New Activity of HSP90 Inhibitors Inducing Down Regulation of ZAP-70 and Inducing Apoptosis in Leukemia Cells

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BACKGROUND

Cancer is in part a result of the ability of pathologically altered cells to evade apoptosis. Therefore, there is a need to identify compounds that can key regulate the key interactions between proteins involved in apoptotic regulation in order to treat cancer. ZAP-70 is considered the best prognostic factor for disease progression and is correlated with poor clinical outcome in CLL patients, in part through its ability to serve an anti-apoptotic function in these cells. A compound with the ability to down regulate ZAP-70 and induce apoptosis specifically in CLL cells would provide an invaluable therapy for patients with aggressive disease.

TECHNOLOGY DESCRIPTION

This invention provides new uses of specific inhibitors of heat shock protein 90 (Hsp90) to induce apoptosis of leukemic cells. Additionally, this technology provides a clinical prognostic marker in cancer cells, based on the detection of apoptosis *in vitro* and the identification of active Hsp90 complexes.

ADVANTAGES

- This invention provides the first evidence that Hsp90 plays an active role in CLL progression/prognosis.
- Inhibiting Hsp90 or ZAP-70 activity or disrupting the interaction between the two molecules directs otherwise resistant cells to undergo apoptosis.
- Hsp90 inhibitors (proprietary or those available in the art) can induce cancer cell apoptosis through the directed down regulation of ZAP-70.
- Hsp90 inhibition leads to the specific down regulation of pathological ZAP-70 in leukemic cells without down regulating ZAP-70 in natural killer cells or healthy T-cells.

APPLICATIONS

- A method and compositions useful to modulate apoptosis in a cell.
- Treatment of patients with CLL or other cell proliferative disorders.
- Prophylaxis in patients with high risk to develop leukemias.
- Determination of cancer risk factors and biological analysis of important signaling pathways in leukemia.
- A method for the identification of novel Hsp90 “client” proteins.
- A method for early diagnosis of CLL and other cancers.
- *In vitro* test that can be used as a clinical prognostic factor, based upon the detection of active Hsp90 complexes and the induction of apoptosis.
- This prognostic assay is amenable to high throughput automatization and could be applied to other types of normal or malignant cells.

STATE OF DEVELOPMENT

This technology is offered exclusively or nonexclusively for U.S. and/or certain foreign countries. A commercial sponsor for potential future research is sought.

RELATED MATERIALS

- Inventor Information—Thomas J. Kipps, UC San Diego Professor of Medicine, Deputy Director Research Operations, UC San Diego Rebecca and John Moores UCSD Cancer Center, Director, CLL Research Consortium.

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OTHER INFORMATION

CATEGORIZED AS
- Medical
  - Disease: Cancer

RELATED CASES
2005-094-0

▶ Blood, 2005, 106:7, “ZAP-70 is a novel conditional heat shock protein 90 (Hsp90) client: inhibition of Hsp90 leads to ZAP-70 degradation, apoptosis, and impaired signaling in chronic lymphocytic leukemia”; Januario E. Castro, Carlos E. Prada, Olivier Loria, Adeela Kamal, Liguang Chen, Francis J. Burrows, and Thomas J. Kipps.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	8,741,578	06/03/2014	2005-094
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Additional Patent Pending

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