### Theonellamide F (TNM-F)

**Chemical compound page**

![Chemical Structure](image)

**Category** | **Parameter** | **Description**
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**Compound information** | Citation | From:
Marine antifungal theonellamides target 3β-hydroxysterol to activate Rho1 signaling
Shinichi Nishimura, Yuko Arita, Miyuki Honda, Kunihiko Iwamoto, Akihisa Matsuyama, Atsuko Shirai, Hisashi Kawasaki, Hideaki Kakeya, Toshihide Kobayashi, Shigeki Matsunaga & Minoru Yoshida

**Chemical descriptors**

SMILES:
```
O[C@@H](CC(N[C@@H]1C(N[C@@H]([C@@H]@Br)C=C(C)/C=C/C3=CC=C(Br)C=C3)CC4=O)=O)=O)=O)=O)=O)
```

InChIKey: DAIPMSNAEZFUGV-BIWASUEOBL

**Chemical compound page**

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**Entries in chemical databases**

Pubchem SID: 93375567

**Availability**

Marine sponge (*Theonella* sp.)

**Additional comments**

TNM-F possesses a bicyclic structure bridged by a histidinoalanine residue. Isolation:

**In vitro profiling**

**Target**

3β-hydroxysterols (e.g. ergosterol in wild-type fission yeast)

**Potency**

-
<table>
<thead>
<tr>
<th>Section</th>
<th>Details</th>
</tr>
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<tbody>
<tr>
<td>Selectivity</td>
<td>3β-hydroxyl group of sterols is essential for the binding of a fluorescently labeled derivative in the in vitro lipid binding assay (Fig. 3).</td>
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<tr>
<td>Potential reactivities</td>
<td></td>
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<tr>
<td>SAR</td>
<td></td>
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<tr>
<td>Mechanism of inhibition</td>
<td></td>
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<tr>
<td>Structure of the target-probe complex</td>
<td>The fluorescently labeled derivative does not bind to phosphatidylcholine, phosphatidylethanolamine, phosphatidyserine and sphingomyeline in a lipid binding assay.</td>
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<tr>
<td>Additional comments</td>
<td></td>
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<tr>
<td>Cellular profiling</td>
<td>Validation of cellular target</td>
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<tr>
<td>Validation of cellular target</td>
<td>Lack of ergosterol biosynthetic genes, e.g. erg2 or erg31 and erg32 in the fission yeast <em>S. pombe</em>, conferred resistance to TNM-F (Fig 4). See also Fig 1, Supplementary Table2 and Dataset 2 for full chemical-genomic profiling. Membrane localization of a fluorescent derivative of TNM-A (Fig 3a).</td>
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<tr>
<td>Validation of cellular specificity</td>
<td>No binding protein has been detected in <em>S. pombe</em> (Supplementary Fig. 1).</td>
</tr>
<tr>
<td>Additional comments</td>
<td>Lack of MVD1/ERG19 in the budding yeast <em>S. cerevisiae</em> confers resistance to theopalauamide, a related marine sponge-derived metabolite (Ho, C. H. <em>et al.</em> Nat. Biotechnol. 2009, 27, 369.). TNM-F causes membrane damage following induction of Rho1 signaling. It also increases 1,3-β-D glucan synthesis, unlike nystatin and amphotericin B.</td>
</tr>
</tbody>
</table>