



ONCOLOGY

A small molecule inhibitor of OPA1 GTPase activity with anti-cancer properties

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TRL scale

Discovery

Lead Optimization

Preclinical

Clinical Phases

What's needed for?

OPA1 is an antiapoptotic protein that plays a fundamental role in the control of the apoptotic cristae remodeling to achieve a complete release of cytochrome c from the mitochondria. Of note, the OPA1 antiapoptotic activity depends on its ability of hydrolyze GTP, since mutations that abolish OPA1 GTPase activity also impair its antiapoptotic function. Disclosed herein is a small molecule that inhibits the GTPase activity of the mitochondrial dynamin related protein OPA1. Also disclosed are derivatives of the said small molecule. The invention further discloses the ability of this said compound and its derivatives to enhance the release of cytochrome c from mitochondria, in response to a pro-apoptotic stimulus, thus sensitizing cells to the induction of apoptotic cell death. The invention belongs to the field of research to improve the treatment of disorders such as cancer and cancer-induced angiogenesis involving the upregulation of the levels of the said protein OPA1.

Advantages

- A high grade of specificity
- Overcome the resistance of cancer cells to currently used therapies
- Inhibitor of OPA1 GTPase activity that can enhance apoptotic release of cytochrome c from mitochondria

Applications

- Use in combinatorial chemotherapy to increase apoptosis sensitivity
- Eradicate cancer drug resistance depending on OPA1
- Curtail cancer angiogenesis especially when cancers become resistant to VEGF inhibitors
- Research tool to inhibit OPA1 and mitochondrial fusion in vitro