NEWS IN BRIEF

NOBEL PRIZE IN MEDICINE – CANCER IMMUNOTHERAPY

James Allison grew up in a small town in Texas where the biology teacher did not believe in evolution. James was so vocal in voicing his protest against this that he was allowed to take classes in the University of Texas. In his life, he had seen the ravages that chemotherapy and radiation wreck on the human body as he lost his mother, two uncles and a brother to cancer. He decided to try a new approach in the battle against cancer.

Allison – who is now Professor at the MD Anderson Cancer Centre in Houston, Texas – received this year's Nobel Prize in Medicine for his work on the protein called CTLA-4 (cytotoxic T lymphocyte 4) on T lymphocytes. This prevents dendritic cells from priming the lymphocyte to recognize cancer cells. In 1997, he and his colleagues developed an antibody that could block CTLA-4. This allowed T lymphocytes to destroy cancer cells, and resulted in cancer remission in mice. For the next 17 years, he passionately campaigned for this mode of treatment. Finally Bristol-Myers Squib decided to go ahead with the development of Ipilimumab, which has now shown remarkable success in patients with malignant melanoma. He continues to work in collaboration with his wife Padmanee Sharma in the field of cancer immunotherapy.

Dr Tasuku Honjo of Kyoto University shares the Nobel Prize this year with Dr Allison. He initially trained as a medical doctor but decided to enter the field of immunology despite advice to the contrary by well wishers. He thought if he failed as a researcher, he would move to the countryside as a rural doctor. His seminal work has been in discovering another checkpoint protein called PD-1, which prevents T cells from attacking tumor cells. Antibodies against PD-1 were found to be extremely effective, especially against lung cancer. Even patients with metastatic lung cancer have gone into long-term remission with this mode of treatment.

This year's Nobel Prize recognizes a new paradigm in cancer therapy – harnessing the patient's own immune system rather than directly attacking cancer cells. (*Nature 1 October 2018*)

NOBEL PRIZE IN CHEMISTRY – EVOLUTION IN A TEST TUBE

Frances Arnold from California Institute of Technology became the fifth woman in history to win the Nobel Prize for Chemistry. She has lived a colorful life that includes hitch-hiking to Washington as a high schooler to protest against the Vietnam War, working part-time as a waitress, and helping Hollywood screen writers accurately portray scientific ideas.

Organisms evolve over centuries following the principles of natural selection. Arnold used the principles of evolution to develop new enzymes, which could catalyze reactions faster than natural enzymes. She introduced random mutations in the genes of bacteria and picked out those mutations which produced better enzymes. Repeated mutations and screening of these bacteria resulted in very powerful enzymes. This breakthrough technique is now used widely in industry to produce chemicals ranging from detergents to medicinal drugs.

She shares the prize with George P Smith who used similar principles to produce a technique called phage display. This results in repeatedly mutating virus genes to produce proteins. In his technique, these phages display the proteins on the cell surface making it easy for scientists to identify them.

The third winner of the prize is Sir Gregory Winters from the MRC Laboratory of Molecular Biology in Cambridge. Winters used the technique of directed evolution to produce powerful antibodies such as Adalimumab, which is used in rheumatoid arthritis. (*Nature 3 October 2018*)

THE MORAL DILEMMA OF THE DENGUE VACCINE

In an insightful editorial in the NEJM, Lisa Rosenbaum discusses the complexities in making public health guidelines, especially related to the dengue vaccine. The question to be addressed is "Can benefit for the majority excuse risk to a minority in public health interventions?" Let us look at the story behind the dilemma.

Dengvaxia is the only available dengue vaccine currently. In April 2016, the Philippines Department of Health implemented the Dengvaxia vaccination program. After vaccinating 830,000 children, they suspended the program when Sanofi disclosed that children who had not been exposed (*i.e.,* were seronegative for dengue prior to the vaccination) were at higher risk for hospitalization and severe illness than those who had been exposed or were seropositive for dengue prior to the vaccination.

There was huge public rumbling following the disclosure. Former Philippines public health under-secretary called it "the biggest government funded clinical trial masked as public health program." The hypothesis for these findings is that in the absence of prior dengue exposure, the dengue vaccine mimics primary infection. A subsequent infection results in severe dengue as is seen in the natural history of dengue infections. The WHO has now made a recommendation for a pre-vaccination screening strategy where only seropositive children are to be vaccinated. This strategy will require an efficient point-of care testing technique, which is now the main challenge. (*NEJM 26 July 2018*)

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