# Nobel prize in Physiology/Medicine- 2018

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Cancer is characterized by the uncontrolled proliferation of abnormal cells which have the capacity to spread to normal tissues and healthy organs. Various therapeutic methods such as surgery, radiation, hormone treatment, chemotherapy, bone marrow transplantation, etc are available for the treatment of cancer, however, advanced cancer remains difficult to be treated requiring novel strategies.

The concept of activating the immune system to attack the tumour cells emerged in the late 19th and 20th century with modest effects due to lack of adequate knowledge to develop generalizable new strategies against cancer.[1] The immune system has the ability to identify "self" and "non-self", thereby identifying and attacking foreign bodies such as bacteria, viruses and other dangers. T cells, a type of white blood cell, have been identified to have receptors which bind to the non-self structures, this in turn triggers and activates the immune system. However, many scientists have identified other proteins which function as a brake to avoid excessive activation leading to autoimmune destruction of the healthy cells and tissues.

The Nobel prize in physiology or medicine for the year 2018, was awarded to James P. Allison and Tasuku Honjo for their invention of cancer therapy by the inhibition of negative immune regulation.

James P. Allison was one of the several scientists who had observed that CTLA-4, a T-cell protein,functions as a brake on T cells. In addition to it, he had also developed an antibody which could bind with CTLA-4 and block its function as a brake thereby releasing the immune system to attack cancer cells (Figure 1).[2] His initial experiment was at the end of 1994, on mice and had been cured.[3] Subsequently in 2010, a study on patients with advanced melanoma showed significant effects and in several patients, there was no remaining signs of cancer.[4]

In 1992, Tasuku Honjo discovered PD-1, another protein on the surface of T- cells and studied its role which was also identified to be similar to CTLA-4but has a different mechanism (Figure 1).[5] In 2012, a study has shown that blocking PD-1 is efficacious in the treatment of various types of cancer including long term remission and possible cure for metastatic cancer.[6]

The invention of "Immune checkpoint therapy" has changed the outcome of advanced cancer in certain groups of people. However, it has been observed that overactive immune responses can be serious and have even life threatening adverse effects but can be manageable. Checkpoint therapy against PD-1 has been proven to be more effective than CTLA-4 in treating renal cancer, lung cancer, lymphoma and melanoma. However, there are new clinical studies indicating that a combination therapy, targeting both CTLA-4 and PD-1 could be more effective, as in patients with melanoma. The discovery of immune checkpoint therapy has provided a new paradigm for cancer management.

## About the Nobel laureates

(Adapted from the press release of The Nobel Assembly at Karolinska Institute)

**James P. Allison** was born in 1948 in Alice, Texas, USA. At the time of the award, he was affiliated to the University of Texas MD Anderson Cancer Center, Houston, Texas and Parker Institute of Cancer Immunotherapy.

**Tasuku Honjo** was born in 1942 in Kyoto, Japan. At the time of the award, he was affiliated to the Kyoto University, Kyoto Japan.

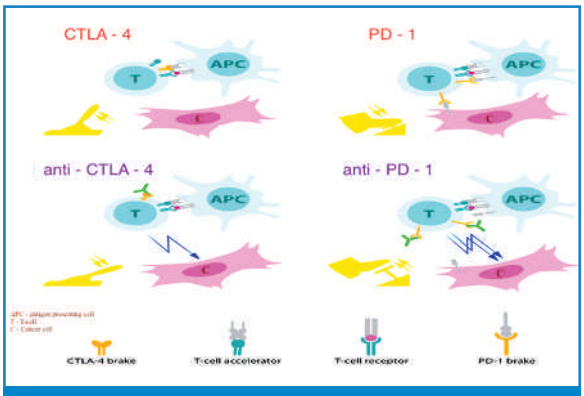


Figure : 1 - Immune system and Cancer Cells

Upper left: T cell receptor binds to the "non-self" immune cells thereby activating T cells. T-cell accelerator protein is required to activate T cells. CTLA- 4 operates as a brake on the T cells and inhibits the function of the accelerator.

Lower left: CTLA - 4 functioning as the brake is inhibited by antibodies (green), thereby activating T cells and attacking cancer cells.

Upper right: T-cell activation is inhibited by PD-1, another T-cell brake.

Lower right: Antibodies against PD-1 block the function of the brake resulting inactivation of T cells and highly efficacious attack on cancer cells.

## References


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**திருக்குறள் 949 / Thirukkural 949:**

உற்றான் அளவும் பிணியளவும் காலமும்
கற்றான் கருதிச் செயல்.

மருத்துவ நூலைக் கற்றவன், நோயுற்றவனுடைய வயது முதலியவற்றை யும், நோயின் அளவையும், காலத்தையும் ஆராய்ந்து செய்ய வேண்டும்.

The learned should ascertain the condition of his patient, nature of his disease and proceed with timely intervention.