

Preventing Cancer

Leader: Stephen Albert Johnston

Team: Stephen Albert Johnston, Luhui Shen, Peter Lee (COH), Keith Kunudson (Mayo).

Summary: Overview: Cancer is the single leading healthcare cost in the US, accounting for ~10% of the total cost. It claims 500K lives a year in the US, 7.5M worldwide. Most of the cancer deaths in the world occur in the developing world. WHO has recently declared that there is a worldwide cancer epidemic. Yet the treatment options offered by the research/medical community are increasingly expensive and complicated, with little real gain. Clearly, a rethink of the problem is in order. Professor Stephen Albert Johnston and his colleagues in the Center for Innovations in Medicine (CIM) approached this problem as inventors and came up with radical, but simple solutions to the challenge of cancer. The three programs for eradication of cancer are detailed below.

Prophylactic Vaccine: After careful analysis we concluded the simplest solution to the cancer problem would be that nobody got cancer. The simplest way to do this would be to administer a vaccine that would prevent people from getting cancer. A preventative cancer vaccine. Most researchers, maybe all, in the area of oncology thought that this was an impossible goal. We thought otherwise and pursued it anyway.

The basic concept is quite simple. It is commonly known that tumors make aberrant proteins. These proteins often have nonsense tails (frameshifts) that consist of peptides the immune system has not seen before. They would be great targets for a vaccine but the presumption has been that these frameshifts were personal – ie they only occurred in that one individual's tumor. Our premise was that this may not be true. Even if each frameshift only occurred in a few per cent of all tumors, if you pooled enough of them you could make a good vaccine. A universal, preventative cancer vaccine. We launched a program to determine if enough of these frameshift antigens could be identified to comprise a preventative vaccine. We have shown that this is indeed feasible. We have taken the effort as far to demonstrate that in mouse models of breast cancer that a prophylactic vaccine is approachable. We were encouraged that our efforts were of some effect when the National Breast Cancer Coalition initiated the Artemis Project to create a prophylactic breast cancer vaccine.

We have pushed the argument from whether it is feasible to create such a vaccine to the practical aspects of implementing it. One concern is the length of time it would take to conduct a phase II efficacy trial if the outcome measure was mortality. To relieve this impediment we invented the immunosignaturing technology that can reveal early evidence of cancer. This technology should speed efficacy trials.

Anti-Metastatic Vaccine: A second concern relative to developing a prophylactic vaccine is that it may be difficult to maintain a high enough immune response to eradicate any tumor. A related concern is that continuous exposure to a high level immune response elicited by the vaccine may have untoward side effects. We have acknowledged this concern and invented a new type of vaccine protocol – the anti-metastatic cancer vaccine. Recall that 90% of cancer deaths are from metastatic tumors. Under this

protocol people would be vaccinated to a low level against any tumor that could arise, using the same antigens as in the prophylactic vaccine. This low level prime response would only be activated if a tumor arose. The primary tumor would boost the vaccine immune response and stop the development of a metastatic tumor. The biology/immunology of such a proposal are sound and we have preliminary evidence that it is achievable.

Amplified Diagnostics: Primary tumors, particularly if discovered early, can almost always be treated with conventional therapies (surgery, chemo, radiation). We have developed a revolutionary concept for early diagnosis of primary tumors that is an adjunct of the anti-metastatic vaccine. People receiving the anti-metastatic vaccine will boost their immune response to tumor antigens as soon as the tumor arises. If they are regularly monitored for these responses, a new tumor could be quickly discovered. Monitoring could be done with a drop of blood sent through the mail. The combination of the anti-metastatic vaccine and the amplified diagnostics would allow preventing metastatic cancer deaths and early discovery of the primary tumor. The amplified diagnostics could even be the basis of new immunotherapeutic approaches to treating the primary tumor.

Value proposition:

We have defined a credible path and program to prevent all cancer and experimentally demonstrated feasible solutions to the problem. We have generated support for the concept of prevention of cancer.

Collaboration objectives:

This is a very broad program that will require, oncology researchers, experts in animal model, immunologists, vaccinologists, clinical trials experts and epidemiologists.

Contact: Stephen Albert Johnston

Stephen.johnston@asu.edu