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Preparation of Novel Pyrazolyl Guanidine as F_1F_0-ATPase Inhibitors

Patent Highlight

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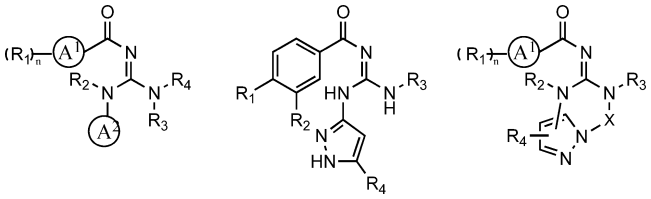
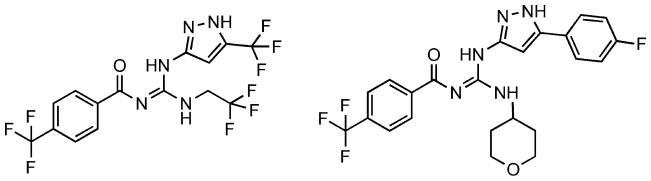
Title:	Preparation of Pyrazolyl Guanidine F_1F_0-ATPase Inhibitors and Therapeutic Uses Thereof		
Patent/Patent Application Number:	WO 2012078874 A1	**Publication Date:**	June 14, 2012
Priority Application:	US 2010-420950P	**Priority Date:**	December 08, 2010
Inventors:	Glick, G. D.; Hurd, A. R.; Taylor, C. B.; Vanhuis, C. A.		
Assignee Company:	Lycera Corporation, USA		
Disease Area:	Immune disorder, inflammatory condition, cancer	**Biological Target:**	F_1F_0-ATPase

Summary: This invention provides pyrazolyl guanidine compounds that inihibit F_1F_0-ATPase (e.g., mitochondrial F_1F_0-ATPase) and methods of using pyrazolyl guanidine compounds as therapeutic agents to treat medical disorders, such as an immune disorder, inflammatory condition, or cancer.

Important Compound Classes:



Examples of Structures:



Recent Review Articles: Chevrollier, A.; Loiseau, D.; Reynier, P.; Stepien, G. Adenine nucleotide translocase 2 is a key mitochondrial protein in cancer metabolism. *Biochim. Biophys. Acta Bioenerg.* **2011**, *1807* (6), 562−567.

Biological Assay: Compounds were tested for activity against F_1F_0-ATPase by measuring the ability of the compound to inhibit ATP synthesis. In addition, the compounds were assessed for cytotoxicity in Ramos cells.

Biological Data: Over 550 compounds were evaluated and showed inhibition of F_1F_0-ATPase in synthesizing ATP. Most potent compounds have an IC_{50} < 10 μM.

Synthesis: Over 550 compounds were prepared.

Additional Information: Inhibitors of mitochondrial F1F0-ATPase may provide a mechanism to control regulation of the apoptotic process and its cellular machinery.

AUTHOR INFORMATION

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Notes

The authors declare no competing financial interest.

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