Tang Prize Laureates Reflect on the Breakthroughs Made Possible by Cytokine Research

TAIPEI, Nov. 27, 2021 /PRNewswire/ -- Following the inspiring opening speech, "Future Perspective of Cancer Immunotherapy," delivered by Nobel Prize and Tang Prize laureate Prof. Tasuku Honjo at the 14th Asia Pacific Federation of Pharmacologist Conference (APFP) on November 26, the 2020 Tang Prize Laureate's Lecture for Biopharmaceutical Science, co-organized by the Tang Prize Foundation and The Pharmacological Society in Taiwan, took place at the 14th APFP at 1:30 p.m. (GMT+8) on November 27. Co-hosted by Dr. Wen-Chang Chang, chair of Taipei Medical University's board of directors, and Dr.Yun Yen, chair professor at Taipei Medical University, this special session featured lectures delivered by three winners for the 2020 Tang Prize in Biopharmaceutical Science, Drs. Charles Dinarello, Marc Feldmann, and Tadamitsu Kishimoto, providing valuable informaiton on the role cytokines play in inflammation and the COVID-19 disease as well as possible treatments.

The first lecture by Dr. Dinarello, titled "Interleukin-1: The Prime Mediator of Systemic and Local Inflammation," began with his purification of leukocytic pryogen from human white blood cells in 1971. It then took him six years to identify two fever-producing molecules, later named IL-1αand IL-1β. In 1977, the research outcomes were published in the Proceedings of the National Academy of Sciences, and for Dr. Dinarello, "that was an important step in the history of cytokine biology," because many people in the field of life science were encouraged to study the immune system's influence on human physiology. As a result, cytokine biology expanded rapidly. He also talked about how after the early experiments in humans, "the history of cytokines being used as a treatment changed dramatically," and the focus was shifted to "inhibiting cytokines, such as IL-1, such as TNF, such as IL-6." To help the audience understand the complicated network constituted by the pro-inflammatory molecules of the IL-1 family, Dr. Dinarello elaborated on the signal transduction of IL-1 family members, their pro- and anti-inflammatory characteristics, and the symptoms of different inflammatory diseases, so as to ease the way for the audience to get a proper grasp of the second half of the lecture which centered on "the clinical application of Il-1 blockade." IL-1 overproduction, as Dr. Dinarello remarked, is a common cause of many diseases. IL-1Ra, on the other hand, can inhibit Il-1αandβ, and block the IL-1R signaling. Anakinra, a recombinant human IL-1Ra has been produced. It is used to treat rheumatoid arthritis and can also prevent glycemic disorders in type 2 diabetes. Moreover, canakinumab, an anti-IL-1βmonoclonal antibody successfully developed by Novartis, has been approved in a variety of diseases, ranging from rare hereditary diseases, rheumatic diseases, autoimmune and inflammatory diseases, to cardiovascular diseases. The most exciting news involving canakinumab is the clinical trial, CANTOS, which unexpectedly proved that canakinumab has an important role in treating cancer. Therefore, Dr. Dinarello believes that blocking IL-1 can usher in the dawn of a new cancer treatment.

