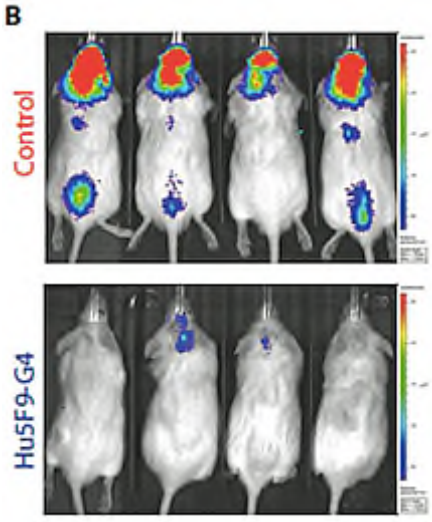
Treating Malignant Pediatric Brain Tumors Using Anti-CD47 Agents

Researchers at Stanford have developed methods of using and administering anti-CD47 agents to treat malignant pediatric brain tumors. These tumors have high morbidity and mortality as they are very difficult to treat. The therapeutics that do exist are so toxic that they can cause severe physical and intellectual disabilities. Thus, there is a need for new cancer therapeutics with high specificity against brain cancer cells and less toxicity to normal brain cells. To help meet this need the inventors have developed methods to treat pediatric brain tumors with immunotherapy agents that block interaction between CD47 and its receptor. These agents can be directly delivered to the cerebrospinal fluid by an implanted continuous delivery device. Disrupting the interaction between CD47 and its receptor eliminates the “don’t eat me signal” that is normally sent to macrophages, thereby allowing the immune system to more effectively fight the cancer. In addition, the inventors have also developed animal models in which the animal is engrafted with both normal human neural cells and brain cancer cells to test the toxicity of potential therapeutics in a preclinical setting. This technology provides new methods for treating malignant pediatric brain tumors and enables more effective preclinical testing of new therapeutics.



Xenograft mouse model of patient-derived pediatric medulloblastoma. Compared with untreated control (top), the mice treated with CD47 blockade (bottom) show a significant decrease in tumor burden.

Stage of research
Using the xenograft models of pediatric brain tumors, the inventors showed that CD47 blockade could be used to treat these brain tumors without toxic effects to normal tissues.

This technology may no longer be available after September 28, 2017.

Applications

- Therapeutic for pediatric brain cancer
- Drug development- animal models for preclinical drug screening and toxicity testing

Advantages

- Xenograft animal models:
  - Enable more effective preclinical drug screening
  - Can be used to test not only the efficacy but also the toxicity of therapeutic agents

- Potential safer and more effective therapeutic to treat pediatric brain cancer

Publications

- Gholamin S, Mitra SS, Feroze AH, Liu J, Kahn SA, Zhang M, Esparza R, Richard C, Ramaswamy V, Remke M, Volkmer AK, Willingham S, Ponnuswami A, McCarty A, Lovelace P, Storm TA, Schubert S, Hutter G, Narayanan C, Chu P, Raabe EH, Harsh G 4th, Taylor MD, Monje M, Cho YJ, Majeti R, Volkmer JP, Fisher PG, Grant G, Steinberg GK, Vogel H, Edwards M, Weissman IL, Cheshier SH. Disrupting the CD47-SIRPα anti-phagocytic axis by a humanized anti-CD47 antibody is an efficacious treatment for malignant pediatric brain tumors. *Science Translational Medicine*. 2017 Mar 15;9(381).
- Digitale, E. Antibody fights pediatric brain tumors in preclinical testing. *Stanford News*. 2017 Mar 15.

Related Web Links

- Cheshier lab
- Weissman lab

Patent Status

- Published Application: US 2018-0258170

Keywords

therapeutic: anticancer, therapeutic: antibodies, therapeutic: immunotherapy, cancer therapeutics, drug screening platform, therapeutic antibodies: cancer, therapeutic target: cancer, pediatric cancer, Cd47

Stanford Reference

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