BG34-200 Engagement With Integrin CD11b for Modulating Tumor-Associated Myeloid Cells in Pancreatic Cancer

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Cancer immunotherapies such as checkpoint inhibitors and CAR-T therapies are becoming a therapeutic option for cancer patients with advanced and metastatic disease. However, clinical success has been limited as tumor cells exploit multiple mechanisms in the tumor microenvironment (TME) to create an immunosuppressive environment, escaping immune destruction. Recent studies have shown that immunosuppressive myeloid cells in the TME are the major mechanism of cancer resistance to immunotherapy. Myeloid cell marker, integrin CD11b, represents a new and innovative target to potentially modulate myeloid cell functions for enhancing immunotherapy. The CD11b integrin can mediate a variety of myeloid cell functions, such as adhesion, migration, differentiation, and proliferation, in response to binding to ligands. Here, we investigate the engagement of myeloid cell marker (integrin CD11b) with in-house developed ligands (BG34 molecules) with an aim to develop a modulatory agent for immunosuppressive myeloid cells. To pursue this, we apply overlapping peptide microarray technology to characterize the binding sequence of CD11b to BG34 molecules with different molecular weights. Five peptide epitopes were identified directing the BG34-200-CD11b binding: L380-K386, Q485-C494, V173-K182, S158-K170, and E237-K247. Defined binding sites allow us to better characterize the impact of immunosuppressive myeloid cells in cancerous tumors. In the future, we recommend mutagenesis studies to explore signaling pathway(s) that are induced by BG34-CD11b binding and essential for antitumor responses. This provides exciting potential for the development of BG34-based immunotherapy for cancer patients who failed to respond to standard of care chemotherapy, radiation therapy, and immunotherapy.

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