Treating Chemoresistance in Chronic Myelogeneous 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 myelogeneous 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 myelogeneous 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

INTELLECTUAL PROPERTY

<table>
<thead>
<tr>
<th>Title</th>
<th>US Patent Application</th>
<th>Filed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods of Treating Chemoresistance and Relapse in Cancer Cells</td>
<td>12/026,554</td>
<td>2/5/2008</td>
</tr>
</tbody>
</table>

CONTACT
Matthew Grunseth, M.B.S.
Manager, Office of Technology Licensing
Telephone: (626) 471-7221 | Email: mgrunseth@coh.org

This material is a summary of public domain and non-confidential City of Hope information. Additional material may be disclosed under a confidentiality agreement.

MK 10-035