Production and Characterization of a Recombinant Bispecific Antibody for the Treatment of AML

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Abstract
Delivering lethal doses of radiation directly to a tumor without damaging surrounding tissue has been one of the biggest challenges in the administration of radionuclide-based cancer therapeutics. The opening question towards the development of novel cancer therapeutics is how to minimize the spread of radiation to normal tissue and maximize the specific targeting of radiation to a cancer cell. Processes such as radioimmunotherapy (RIT) use radiolabeled antibodies to target cancer tumors and while this process has shown some clinical success the excess exposure of radiation to healthy tissue limits its desirability as a therapeutic treatment. Other methods include pre-targeted radioimmunotherapy (PRIT), a two-step system where the exposure of radiation to normal tissue is minimized as the bi-specific antibody is first bound to cancer cells, then a clearing agent removes unbound antibody from the bloodstream just prior to administration of the radiolabeled second step. This ensures radiation is sent directly to affected cancer cells. This development of PRIT is expected to directly target cancer cells, improve biodistribution and serve as a better therapeutic alternative compared to RIT. My research is going to involve producing and characterizing the bispecific antibody so radiation is able to directly target affected cancer cells and provide a less toxic way for radiation to travel in the blood.

Methods
1. Produce large-scale batches of plasmids containing sequences coding for heavy and light chain
2. Transfect plasmids into HEK cells
3. Harvest supernatants after several days
4. Purify over a Protein A column
5. Assess product by PAGE and flow cytometry
6. Pilot biodistribution
7. Full time course biodistribution

Results

Conventional Radioimmunotherapy (RIT) vs Pretargeted Radioimmunotherapy

One-step Radioimmunotherapy
While one step radioimmunotherapy has shown to successfully kill cancer cells, PRIT serves to reduce binding of radiation to non-target tissues so less toxicity is incurred during treatment.

2 Step Pretargeted Radioimmunotherapy

30F11 Bispecific

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References