SPECTRUM
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Special Issue - Nobel Prizes 2018

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Nobel Prize in Biology

Block the Blocker!

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The year 2018 has proved to be a remarkable year for the field of immunology. The Nobel Prize for Physiology or Medicine 2018 was bagged by two immunologists, Dr. James P. Allison and Dr. Tasuku Honjo, for their discovery of 'checkpoint inhibitors for cancer therapy'.

Undoubtedly dreadful, cancer is a term given to a bunch of diseases, all of which stem from uncontrolled growth of our own cells. These cells may abnormally acquire the ability to migrate to various organs of the body. Interestingly, almost every one of us may have had abnormal growth of cells at some point in our lives. The fact that we are unaware of it is because our body is always on the guard and puts up a strong fight to eliminate such abnormal cells. This is all thanks to our immune system which performs the crucial task of protecting our body from 'errant self cells' as well as 'outside invaders'. This is achieved by immune cells constantly surveying the body, a phenomenon called 'immune surveillance'.

The immune system comprises of a variety of blood cells and important organs such as thymus, bone marrow, and lymph nodes. In the present context, two cells are particularly important - antigen presenting cells (APCs) and T cells. APCs constantly survey the body and if they find a foreign or abnormal cell, they bring it to the notice of T cells. The latter cells start hunting down these entities and execute their destruction. Interestingly, T cells have in-built 'accelerator' as well as 'brake' proteins whose function is to either accelerate an immune response or dampen it, respectively. It is an elegant way to balance destruction with not too much destruction such that the body's own cells are not harmed. However, destroying cancer requires a tough combat and these brake proteins on T cells may cause a major hindrance. This is precisely what the Nobel laureates had sought out to understand. They undertook extensive research on T cells, albeit in different parts of the world. (Dr. Allison is an American immunologist and Dr. Honjo is a Japanese immunologist).

Dr. James P. Allison and Dr. Tasuku Honjo

Dr. Allison discovered a protein called CTLA-4 (in the year 1994) and Dr. Honjo discovered a protein called PD-1 (in the year 1992), both appearing on the surface of T cells. However, these proteins functioned by using different mechanisms. What they had in common is that both served to prevent an immune response! So, once freed from these proteins, T cells can elicit an immune response and kill thousands of cancer cells. Thus, Dr. Allison and Dr. Honjo independently believed that blocking CTLA-4 and PD-1, respectively, could be a successful strategy for treating cancer. They worked in an era during 1990s wherein modulating the immune system to treat cancer seemed rather unrealistic and the only perceivable treatment options were surgery, radiation and/or chemotherapy. Despite not receiving much recognition for their work initially, they persisted with their research believing that some day this could be an effective therapy for advanced cancers. Ultimately, the FDA approved drugs that blocked CTLA-4 and PD-1, called 'checkpoint inhibitors' and both drugs have proved successful for treating various advanced cancers that were previously untreatable. In fact, making a combination of these blockers is also being considered. Of course, this sort of immunotherapy comes with a lot of side effects and is also thought to be an

extremely expensive treatment option. Nonetheless, it was a significant step which required a brilliant team and tremendous hard work to tackle one of humanity's greatest challenges - cancer.

Suggested Reading
https://www.nobelprize.org/prizes/medicine/2018/
https://www.cancerresearchuk.org/about-cancer/cancer-in-general/treatment/immunotherapy/types/checkpoint-inhibitors

Nobel Prize in Chemistry

Lessons From Evolution

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Chemistry is the play set that nature has used to breed a complex set of biochemicals like carbohydrates and proteins, and proteins are where most biological functionality lies. From the incredible macromolecules that fix carbon dioxide to provide us food, to the ones that digest the meals we eat, proteins (enzymes) perform varied chemical reactions. The diversity and potential of proteins to catalyze biochemical reactions forms the bedrock of this year's Nobel Prize in Chemistry.

