CD24 and PD-1 Co-Inhibition for Treatment of Malignant Pleural Mesothelioma

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Objectives:

To determine if CD24 blockade would potentiate the effectiveness of immune-checkpoint inhibitors in mesothelioma models.

Background:

Malignant mesothelioma is an aggressive neoplasm mainly due to prior exposure to asbestos. Pemetrexed plus cisplatin chemotherapy is the current standard treatment but prognosis of the disease remains poor. New treatment options including targeted therapy and immunotherapy are available but results from recent clinical trials using immune-checkpoint inhibitors were disappointing. Therefore, identification of novel target for immunotherapy requires further investigation.

Methodology:

1. The molecular mechanisms of CD24 mediated immunosuppressive effects in mesothelioma was investigated through cells and animal models.
2. The therapeutic potential of CD24 and PD-1 co-inhibition was examined.
3. The tumor immune microenvironment in patient tissue was also studied.

Impact:

Preliminary data of the effectiveness of C24 blockage with current immune-checkpoint inhibitor PD-1 was gained through this preclinical study. The data would help to develop novel treatment options for mesothelioma.

Result and Conclusion:

<u>Mesothelioma cell model</u>

1. CD24 inhibition enhanced macrophage phagocytosis of mesothelioma cells.
2. MTAP overexpression could amplify the above phagocytosis effect.

<u>Mouse mesothelioma model</u>

1. Single anti-CD24 or anti-PD-1 treatment showed minimal efficacy.
2. The combinative treatment of anti-CD24 and anti-PD-1 significantly reduced tumor volume.