The second speaker, Dr. Feldmann, shared his views on "Translating Molecular Insights in Autoimmunity into Effective Therapy." The emphasis of the first half of his lecture was on how he discovered that anti-TNF can be effective in treating rheumatoid arthritis. Administrating either high or low doses of this drug can block TNF while also rapidly reducing the production of other inflammatory mediators. In their earlier experiments, Dr. Feldmann and his team demonstrated that around 50% of people with rheumatoid arthritis responded to the combination therapy using anti-TNF and the cancer drug methotrexate. That led him to believe that "we've got a long way to go before every patient is cured." During the second half of the talk, Dr. Feldmann informed us that "TNF is a very unusual meditator, because it has two different targets: TNF receptor-1(TNFR1), which drives inflammation, and TNF receptor 2, which does the very opposite. So if you block all of TNF, you block of receptors. You block inflammation, but you also prevent the body's attempt to dampen down the inflammation." Therefore, he and his colleagues are "in the process of generating tools" and has already blocked TNFR1 without change the function of regulatory T cells. In addition, Dr. Feldmann mentioned the potential of anti-TNF for addressing many unmet medical needs, such as treating fibrosis of the hand by injecting anti-TNF into the palm. However, he pointed out the two obvious disadvantages of the anti-TNF he first developed: it was cost-prohibitive and "it was an injectable drug." Thus, to develop "cheaper drugs that could be delivered by mouth" would bring greater benefit to the society. Throughout the lecture, Dr. Feldmann kept bringing up many people with whom he was or is collaborating for different projects and experiments, as he tried to drive home the message that what he had learned from these experiences was "how to work effectively with others" to ensure continuous breakthroughs in their research. It has been the hallmark of his career to find "talented people to work with," and, "together with them," to achieve much more "than we could alone."

Presenting the third lecture on the topic "Interleukin-6: From Arthritis to CAR-T and COVID-19," Dr. Kishimoto drew the audience's attention to how IL-6 was discovered, why IL-6 is a pleiotropic molecule, and why IL-6 "is responsible for both antibody production as well as inflammation induction." He also shed light on IL-6's effects on autoimmune diseases and how IL-6 can trigger cytokine storms. Early on in his talk, Dr. Kistimoto made clear that the overproduction of IL-6 has found to be associated with many diseases, such as cardiac myxoma, Castleman's disease, rheumatoid arthritis, and systemic onset of juvenile idiopathic arthritis (JIA). To tackle the inflammatory responses provoked by IL-6 overproduction, Dr. Kishimoto and his team tried to treat patients by blocking IL-6 signals. Subsequently, tocilizumab, a recombinant humanized anti-IL-6 receptor monoclonal antibody, was successfully developed and has been approved for use in more than 100 countries for the treatment of rheumatoid arthritis and JIA. With regard to how the production of IL-6 is regulated and why IL-6 overproduction often occurs in chronic inflammatory diseases, Dr. Kishimoto explained that the stabilization of IL-6 strongly depended on its messenger RNA. To rescue patients suffering from CAR-T cell-induced cytokine storms, many in the medical profession now will use tocilizumab to cushion the side effects of this therapy. In view of this example, Dr. Kishimoto and his team speculated that

tocilizumab can also be effective in helping seriously-ill COVID-19 patients combat cytokine storms. Several large-scale clinical trials proved that it can lower the possibility of requiring invasive ventilation or the risk of death. For this reason, the US Food and Drug Administration and the World Health Organization have both issued an Emergency Use Authorization for tocilizumab for the treatment of COVID-19 patients. In this lecture, Dr. Kishimoto gave us a comprehensive overview of the research on IL-6 he led his team in carrying out over the past 50 years. It was a journey that took them from basic research to drug development and clinical application.

These three lectures by the 2020 Tang Prize laureates in Biopharmaceutical Science will be premiered on the Tang Prize YouTube channel from 4 p.m. to 7 p.m. (GMT+8) on November 27. To watch the complete version of the "2020 Tang Prize Laureate's Lectures for Biopharmaceutical Science," please consult the schedule below.

- Dr. Charles Dinarello - Interleukin-1, the prime mediator of systemic and local inflammation
  11/27 16:00 Taipei time (GMT+8) https://youtu.be/gVXKCkTKkcg
- Dr. Marc Feldmann - Translating Molecular Insights in Autoimmunity into Effective Therapy
  11/27 17:00 Taipei time (GMT+8) https://youtu.be/_M3R9WFtDt4
- Dr. Tadamitsu Kishimoto - Interelukin-6: From Arthritis to CAR-T and COVID-19
  11/27 18:00 Taipei time (GMT+8) https://youtu.be/93rNLo5QMQc

SOURCE The Tang Prize Foundation

For further information: Clare Liu, Email: thetangmedia@tang-prize.org, Phone Number: +886-2-8772-5188#103
