

Physiology and Medicine: The Gifted Saga of the Last Decade

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Summary

Over the last century, Science and Technology moved forward and witnessed exceptional inventions and discoveries due to individual and collaborative research efforts. This momentum opened doors for the deep understanding of biological systems by which it permitted the advancement in technologies and designing of new tools in biomedical field. Since 1901, discoveries and inventions in various fields of science (Chemistry, Physics, Physiology and Medicine, Economics) including literature which can influence the betterment of human race were being awarded with Nobel Prize. Over the past decade, numerous groundbreaking discoveries in physiology and medicine have been reported. This short note is intended to summarize the significance of these findings and few remarkable controversies associated with them.

Introduction

To develop suitable treatment systems for a disease, it is important to understand the human molecular physiology, and the causative agents of the disease. Due to advances in biomedical sciences, the cutting edge technologies improved the human health care systems. The first Nobel Prize in Physiology and Medicine has been awarded to Emil Adolf von Behring (1901) for his work in immunology and second recipient was Ronald Ross for his work on Malaria in 1902. Later on, numerous exceptional findings in many areas of physiology and medicine such as fundamental biology, cell and molecular biology, Immunology and infectious diseases, neurology, genetics, microbiology/parasitology and other branches have been presented with the prize. There are some remarkable findings such as vaccination, pasteurization, etc., which were awarded with the Nobel Prize in the early 19th century [1,2].

At the turn of 20th century the world has witnessed benchmark innovations and discoveries such as depiction of DNA Double helix which is considered as scientific excellence [3,4]. To continue the legacy many of the genetic experiments such as discovery of genetic coding (1968), genetic control of enzymes (1965), problems of molecular genetics (1978), mobile genetic elements (1983) and genetic control of early embryonic development (1995) genetic regulation of organ development and programmed cell death (2002) were awarded the Nobel Prize [5]. Microbiology, Immunology and infectious diseases are the most frequently awarded fields of medicine and physiology, over the century. The first half of the 20th century is dominated by microbiologists whereas the second half is awarded to the immunologists [6]. In Physiology and Medicine Nobel Prize has been awarded 106 (38 one laureate, 32 times shared by 2 laureate and 36 times shared by 3 laureate) times (1901-2015) to 210 researchers from all parts of the globe [5]. In Physiology and Medicine Nobel Prize has been awarded 106 (38 one laureate, 32 times shared by 2 laureate and

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RNA Interference- 2006

The discovery of RNA interference (RNAi) which completely explained the fundamental mechanism of gene regulation has been awarded the Nobel Prize in 2006. It is considered as a revolutionary discovery in understanding the gene expression, gene silencing and evolution [7,8]. In their studies, Fire and Mello found that double standard RNA (dsRNA) is more effective than single standard RNA (ssRNA) in interfering with the function of endogenous gene [9]. RNAi could be useful as a potential drug in viral infection, tumor treatment, and in gene mutation related disease treatments. However, many questions related to the basic mechanisms, potential applications and improved therapeutic opportunities needed to be addressed in near future [7,8].

Gene Targeting (Gene Knockout)-2007

The 2007 Nobel Prize was awarded to three scientists for development of gene targeting (knockout) in mouse embryonic stem cells. This discovery opened the gates for genomic studies and regenerative medicine. Mouse Embryonic Stem cells allow specific targeting modification, which dragged the attention of these three laureates [9-12]. Embryonic stem cells have a tendency to deliver experimental genetic manipulations, thereby, improve the theoretical understanding and biomedical benefits [11]. Emerging technologies such as gene targeting need to be tested and validated effectively, by which significant complex biological questions would be answered [10]. Their work has significantly impacted developmental biology, cancer science, regenerative medicine, epigenetic reprogramming and maintenance of pluripotent Cells [13,14].

