Anti-hCD47 Antibody: Potential Cure for Cancer

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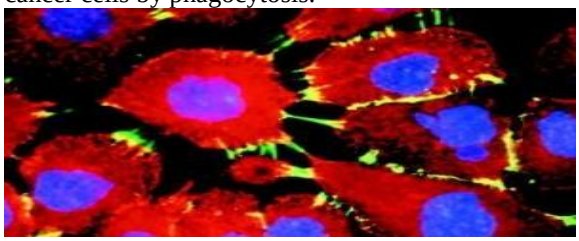
BME 181 Second Presentation, April 8, 2013 <jp32012@gmail.com>

***Abstract*—Researchers at Stanford University have discovered "a single therapy that uses our own immune system to effectively attack all cancers with almost no side effects." After success with mice, scientists are hopeful heading into human trials.**

I. Introduction

In 2008, cancer accounted for 7.6 million deaths worldwide, 13 percent of the total deaths in 2008. Clearly, the human race has faced immense frustration when it comes to treating cancer. However, a new hope is on the horizon. Anti-hCD47 antibody blocks the surface protein CD47 found on normal and cancerous cells. CD47, a "cellular cloaking device," transmits a "don't eat me" signal to macrophages, which consume foreign matter and harmful cells. Cancer cells boost their amount of CD47, which results in macrophages ignoring them, enabling the cancer to metastasize. Anti-hCD47 blocks the CD47 "don't eat me" signal, so that macrophages eat the cancer cells by phagocytosis.



Cancer cells in the bladder are shown above.

II. Methods

CD47's "don't eat me" signal is transmitted when signal regulatory protein-α (SIRPα) on macrophages binds to the CD47. The binding initiates a signaling cascade that inhibits phagocytosis. Blocking monoclonal anti-humanCD47 antibodies, or anti-hCD47 mAbs, which include B6H12.2 and Bric126, specifically bind to the antigen CD47. When an anti-hCD47 mAb binds to a CD47 protein, the "don't eat me" signal of the CD47 is blocked, subjecting cancer cells to phagocytosis. Since cells present the occurrences within themselves to other cells at the surface, immune cells can detect abnormal cells and destroy them. The genetic changes that bring about a cancer cell result in the protein calreticulin being presented at the surface of the cell, which transmits an "eat me" signal, communicating to macrophages that the cell is abnormal. Disabling the protective CD47 barrier exposes the calreticulin "eat me" signal of the cancer cells. Despite being exposed to the anti-hCD47 mAbs, normal cells are not eaten because they do not ouput an "eat me" signal.

III. Results

The results of anti-hCD47 mAbs on mice have been incredible. All human leukemic blood cells were eliminated within a day after a single dose of the antibody was injected into one mouse. Experiments on mice have shown that the anti-hCD47 mAbs are successful in treating human tumors as well as human cancers that have already spread; large tumors have shrunk and some smaller tumors have even been eliminated altogether. In a complete series of experiments at Stanford on mice that had human acute myelogenous leukemia, the cancer was erased in a majority of the mice. In addition, the anti-hCD47 mAbs prevent cancer from metastasizing, or spreading from the original tumor. Not surprisingly, tests showed that the greater the amount of CD47 expressed by cancer cells, the lesser the chance that the subject survived. Also, the effectiveness of the antibody therapy was inversely proportional to the initial tumor size.

IV. Discussion

There are nearly no negative effects of the anti-hCD47 mAb treatment. Large doses of anti-hCD47 mAbs do produce a temporary anemia, but the red blood cell count quickly recovers. The antibody therapy would not be advisable after chemotherapy because normal cells are damaged due to the high stress of chemo; thus, noncancerous cells would have calreticulin on their surfaces. Blocking CD47 would subject the noncancerous cells to phagocytosis.

Anti-hCD47 mAbs, which can be grown in unlimited amounts, would likely be most effective when the tumor is maximally debulked; then, the tumor can be cut out by focused radiation therapy. The effectiveness would further increase if used alongside antibodies that strengthen the "eat me" signals from surface proteins like calreticulin.

Nearly every type of cancer has the potential to be successfully treated by the antibody, excluding a few types that use unknown methods to avert macrophages. Moreover, the anti-CD47 antibody would enhance the efficacy of other treatments that utilize immune cells to attack cancer. However, the microenvironment of a nontransplanted human tumors has the potential to introduce additional immune suppressing factors.

The Stanford research lab has received a $20 million grant from the California Institute for Regenerative Medicine to begin human trials of the antibody, which are expected to begin in late 2013 or early 2014.

References

[1] World Health Organization, Jan. 2013. Web. <http://www.who.int/mediacentre/factsheets/fs297/en/>
[2] *Wikipedia*. Wikimedia Foundation, 29 Mar. 2013. Web. <http://en.wikipedia.org/wiki/Monoclonal_antibodies>
[3] *PubMed Central*. National Academy of Sciences, 26 Mar. 2012. Web. <http://www. ncbi.nlm.nih.gov/pmc/articles/PMC3340046/>
[4] Stanford Medicine, Summer 2012. Web. <http://stanmed.stanford.edu/2012summer/ article7.html>
[5] Medical Daily, 28 Mar. 2013. Web. <http://www.medicaldaily.com/articles/14434/20130328/cancer-treatment-cd47-miracle-bullet-breast-colon-bladder-antibody-eat-macrophage-immune.htm>