

Editorial Board



B. K. Kishore
M.D., Ph.D., MBA



Soumya R. Neravetla
M.D., FACS



Kusum Punjabi
M.D., MBA, FACEP



Kavitha Das
BDS, MPH, MS

Editorial



jean-philippe-delberghe-unsplash

Launching JAAPI

The Peer-Reviewed Journal of AAPI

Bellamkonda K. (BK) Kishore

M.D., Ph.D., MBA, CBiol, FASN, FRSB, FAPS, FAHA

University of Utah Health, Salt Lake City, Utah

Email: nephron369@yahoo.com

*The glory of medicine is that it is constantly moving forward, that there is always more to learn.
The ills of today do not cloud the horizon of tomorrow, but act as a spur to greater effort.
– William James Mayo, M.D.*

As we entered the 21st century twenty years ago, knowingly or unknowingly we also entered into an age of information explosion. For the first time in history, the humanity is feeling that it cannot cope up with the pace at which information is pouring into the world from all possible corners and portals. As physicians and scientists, we are realizing that there is no dearth of information, but there is a dire necessity for more time to process information and to manage it. To meet this demand, in the past two decades, several internet portals, such as [WebMD](#) and [Faculty Opinions](#) have been offering processed and ready to read and digest information as small packets, just like the fast food chains offer us ready to eat food items in boxes. Such knowledge portals are extremely useful for practicing clinicians as well as researchers, who may not afford to spend time going through extensive and complex scholarly publications. These portals also complement CME programs in reducing the ever widening knowledge gap. We definitely need journals and other resources that can churn wide range of information and present the gist of knowledge in a simple format, just like extracting butter by churning yougurt. Many professional societies or associations have realized this fact and are providing processed information as a ready-to-use source of knowledge to their members through publications that often complement or run parallel to the high impact scholarly journals that already exist. One such example is the recently launched [Kidney360](#) of the American Society of Nephrology (ASN), which complements the [two high impact kidney journals](#) it already publishes. In fact, while doing so, the ASN has introduced two new concepts. One is moving nephrological care from US-centric to global-centric one, and providing an open access source of information to kidney patients as

well. At a time when most educated patients are googling about their illnesses before visiting a doctor, an authentic source of information about diseases provided by dedicated physicians is more welcoming than the information spread by amateurs on the internet. Medical education and clinical knowledge are no more the privilege of medical schools or hospitals or clinical grandrounds alone. The new concept is, the best way to combat misinformation is to proactively provide true information. In this context, the real meaning of *doctor* as *teacher* in Latin is more relevant today than ever before.

As the leading organization for Indian Physicians outside India, AAPI has been the dynamo of force in the United States and India. It is well poised to address global healthcare issues affecting both developed and developing countries, as well as rapidly emerging economies, such as the BRICS countries. As part of these efforts, AAPI has initiated several projects, and has been conducting Global Healthcare Summits (GHS), and various awareness campaigns, such as the Obesity Awareness Campaign. The ongoing coronavirus pandemic has added another dimension to the educational outreach capability of AAPI in the form of a series of high-quality webinars by experts in the field. In fact, the pandemic has brought out the best in AAPI. Yet, there is room for a medical journal to enhance the professional and academic outreach and outlook of AAPI to the larger cross section of the world and to serve as its voice spreading its vision and mission, namely, *to facilitate and enable Indian American Physicians to excel in patient care, teaching and research and to pursue their aspirations in professional and community affairs*. While doing so, they have the potential to transform AAPI into a Global Healthcare Institute. In line with these aspirations, about a year ago, in its Governing Body meeting in the Long Island, NY on February 8, 2020 AAPI announced its decision to launch a peer-reviewed medical and health journal. It was a collective decision made by Dr. Suresh Reddy, then President and Dr. Sudhakar Jonnalagadda, then President-Elect. They entrusted the responsibility of preparing the launchpad for the journal to me. Following that, in collaboration with Drs. Soumya Neravetla, Kusum Punjabi and Kavitha Das, Sushruta Medical News (SMN), a non-peer-reviewed medical and healthcare bulletin was started with monthly issues containing quality publications. With the success of SMN and the groundwork prepared, now we are ready to launch JAAPI, the peer-reviewed Journal of the AAPI, with its inaugural issue coming out soon. Since this is the last issue of Sushruta Medical News, we dedicate it to present the groundwork prepared for JAAPI, which includes the Editorial Advisory Committee, the inaugural Editorial Board, details about the vision, mission, and scope of JAAPI as well as its structure and future expansion. More details will be provided in due course as the JAAPI moves forward decisively.

