Lay abstract LILT Trivedi

Abstract:

Amidst a raging viral pandemic currently devastating the world, we must also remember that ***about 15-20% of all cancers are caused by infectious agents. Every year, viruses make over 1,3 million people sick with cancers across the globe.*** Epstein-Barr virus (EBV), is peerless in its ability to turn a normal B lymphocyte with a defined life span, into an indefinitely growing immortalized cell, which potentially can go rogue and become a lymphoma.

Most such cancers occur in people with functioning immune defenses because viruses have deviced clever strategies to compromise host immunity to survive, thrive and infect new individuals.

We have shown that EBV usurps immune checkpoint (IC) controls and makes the cancer cell invisibile to the immune system. To evade recognition by the immune system, EBV increases expression of a protein called PD-L1 on infected cancer cells. We also found that a noncoding small RNA, miR-34a, is quite effective in reducing PD-L1 in lymphoma cells.

Antibodies to immune checkpoint proteins like PD-L1 are used as an immunotherapy tool but unfortunately, only a small fraction of the patients have a beneficial outcome. With an urgency to improve immunotherapy, I put forward a unique RNA aided combinatorial immunotherapy approach in the present proposal. ***We will test efficacy of miRNAs and IC blocking antibodies in preclinical biomimetic 3D microfluidic chips by using tumor cells and T cells from the same patient, a technology that I've patented jointly with Harvard Medical School.*** Using this approach, we can identify whether a patient's T cells are activated and are eliminating tumor cells within a few weeks. I am confident that this highly translational proposal will lead to improved immunotherapy of not only virus associated cancers but also other types of tumors.