Structure-based design of novel quinoxaline-2-carboxylic acids and analogues as Pim-1 inhibitors

<table>
<thead>
<tr>
<th>IC₅₀ (µM)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.074</td>
</tr>
<tr>
<td>K812</td>
<td>38.9</td>
</tr>
</tbody>
</table>

DATE(S)
du 12 novembre 2018 au 31 décembre 2018

LIEU(X)
Site Grandmont

Faculté de Pharmacie- Philippe Maupas
We identified a new series of quinoxaline-2-carboxylic acid derivatives, targeting the human proviral integration site for Moloney murine leukemia virus-1 (HsPim-1) kinase.

Seventeen analogues were synthesized providing useful insight into structure-activity relationships studied. Docking studies realized in the ATP pocket of HsPim-1 are consistent with an unclassical binding mode of these inhibitors. The lead compound 1 was able to block HsPim-1 enzymatic activity at nanomolar concentrations (IC_{50} of 74 nM), with a good selectivity profile against a panel of mammalian protein kinases. In vitro studies on the human chronic myeloid leukemia cell line KU812 showed an antitumor activity at micromolar concentrations. As a result, compound 1 represents a promising lead for the design of novel anticancer targeted therapies.

**Keywords**
quinoxaline; Pim-1; kinase inhibitor; anticancer targeted therapy.


https://doi.org/10.1016/j.ejmech.2018.04.056
À lire aussi

Vacances de Noël de la Faculté de Pharmacie

Une double conférence organisée par les associations Interpharma et Officina sur "le rôle du pharmacien dans les métiers du marketing, de la vente et du digital" et "L'officine du futur, connectée, robotisée et centrée sur le patient".

La licence pro FoQCos lance sa première Newsletter, FoQCos News!

Haut de page