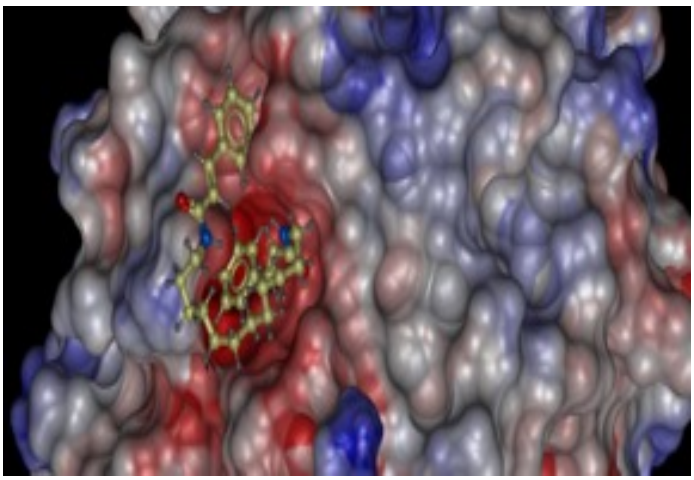
CHAPMAN UNIVERSITY | Office of Research

Bis-Cinnamamide Derivatives as Novel APE/Ref-1 Inhibitors for the Treatment of Human Melanoma

Chapman Case #2022-002

Market Need

Melanoma can be one of the most aggressive types of cancer and it is becoming more common. Moreover, a significant portion of melanoma patients are resistant to chemotherapy and immunotherapy treatments, giving rise to a need to develop new and effective treatment strategies to improve melanoma therapy to tackle drug resistance and sometimes severe events associated with immunotherapy. A key player in melanoma development is an enzyme called APE/Ref-1 that significantly upregulates melanoma cells, resulting in the stimulation of disease progression and development of drug resistance. Subsequently, depleting the amount of APE/Ref-1 enzyme in melanoma cells would significantly reduce tumor growth, thus forming the mechanistic rationale behind inhibiting APR/Ref-1 as a novel treatment strategy of melanoma.



Chapman Solution

Dr. Sun Yang and Dr. Keykavous Parang of Chapman University, along with Dr. Richard Chamberlin and Dr. Frank Meyskens of UC Irvine, have invented a novel inhibitor that can inhibit the activity of the APE/REF-1 protein by selectively blocking the redox regulatory activity of APE/Ref-1 in melanoma cells. In comparison to other well-studied APE/Ref-1 inhibitors (E3330 and E2009), the Chapman Inhibitor showed significant inhibition of melanoma proliferation at low concentration less than 0.1 μM, whereas the required concentrations of E3330 and E2009 were 6.6 μM and 5.3 μM respectively. Further, a particular design of the Chapman Inhibitor has shown effective tumor growth inhabitation in vivo with dosage of as low as 5mg/kg i.p daily, without producing any apparent systemic toxicities. After a 21-day treatment, the tumor size reduced to 44.7% of the control.

Applications

- Potential new drug to treat melanoma

Key Publication

- Bis-Cinnamamide Derivatives as APE/Ref-1 Inhibitors for the Treatment of Human Melanoma, MDPI, April 2022.

Intellectual Property

- Provisional patent application filed

Stage of Development

- *In vivo* and *in vitro* demonstrations of significant inhabitation of tumor growth and tumor size
- Available for licensing and further research collaborations

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