Human Papillomavirus and Human Immunodeficiency Virus- 2008

Over the years, there was no clue for most of the viral diseases such as Cancer and AIDS that challenged the man kind and Science as well. To cure any disease it is most important to have an idea about its causative agent, physiology and molecular structure. The 2008 Nobel Prize has been awarded to outstanding and lifesaving findings of HPV and HIV. Harald zur Hausen discovered papillomavirus [15], which is the second most risk of cancers and Françoise Barré-Sinoussi and Luc Montagnier discovered human immunodeficiency virus [16,17]. These findings helped in development of diagnostic options and biosynthetic vaccines for cervical cancer [18] and AIDS [19]. Of course, both the findings answered the long lasting global burdens; this is the prize of

the decade, which has remarkable conflicts. There is evidence that the discovery of Human papillomavirus (HPV) has potential commercial benefits to one of the leading biopharmaceutical companies [20]. On the other hand, Human Immunodeficiency Virus (HIV) discovery has different issue, where one scientist left out, which surprised the world including one of the co-recipients of the prize [21,22].

Discovery of Telomeres and Telomerase Enzyme- 2009

This is one of the awards presented to the solution of one of the secrets in Biology. How the chromosomes are protected? How the ends of the chromosomes are replicated? These questions are remained for many years. In 1978 the first telomere sequence has been identified and later the discovery of telomerase enzyme revealed the secret behind the unsolved problem [23]. These findings, advent the understanding of the telomeres and the activity of the telomerase enzyme in normal cells and cancer cells as well [24-26]. This discovery update the current knowledge about the telomere replication, where lot of twists and turns are located and specifically, improved understanding of non-Watson and Crick forms of DNA sequences. Other than this, these findings have clinical significance in understand the aging. This is one more special award of the decade; the recipients are either close colleagues (Blackburn and Szostak) and or mentor and student (Blackburn and Greider). This prize has remarkable significance in Nobel history that for the first time 2 women awarded the Nobel Prize in the same year field and year.

In Vitro Fertilization-2010

In Vitro fertilization is the cause of the smiles on the faces of childless couple around the world and this could deserve the Nobel Prize and considered as one of the most courageous discovery of the current times [27]. In 1968, Edwards et al. for the first time reported the *in vitro* fertilization convincingly. After the *in vitro* fertilization reported, Edwards had a tough time and series of professional attacks on him in all possible ways that included ethical and political. "The massive press interest of the late 1960s was unabated in the ensuing years, and so Edwards was faced with a choice: either he could keep his head down and allow press fantasies and speculations to go unanswered and unchallenged, or he could engage, educate and debate"[28]. Finally, the battle ended and IVF has been awarded Nobel Prize in 2010 and Dr. Edwards passed away in 2013 but IVF became immortal.

Innate and Adaptive Immune Response and Dendritic Cell- 2011

Over the last century ground breaking discoveries reported in the field of immunology; however, there are questions yet to be answered. The understanding of basic immunology where numerous cells, tissues and molecules are involved is a big deal to the researchers. The basic immune system functions are revealed that how an organism (from insect to mammal) senses the infection and responds to it? This time innate and adaptive immunity mechanisms have been awarded the prize for discovery of Host defense system in mammals [29,30], in insects [31] and for the discovery and roles of dendritic cells in adaptive immunity (Ralph Steinman). Sometimes, individual discoveries open the gates for new scientific field, Ralph Steinman discovery is one of those kind, which transformed into novel medical applications [32]. After the years of dedicated work and seminal

discoveries at the age of 68 (2011) Ralph Steinman passed away few days before the Nobel committee announced the award [33].

The Induced Pluripotent Stem Cells- 2012

In few cases, hypotheses are gone wrong and the negative results of these experiments leads to new scientific discoveries. One of the most interesting major breakthroughs of this kind reported in last decade is the finding of Induced Pluripotent Stem Cells (iPS cells), for which 2012 Nobel Prize has been awarded. After a series of attempts to find out the research work for his doctoral program, Shinya Yamanaka, encountered with couple of negative results and further analyses of those results led to new state of the art of science and so called 'induced pluripotent stem cells (iPS cells)' [34]. These findings reported that the forced expression of certain transcription factors can induce the pluripotency and led to development of effective reprogramming methods of iPS cells [34]. On the other hand, John B Gurdon the co-recipient of 2012 Nobel Prize, worked with eggs and embryos of frogs (*Xenopus*) and reported reprogramming by nuclear transplantation [35]. These findings improved the understanding of nuclear reprogramming, of embryonic development, and of cellular differentiation. Gurdon work has paved the way for regenerative medicine [35,36]; and also this discovery led to the further research in regenerative medicine and reprogramming field.

