Z, Gao C, Chen W, Huang Q, Yee JK, Bhatia R, Chen WY. BCR-ABL gene expression is required for its mutations in a novel KCL-22 cell culture model for acquired resistance of chronic myelogenous leukemia. J Biol Chem. 2010 Feb 12; 285(7): 5085-96.

INTELLECTUAL PROPERTY

Title	US Patent Application	Filed
Methods of Treating Chemoresistance and Relapse in Cancer Cells	12/026,554	2/5/2008

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