I take this opportunity to thank all those who supported our efforts and encouraged us in publication of Sushruta Medical News, and in preparing the launchpad for JAAPI. First, I would like to thank Drs. Suresh Reddy and Sudhakar Jonnalagadda for the confidence they bestowed on me, and for their sustained and unconditional support during the past one year which made launching of JAAPI possible today. Second, I thank my co-editors of Sushruta Medical News, Drs. Soumya Neravetla, Kusum Punjabi and Kavitha Das, who worked hard in bringing out 11 monthly issues of SMN despite constraints imposed by the pandemic. I thank all authors who contributed to SMN. I am indebted to the energetic members of the Editorial Advisory Committee, who generated value and synergy, namely Drs. Manoj Shah, Suresh Karne, Raj Alappan, and Ramasubbareddy Dhanireddy, and the two wise Editorial Advisors, Drs. Vikas Khurana and Vemuri Murthy. Without the unconditional support of these dedicated professionals, JAAPI could not be realized so soon. Finally, I thank the AAPI Executive Committee Members of 2020 and 2021, and those who volunteered as Editorial Board Members. Together we can take JAAPI to new heights and sustain it. As the Canadian physician William Osler said, *medicine is a science of uncertainty and an art of probability*. But JAAPI should help us to overcome those by showing us the direction in which we have to tread. Of course, that is possible by following the advice of Benjamin Franklin: *either write something worth reading or do something worth writing about*. The choice is ours.

Hyperlinks: Hyperlinks in the text take to their respective websites or media.

Disclosure: Author declared no competing interests.



AMERICAN ASSOCIATION OF PHYSICIANS OF INDIAN ORIGIN

December 14, 2020

President

Sudhakar Jonnalagadda, MD

(912) 309-0340

aapipresident@aapiusa.org

President-Elect

Anupama Gotimukula, MD

President-elect@aapiusa.org

Vice President

Ravi Kolli, MD

vicepresident@aapiusa.org

Secretary

Amit Chakrabarty, MD

secretary@aapiusa.org

Treasurer

Satheesh Kathula, MD

treasurer@aapiusa.org

Immediate Past President

Suresh Reddy, MD

redyaapi@gmail.com

Chair, AAPI Board of Trustees

Sajani Shah, MD

sajanishah@yahoo.com

YPS President

Ami Baxi, MD

ami.baxi@gmail.com

MSRF President

Kinjal Solanki, MD

kinjal.solanki15@gmail.com

Regional Directors

Sujeeth Punnam, MD

sujeeth.punnam@gmail.com

TBD

Hemant Vallapureddy, MD

ilulug@yahoo.com

Roshan Shah, MD

rosh.shah@gmail.com

Meher Medavaram, MD

meherm@comcast.net

Dharmesh Gandhi, MD

dvgandhi2002@yahoo.com

Sunil Kaza, MD

sunnymd@gmail.com

Subbarao Bollepalli, MD

subbarao@snet.net

Himanshu Pandya, MD

pandyamd@yahoo.com

Sumul Ravai, MD

dravai@gmail.com

Bhushan Pandya, MD

bhpm2004@yahoo.com

Malti Mehta, MD

mehtapcmd@gmail.com

Board of Trustees

Chair

Sajani Shah, MD

sajanishah@yahoo.com

Bhavani Srinivasan, MD

docbhavani@gmail.com

Sapna Aggarwal, MD

sapnaaggarwal@verizon.net

Mukesh Nigam, MD

mkn9900@yahoo.com

Kusum Punjabi, MD

kusumpunjabi@yahoo.com

Tarak Vasavada, MD

tarak@vasavada.us

Jagdish Gupta, MD

jagdishgupta@gmail.com

Raghu Lolabhattu, MD

raghujyothi99@yahoo.com

V. Ranga, MD

vrangamd@gmail.com

Seema Arora, MD

seemaaroramd@aol.com

Stella Gandhi, MD

stella_gandhi@yahoo.com

Pooja Kinkhabwala, DO

pkinkha@gmail.com

General Counsel

Hari Shivshankar Lal, Esq.

