Therapeutics & Vaccines

Synstatin "SSTN$_{I/V}$" Disrupts Cancer Growth

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WARF: P160224US02

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The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing a novel 'fusion' peptide shown to inhibit syndecan-1 activation of two receptors that play a key role in tumor growth, IGF-1R and VLA-4.

The peptide inhibits binding and activation of the receptors and can thus block survival and invasion of numerous cancer cells, tumor-induced angiogenesis and homing of leukocytes in immune diseases, solid tumors and lymphomas/leukemias/myeloma.

Overview

Leading UW–Madison oncologists previously showed that the matrix receptor syndecan-1 (Sdc1/CD138) – a matrix receptor highly expressed in multiple myeloma – captures and activates multiple cell surface receptors. Among these receptors are the insulin-like growth factor-1 receptor (IGF-1R) and very late antigen-4 (VLA-4, also known as the α4β1 integrin).

IGF-1R provides survival signaling for many tumor cells, including myeloma, as well as for activated endothelial cells. VLA-4 is expressed on leukocytes (lymphoid and myeloid) and their malignant counterparts, including myeloma, and has a major role in cell adhesion, extravasation from the blood stream and invasion. VLA-4 also provides resistance to chemotherapy, a mechanism known as Cell Adhesion-Mediated Drug Resistance or CAM-DR.

Thus, targeting one or both of these important receptors with a single drug holds great promise for disrupting cancer growth.

The Invention

The researchers have now developed a fusion peptide with sequences derived from the extracellular domain of syndecan-1. The peptide, SSTN$_{I/V}$, includes an IGF-1R-binding segment and a VLA-4-binding segment. It demonstrates significant bioactivity *in vitro* against cancer cells, immune cells and endothelial cells.

The researchers envision an immediate clinical application in myeloma, a cancer with no known curative therapies that appears highly susceptible to SSTN$_{I/V}$.

Applications

- Potential cancer/tumor therapeutic

Key Benefits

- Targets growth, survival and invasion of tumor cells
- Targets tumor angiogenesis
- Does not affect normal tissue
- Stable in serum

- May be affective against tumor cells resistant to IGF-1R inhibitors
- No other drugs like it are available.

Stage of Development

As the new peptide should retain all the activities of SSTN-IGF1R, and have additional inhibitory properties due to its VLA-4 blocking properties as well, the researchers anticipate that it will block tumor survival and angiogenesis *in vivo* like SSTN-IGF1R, but also block tumor invasion, leukocyte invasion and additional mechanisms in angiogenesis due to the VLA-4 blocking activity.

The researchers have shown conclusively *in vitro* that the new peptide blocks tumor cell migration, tumor growth and angiogenesis. It does so by targeting syndecan-1-coupled ternary receptor complexes on both activated endothelial cells and the tumor cells. Additionally, it remains stable during prolonged incubation in serum.

Additional Information

For More Information About the Inventors

- Alan Rapraeger

Related Technologies

- For information about other cancer-fighting synstatins developed by the researchers, see WARF reference numbers:
- P06390US02
- P120300US03
- P120259US03

Publications

- Beauvais D.M., Jung O., Yang Y., Sanderson R.D. and Rapraeger A.C. 2016. Syndecan-1 (CD138) Suppresses Apoptosis in Multiple Myeloma by Activating IGF1 Receptor: Prevention by SynstatinIGF1R Inhibits Tumor Growth. Cancer Res. 76(17): 4981-4993.

Tech Fields

- Therapeutics & Vaccines : Oncology

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