SPARK
AT STANFORD

Project sk13190

Enhancing host-anti-tumor response by preventing thrombin cleavage of osteopontin

Executive Summary

Modulation of macrophages by inhibition of thrombin cleavage of osteopontin (OPN) prevents suppression of host-anti-tumor immune response and up-regulates tissue repair instead of fibrotic reactions. We have identified a monoclonal antibody that prevents thrombin cleavage of OPN and shows efficacy in *in vivo* models.

Unmet Need

Despite significant survival improvements due to immunotherapy and targeted therapy, prognosis for patients with many cancer types such as unresectable or metastatic malignant melanoma remains poor.

Approach

Our therapeutic will prevent thrombin-cleavage of OPN thereby enhancing the host's anti-tumor immune response via modulation of tumor-associated macrophages resulting in an effective adjunctive therapy for cancer treatment. It may also block pathological fibrosis in various fibrotic diseases.

Milestones Achieved

- Established proof of concept in mouse models of melanoma and colon cancer
- Developed a monoclonal antibody which is capable of blocking OPN cleavage and shows in vivo anti-cancer activity
- Humanized version of the mouse antibody is under development

Value Proposition

Our therapeutic will improve survival and quality of life for patients with cancer.

Publication

Peraramelli *et al.* Thrombin cleavage of osteopontin initiates osteopontin's tumor-promoting activity. J Thromb Haemost. 2022 May;20(5):1256-1270. PMID: 35108449

IP Status

Patent application published US 20220324956A1

Team

Lawrence Leung (ex Chief of Staff, Palo Alto VA; Prof of Medicine)
John Morser (ex Scientific Director, Cardiovascular Research, Berlex)
Timothy Myles (ex Senior Scientist, Hematology, Bayer)

No anticoagulant effect differentiates A6 from all clinical anticoagulants.

In the process, OPN-KI mice heal with less fibrosis too.