Protein function depends upon protein structure i.e., if one can change the structure of protein, the function can be changed. Frances Arnold, decided to harness this incredible evolutionary potential of proteins to carry out chemical reactions that were difficult for conventional chemists. So, how does one go about changing protein structure? It's all about the "Base". Change the sequence of nucleotides coding for the proteins and you change the way the amino-acids organise and assemble, which generates a new structure and hence a new function. Frances Arnold utilized this evolutionary potential, creating super-enzymes from pre-existing enzymes, using the process which we now know as "Directed Evolution". From her early work in 1993, Frances utilized simple labstrains of bacteria to (1) produce a certain enzyme of interest (2) modify it to perform better for the same reactions or catalyse a completely new reactions e.g. mutating the genetic code of the enzyme Subtilisin and then introducing these mutated genes into bacteria that produced thousands of different variants of this protein. In nature, the variations are regulated by 'natural selection', but Arnold used 'selection' to screen for best enzymatic activity of subtilisin. Once she got a version that performed better than the naturally occurring enzyme (wild-type), she subjected this sequence to second and third cycles of selections, generating sequences that perform many fold better than the wild type. This improvement for a desired characteristic was later called 'directed evolution'. This incredible work landed Frances Arnold one half of the Nobel Prize, making her only the fifth woman in history to achieve this feat.

Directed evolution evolved into a more useful technique when George P Smith and Greg Winter married this idea to "phage display" producing anti-bodies for medicinal use. Bacteriophages are viruses that use bacteria as a host to replicate and mass produce any gene sequence present within the viral coat. Smith and Winter had the idea to use phages that harbours a DNA sequence that code for a basic antibody. These modified 'phages' were then used to infect bacteria. In each cycle the virus mutates these antibody protiens. These mutations lead to evolution of these antibodies which now are selected by "screening" to bind to a disease-protein. The phage "displays" these evolved antibodies on the coat (i.e., Surface) and these can be screened by "fishing" them out by a "target" protein. Over generations of doing this, chemists can evolve very specific antibodies for a target protein.

Greg Winter and his colleagues founded a company based on the phage display of antibodies e.g., generating an antibody for TNF-alpha, that drives inflammation in many autoimmune diseases. In 2002, the pharmaceutical was approved for the treatment of rheumatoid arthritis and is now also used for treating different types of psoriasis and inflammatory bowel diseases.

The 2018 Nobel Prize in chemistry is an excellent example of interdisciplinary research bringing about technologies that lead to greener chemicals industry, produce new materials, manufacture sustainable biofuels, mitigate disease and save lives.R(evolutionary) Chemistry indeed.

Frances Arnold, George P Smith and Greg Winter

Nobel Prize in Physics

The Power Of Light

Cyrus Khan, Freelance Science Writer.

The Nobel Prize in Physics honoured two discoveries in the physics of lasers this year. What makes these discoveries both stand out is the simplicity of their idea and execution.Half of the prize was awarded to Arthur Ashkin, who at age 96 now holds the distinction of being the oldest person to receive a Nobel. Ashkin came up with the novel concept of

'optical tweezers', which as the name suggests, holds small delicate things in place using just light from a laser beam.Now you may wonder how can light hold something. In everyday situations, the invisible waves of light that fall on us say from the sun or a tubelight do not seem to exert any force, however, light waves can exert a tiny little force that can actually push light objects. This 'radiation pressure', is somewhat like a wind. Even though we cannot see the wind, on a windy day, there are so many fast moving air particles racing in our direction that we feel a gentle push. Light is also composed of tiny particles called photons, which can have a similar effect, which is much more noticeable when in all the particles are moving together in the same direction (like in a laser).In his later work, Ashkin used optical tweezers to move around and study individual bacterial cells, which could not be done before without destroying them. Being able to hold small incredibly tiny objects was a tremendous boon to the field of biology and chemistry as well, and for his clever fundamental idea and execution, Ashkin was awarded the prize in Physics.

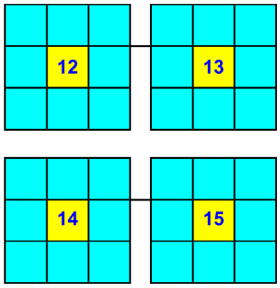
The second half of the prize was shared between Gérard Mourou and Donna Strickland for developing a revolutionary technique to make extremely powerful short pulses of light. High-intensity pulses of laser light have enabled several applications from precision machining to laser fusion experiments. Power is energy divided by time, and can be increased by either increasing the pulse energy, or decreasing the width of the pulse in time (or both). Initially after the development of the laser, it seemed impossible to increase the intensity of the optical pulses without frying the amplifier itself! The solution that Strickland and Mourou came up with was to stretch the initial pulse in time to reduce its peak power. Such a longer pulse could be amplified without destroying or damaging the components of the amplifier. The amplified high-energy pulse could then be compressed to create a dramatically more powerful pulse than the original one. This technique, called 'chirped pulse amplification' is the basis for generating ultra-high intensity laser pulses today. These allow applications in industry and medicine – for example in modern laser eye surgery (that millions of people now undergo every year) to make the delicate cuts to the cornea required to correct vision, and in basic research where such extreme intensity light allows researchers to create conditions in the lab like those in the interiors of stars. The ingenuity of the arrangement and its technical implementation that Mourou and Strickland (who was a PhD student at the time, it was her first paper!) came up with completely changed the way high-power lasers could be used, and the Nobel prize is a well-deserved and timely recognition.