lalslw@msn.com

Administrative Director

Vijaya Kodali

vkodali@aapiusa.org

Dear AAPI Friends,

In order to facilitate transition of the current Sushruta Medical News into a peer-reviewed Journal of the American Association of Physicians of Indian Origin (JAAPI), and for carrying out the groundwork needed for establishing a professional quality JAAPI, I hereby authorize the formation of an Ad hoc Editorial Advisory Committee with the following membership for the year 2020-21. This Committee will be responsible for the work needed to launch JAAPI and has the autonomy to take appropriate decisions as deemed beneficial for the entrusted work.

Ad hoc Editorial Advisory Committee of JAAPI (Journal of the AAPI)

Chair: Bellamkonda Kishore, M.D.

Co-Chairs: Soumya R. Neravetla, M.D.

Kusum Punjabi, M.D.

Kavitha Das, BDS

Members: Ramasubbareddy Dhanireddy, M.D.

Manoj Shah, M.D.

Suresh Karne, M.D.

Rajendran Alappan, M.D.

Advisors: Vemuri S. Murthy, M.D.

Vikas Khurana, M.D.

Contact the Committee at: smn@aapiusa.org

Sincerely,

Sudhakar Jonnalagadda, MD

President, AAPI



P: (630) 990 2277

F: (630) 990 2281



www.aapiusa.org

www.aapiconvention.org



600 Enterprise Dr., Ste. 108

Oak Brook, Illinois 60523



info@aapiusa.org

Tax ID: 38-2532505

About JAAPI: JAAPI is a peer-reviewed medical and health journal published by the AAPI. In line with the vision and mission of AAPI, JAAPI is dedicated to facilitate Physicians to excel in patient care, teaching and research, and pursue their aspirations in professional and community affairs. JAAPI is open to contributions from physicians and scientists of all backgrounds and from all over the world.

Scope of JAAPI: JAAPI publishes a variety of articles, such as original research articles, clinical studies, reviews, perspectives, commentaries, case studies etc., covering all aspects of medical sciences, clinical specialties, and healthcare, including epidemiology, and policy and legislative issues. Articles submitted to the JAAPI must be original and should not have been published previously or under consideration for publication elsewhere, except in abstract form in proceedings of conferences or meetings. Based on the type of the article, the length and specifications vary.

Publication Model: JAAPI will be published as completely Open Access in electronic form (PDF). These will be archived in AAPI website, and the link to URL for each issue will be emailed to AAPI Members. A limited number of hard copies will be printed for promotional purposes and for displaying at AAPI Conventions and other professional meetings or for distributing to libraries or dignitaries. There will not be any submission fee or publication charges to the authors. Although materials published are copyrighted by the AAPI, others can cite or reproduce figures, schemes and pictures published in JAAPI without paying fee, but by giving due credit to JAAPI. This will ensure rapid dissemination of materials published in JAAPI and thus help to boost its Impact Factor.

Registration and Indexing: Soon after publication of the inaugural issue, JAAPI will obtain ISSN (International Standard Serial Number) for both electronic and print versions. After a year of publication, JAAPI will be eligible for applying for registration with MEDLINE. If successfully registered, JAAPI will be indexed in the PubMed operated by the National Library of Medicine. JAAPI will also be registered for indexing in other major bibliographic databases, such as SCOPUS (managed by Elsevier), EMBASE (Excerpta Medica Database), DOAJ (Directory of Open Access Journals), Ovid (Walter Kluwer Ovid Database) and BioMed Central Database. JAAPI will be added to ResearchGate, an European social networking site for scientists and researchers to share publications, discussions and collaborations. JAAPI will also create a Twitter handle so that physicians, healthcare professionals, academicians and scientists can follow the highlights of articles published in JAAPI.