Machinery Regulating Vesicle Traffic and the Transport System- 2014 Nobel Prize

In 2013, three researchers shared Nobel Prize for the ground breaking discovery of "machinery regulating vesicle traffic and the transport system in the cells" [37]. One of the three laureates, Rothman worked on the membrane fusion of the cells and showed how the vesicles transport the proteins in various components of the cell [38]. Whereas the other two Randy Schekman and Thomas Südhof worked on molecular basis of neurotransmitter release at the junction of nerve cells and between nerve and muscle cells. Randy Schekman showed that how the genes and proteins control the secretory pathway in Yeast [39]. Südhof showed the molecular machinery of neurotransmitter release and discovered the molecular mechanism by which Ca^{2+} ions trigger synaptic vesicle fusion [40]. The most interesting fact behind this study is that, all three studies have a close relationship and inspired by studies that are honored with Nobel Prize earlier.

Brain Navigation System: Grid Cells, Place cells and Memory-2014 Nobel Prize

Cognitive psychology, Brain function and behavior are at the center of neurology over the years. But the questions like who we are? and where we are? were not revealed. Advancements in the field of neuroimaging and neuropsychology have improved the understanding and discovery of Place cells [41,42], Grid cells provided deeper insights in brain and spatial memory [43,44]. The place cells in the hippocampus signal the position, when an animal enters a particular place of its environment. The grid cells found in entorhinal cortex provides the brain with a navigation system. The combination of place cells and grid cells improve the knowledge of animal's position [42-44]. This award is considered as a special prize of the decade, which is shared by the mentor and students (O'Keefe is mentor of Moser MB and Moser EI) and wife and husband (Moser MB and Moser EI).

Discovery of Avermectin and Artemisinin- 2015 Nobel Prize

The Nobel Prize 2015 has been awarded to the “Simple Natural and Basic Science”. Three researchers, Bill Campbell and Professor Satoshi Ōmura for the discovery of avermectin and Youyou Tu for the discovery of the artemisinin awarded the prize. These discoveries revolutionized the therapeutic options for parasitic diseases such as Onchocerciasis (River blindness), Lymphatic filariasis, Malaria, etc., which significantly reduced the percentages of the morbidity and mortality [45-47]. These findings raised the interest in natural products and their therapeutic applications not only for parasitic diseases but also to lethal threats such as cancer and AIDS. The benefits to the mankind of and global impact of these discoveries are immeasurable [48-50]. Finally, the gifts of nature have been gifted.

Conclusion

As fundamental science advances day by day, every new invention or discovery has its impact on human healthcare and helps to improve the livelihood. As mentioned above, most of the findings in basic science have been gifted with Nobel Prize in last decade. For example, the prizes of 2015, 2013, 2011, and 2009 awarded to fundamental understanding of science, whereas prizes of 2012, 2011, and 2006 awarded to the fields that opened new fields in Biology. iPS cell technology opened new branch of biology, Regenerative Medicine and has great impact on embryonic development and developmental biology. The finding of place cells and grid cells advanced the cognitive psychology and neuroscience. RNAi has answered many questions regarding evolution and opened the opportunities for development of therapeutic strategies. 2007 prize has been awarded for gene targeting technology, the finding that led to Molecular Biology. 2010 prize for “re-creation” (*in vitro* fertilization) which is opposed by religious beliefs but accepted by science. We can say 2008 prize has direct impact on human health care improvement, the discovery of HPV and HIV which gave relief to the world from two major burdens (cervical cancer and AIDS) of mankind. In conclusion, continuous research is required to update our current knowledge in both fundamental and applied science by which our health care puzzles will be solved.

Conflict of Interest

This article is being written to summarize the highest level of findings and the pain has been taken by the inventors. Overall, this paper is author's soul interest, passion and enthusiasm in science but not to criticize. It is neither a scholarly study nor an in-depth story of the lives of these people.

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