Synergistic Tumor Treatment with IL-2, an Integrin-Binding-FC Fusion Protein, and a Cancer Vaccine
Technology #18598

Applications

This technology is method of treating cancer by delivering a combination of IL-2, an integrin binding knottin-Fc fusion protein, and a cancer vaccine that has wide-ranging potential as a cancer immunotherapy.

Problem Addressed

Cancer immunotherapies harness patients’ own immune systems to fight cancerous lesions. Immunotherapies such as tumor-specific monoclonal antibody treatment, immunostimulatory cytokine treatments, and immune checkpoint blockade therapies have demonstrated efficacy in a wide variety of cancers including melanoma, breast cancer, colon cancer, and lung cancer. However, there are still many challenges in the field of cancer immunotherapies. Firstly, most immunotherapies need to be specifically tailored to each cancer subtype. Additionally, predicting therapeutic outcome is difficult, and different patients with the same cancer and therapeutic dosing might exhibit either robust tumor remission or complete failure of treatment. Finally, cancers that lack known tumor antigens or have low antigenic burden are almost impossible to target with current immunotherapies. These inventors have engineered a combination therapy that is able to address these issues in cancer immunotherapy.

Technology

This technology is a three-component combination immunotherapy composed of a pharmacokinetically improved IL-2, a knottin-Fc fusion protein, and a cancer vaccine. IL-2 is a cytokine that can activate both innate natural killer (NK) cell immunity and adaptive T-cell immunity. IL-2 treatment is currently approved for use in treating several cancers. However, IL-2 therapies are highly toxic due to the short half life that necessitates very high dosing. The first component of this invention is a pharmacokinetically (PK) improved IL-2. These inventors fused IL-2 to albumin or Fc, which stabilizes the serum circulation half-life of IL-2. The second component of this invention is a bi-functional Knottin-Fc fusion protein that targets the molecule to cancer cells and induces an immune response. Knottins are compact, exceptionally stable proteins that are useful as molecular scaffolds. These inventors engineered knottin derivatives that selectively bind cancer-associated integrin proteins, which allows specific binding of the knottin-Fc fusion protein to cancer cells. Fc peptides are an immunogenic component of antibodies, and cells bound to Fc fragments surface are targeted by NK cells for destruction. Upon binding to Fc on a target cell, NK cells release cytotoxic compounds directly into the Fc-bound cell and release cytokines that stimulate local inflammation and adaptive immunity responses. The inventors demonstrate that in vivo administration of PK-IL-2 and knottin-Fc results in robust tumor regression and increases in lifespan in a variety of mouse cancer models. Additionally, this treatment paradigm works synergistically with existing cancer vaccines such as immune checkpoint blockade therapies. The inventors demonstrate that mice treated with a combination of PK-IL-2, knottin-Fc, and anti-CTLA4 or anti-PD1 antibodies have impressive, lasting therapeutic responses.
Advantages

- Longer serum half-life of IL-2 through fusion to albumin or albumin binding peptides
- Targeting of immunogenic Fc to cancer cells through binding to cancer-associated integrins
- Potential as a generalized cancer immunotherapy since cancer-associated integrins are overexpressed in diverse cancer types
- Synergistic therapeutic response when combined with immune checkpoint blockade or tumor-specific antibodies

Categories For This Invention:

Life Sciences
Clinical Applications
Oncology
Therapeutics
Antibody (Therapeutics)
Drug Delivery
Peptide
Protein

Intellectual Property:

Synergistic tumor treatment with IL-2, and integrin-binding-Fc fusion protein, and a cancer vaccine
PCT
2017-139570

Inventors:

Darrell Irvine
Jennifer Cochran
Dane Wittrup
Byron Kwan
Cary Opel
Kelly Moynihan

External Links:

Irvine Lab
http://irvine-lab.mit.edu/
The Wittrup Lab
http://kdw-lab.mit.edu/