Editorial Board: The Editorial Board of JAAPI consists of one Editor-in-Chief, several Deputy Editors covering different areas of medicine and health care, Editorial Board Members and Editorial Interns. In addition, there are Editorial Advisors to oversee long-term performance and stability of JAAPI and to help the Editorial Board Members in logistics, administrative and fiscal issues. The Editor-in-Chief and Deputy Editors are chosen based on their academic standing and/or professional experience in editing and reviewing manuscripts for journals. The Deputy Editors will handle the review process of submitted papers with the help of internal (Editorial Board Members) and external reviewers. Editorial Interns are YPS or MSRF members who would like to obtain training in editing for journals. They will work with the Deputy Editors. Only manuscripts that meet professional and scientific standards will be accepted for publication. Review process is single-fold blinded on the authors side. But after acceptance of papers, the names of the handling Editors and Reviewers will be published on the front page of the article. This new trend started by some European journals is gaining momentum as it gives due credit to the Editors and Reviewers and ensures fair review process. Finally, AAPI membership is required for all Editorial Board Members, who are expected to promote the vision and mission of AAPI through JAAPI.

CME Credits for Peer-Review Process: After indexing by PubMed, working through AAPI, JAAPI will obtain CME Credit eligibility for its reviewers by the Accreditation Council for Continuing Medical Education of the American Medical Association. Currently, several journals are offering CME credits to their reviewers.

Journal Periodicity: Initially, the JAAPI will have three issues per year (Spring, Summer, and Fall). As the journal picks up momentum and article submissions increase, the periodicity will be quarterly or even more frequent.

Types of Articles JAAPI Accepts:

- **Original Research Articles:** These describe original scientific or clinical research conducted on in vitro or animal models or human subjects after obtaining approval by the concerned institutional animal care and use committees or human subjects research review boards. The research should comply with the guidelines and regulations of US Public Health Service. The original research articles can be up to 3,000 words in length, excluding title page, abstract, legends and references. Maximum 7 figures or tables are allowed. Additional figures or tables need to be justifiable for the article. Supplemental Information (SI) containing data and text, such as methods, are allowed for deposition.
- **Review Articles:** The review articles can address any contemporary issue in medical or clinical sciences, or healthcare, including epidemiology, and policy and legislative issues. The reviews should provide in depth analysis of the topics but should not be just presenting catalog of information. The review articles should be balanced and should cite relevant literature without bias. The review articles can be up to 3,000 words, excluding title page, abstract, references, and legends. Not more than 5 figures and tables combined. There is no limit on the number of references, but they should be recent and relevant ones.
- **Clinical Studies:** Clinical trials can be either observational or retrospective analysis of data or prospective randomized studies. All clinical studies should be conducted in accordance with the regulations and guidelines, documenting informed consent, protection of research subjects, inclusion of minorities etc., as per the guidelines of the US Public Health Service. Rigorous statistical analysis should be followed. Raw data should be made available for analysis if required. These articles can be up to 3,000 words, excluding title page, abstract, tables, legends, and references. Maximum number of figures or tables are 7 combined. Additional figures or tables should be justifiable for the study. Supplemental Information (SI) is allowed for deposition.
- **Brief Reports:** Brief reports of contemporary issues of high significance are accepted to disseminate information. These reports are up to 1,200 words in length, excluding title page, abstract, legends and references. About 3 tables or figures combined are permitted. Maximum 15 references are allowed.
- **Letters to the Editor:** Letters to the editors on topics of high importance or on the articles published in JAAPI are welcome. These should be focused and carry significant take home message, rather than a simple presentation of one's own perspective on the topic. These can be up to 600 words in length with 6 references, 2 small tables or figures maximum. The authorship should be limited to 2 or 3. No abstracts are allowed.
- **Articles on Diagnosis and Treatment Review:** Article describing latest methods, approaches and technologies in diagnosis and treatment can be up to 2,000 words, excluding title page, abstract, references, and legends. Figures and tables should be limited to five combined.
- **Case Studies or Clinical Challenges:** Case presentation with about 250 words, followed by discussion of 500-600 words, 1-2 small figures, and less than 10 references, are welcome. The authorship should be limited to 3 unless it involves trainees. Proof of patient consent should be provided.
- **Perspectives on Contemporary or Controversial Topics:** These should be thought-provoking with intuitive analysis rather than presentation of facts. Some degree of speculation and hypothesis is