Arthur Ashkin, Gérard Mourou and Donna Strickland

Through The Lens

Identify this coastal bird. It has a harsh wailing call. You will usually spot it on a ferry ride to Alibaug.

Stimulate Your Grey



Can you put the numbers 1 to 8 in each of the squares so that each side adds up to the middle number?
Source-http://www.mathsphere.co.uk/resources/MathSphereMathPuzzles.htm

Science In Daily Life

For Breezy and Bright Mornings

Peehu Pardeshi, Senior Research Officer, Doctors For You(NGO)

Imagine waking up to a beautiful shiny morning on a clear sky day. Imagine a large window bringing in the pure sunlight filtered through happily swaying trees. Feel the freshness of the breeze on your cheeks. What is your mood now? Do you feel refreshed and enthusiastic? Oh yes, you do!

Now imagine a contrary situation. Imagine a dull and damp room with a small half-open window overlooking another dull house. Feel the suffocation of the stale air standing still in the room. I could go on describing further, but I am sure you are feeling depressed already!

Now if just by imagination of the second scenario, you could generate a feeling of sadness and gloom, what

would be the condition of the people actually staying in these houses? The answer seems obvious.

This observation is now backed by science. These exact questions were asked in a scientific manner and the answers recorded. As happens in any scientific project, a preliminary observation was made, a hypothesis generated and then it was tested using scientific method of inquiry. The preliminary observation was that in a housing colony there were unusually high number of persons suffering from Tuberculosis. It was also observed that the buildings were laid out very close to each other. The houses were very small and stuffy. It was already known to the scientists that Tuberculosis spreads through coughing and sneezing and the chances of the spread increase in damp and crowded places. Based on this, a hypothesis was generated that the high burden of Tuberculosis could be associated with the poor housing conditions of the people in the colony. The aim of the study was to find if the architectural factors in the colony had any impact on the well-being of the residents.

With this aim, the enthusiastic researchers set out to survey the households with the help of a questionnaire in hand. They found out that, families staying on lower floors had higher chances of having a tuberculosis patient, as compared to those staying on the higher floors. Also, overcrowding in the house due to the small size of the house and large number of family members, posed a risk for Tuberculosis. All this could be attributed to the poor design and layout of the house and close clustering of the buildings in the colony. One of the defects was that there were windows only on one side of the house. So, the air had no path to exit and hence, there was no cross-ventilation. Some people had overcome this problem by installing exhaust fans, but all were not rich enough to do so. The buildings were located very close to each other which did not allow sunlight to enter the houses on lower floors.

Thus, the scientists realized that denying good housing conditions to the poor people of the society was hampering their growth and well-being and was in turn affecting the whole city. They also found out that the difference in the design of the houses for poor and those of the rich was not by chance, but a carefully planned one! In order to accommodate maximum number of people in minimum amount of space, some people had bent the rules and allowed close clustering of the buildings. To address this discrepancy, architects and doctors together are appealing to the government to review the practices of affordable housing schemes and stop the poor designing. The researchers and architects have also suggested some changes in the already existing houses to make them more ventilated. One of the suggestions was to install exhaust fans. Another was to change the windows from sliding to fully openable which would allow greater area for ventilation. Can you think of some more changes? What would you do to make your own house more airy and bright? If you were an architect, how would you design and position your house with respect to the sun? Would you like to lend a helping hand in creating the locality of our dreams as imagined at the start of this story?

Thought Byte

"When you look down from an aircraft, people, houses, rocks, fields, trees, all appear as one homogeneous landscape. It is very difficult to distinguish one from another. What you have just read is a similar bird's eye view of my life seen, as it were from afar. This is the story of the period ending with the first Agni launch – life will go on. This great country will make enormous strides in all fields if we think like a united nation of 900 million people." -*Dr. APJ Abdul Kalam*, in his autobiography *'Wings of Fire'*
(Co-author - Arun Tiwary) Published by Universities Press

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