p57 was first discovered as a Cyclin Kinase Inhibitor (CKI) in the Cip/Kip family

p57 shares structural homology with both p21 and p27

p57 indirectly represses E2F-mediated transcription and promotes differentiation through MyoD activation

The cellular functions of p57KIP2 exceed those of the rest of the CDK inhibitor family.

Most p57 null mutants die after birth and display severe developmental defects

CDKN1C is paternally imprinted and maternally expressed

Multiple epigenetic and genomic alterations of chromosome region 11p15.5 are responsible for Beckwith-Weidemann Syndrome

There are many compounds that can reactivate p57 and have been developed as therapeutic strategies for cancer.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Method of reactivation of p57&lt;sub&gt;KIP2&lt;/sub&gt;</th>
<th>Use in cancer therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flavopiridol</td>
<td>↑ p57&lt;sub&gt;KIP2&lt;/sub&gt; transcription</td>
<td>Phase II trials for hematological cancers</td>
</tr>
<tr>
<td>BMS-387032</td>
<td>↑ p57&lt;sub&gt;KIP2&lt;/sub&gt; by transcription factor E2F1</td>
<td>Phase I trials for solid tumors and B lymphoid malignancies</td>
</tr>
<tr>
<td>HDAC inhibitors (SAHA)</td>
<td>↑ p57&lt;sub&gt;KIP2&lt;/sub&gt; by increasing promoter accessibility</td>
<td>FDA-approved treatment for T cell lymphoma</td>
</tr>
<tr>
<td>Imatinib</td>
<td>↑ p57&lt;sub&gt;KIP2&lt;/sub&gt; transcription</td>
<td>Clinically used to treat CML</td>
</tr>
<tr>
<td>PACAP</td>
<td>↑ p57&lt;sub&gt;KIP2&lt;/sub&gt; transcription</td>
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<tr>
<td>Green tea polyphenols</td>
<td>↑ p57&lt;sub&gt;KIP2&lt;/sub&gt; transcription in non-cancer cells</td>
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</tbody>
</table>

References