permitted provided they are supported by rational analytical base. These articles can be up to 1,200 words, excluding title page, abstract, legends and references. Less than 3 tables or figures combined are allowed. References should be limited to the required ones.

- **Commentaries on Published Papers:** Commentaries on published papers are accepted if they provide a different post-publication perspective not explicit or missed in the original publications. These can either positively or negatively impact the original publication. But the emphasis is how the original publication can impact clinical practice or evidence-based medicine. These can be 600-800 words in length with one or two figures or tables, and limited references. No abstract is allowed. Authorship should be limited to one or two.
- **Bench-to-Bedside or Bedside-to-Bench:** Authors can take laboratory findings to clinical settings or bring clinical dilemmas to laboratory research. Special emphasis should be made on the process of moving the subject from bench to bedside or vice versa. This type of articles can be up to 1,200 words in length, excluding title page, abstract, legends and references. Not more than 3 tables or figures combined are allowed. References should be limited to the required ones.

References Style: JAAPI follows the same style as JAMA for presentation of references, which can be found in the following URL. <https://www.bibguru.com/c/jama-citation-generator/>

Disclosures: All authors should disclose relevant industry relations, including speaker's bureau, research grants, travel funds, stocks in excess of \$10,000 owned by them or their immediate family members, etc., which can be construed as conflicting with the content of the article being submitted. When in doubt whether a particular industry relation is a conflict, the authors should consult the editorial office.

Plagiarism: When citing a published report or paper, authors should ensure that passages are not reproduced verbatim, as that is considered as plagiarism, even if the source is cited. Authors should rewrite such passages in their own words. JAAPI will eventually subscribe to a professional plagiarism detection service to comply with the existing standards in journal publication. When figures or schemes from other publications, including the previous publications of the authors, are used in the articles, copyright permission to do so should be obtained. It is author's responsibility to obtain copyright permission through Copyright Clearance Center (<https://www.copyright.com/manageAccount.action>). Proof of obtaining copyright permission should be provided to JAAPI. For assistance, authors should contact editorial office.

Proprietary Names: While citing names of drugs or medications, authors should avoid brand names and use generic or pharmacological names only.

Advertisements: JAAPI welcomes advertisements from pharma industry, private companies or businesses, clinical and professional practices or educational webinars or CME programs or promotion of books on medical and health issues by the authors. However, JAAPI does not accept advertisements related to elections for positions in the AAPI or its chapters or other organizations or political lobbying or religious issues or others that are not professional in nature. All advertisements will be of full page. The pricing is \$1,000 for inside page, \$2,000 for outside of back cover, and \$1,500 for inside of front or back covers. Checks should be made payable to AAPI with JAAPI-Ad in the memo line. Funds raised through advertisements will be used to pay for the expenses incurred for running JAAPI.

Contact Information: A dedicated portal for JAAPI will be created in AAPI website soon. Until that time, for further information about JAAPI or to submit articles, please send an email to smn@aapiusa.org One can also directly contact the Editor-in-Chief or any Deputy Editor, who will be willing to respond to your questions.

Editorial Board of JAAPI

Editor-in-Chief

Bellamkonda K (BK). Kishore

M.D., Ph.D., MBA, CBiol, FASN, FRSB, FAPS, FAHA
Nephrology & Hypertension; Nutrition & Integrative Physiology; and
Center on Aging, University of Utah Health, Salt Lake City, UT

Deputy Editors

Raj Alappan

M.D., DTCD, DM., FACP, FCCP, FASN
Nephrology & Hypertension, Medical School of Georgia,
Augusta, GA; Mercer University, Macon, GA

Madhusudan Bhandary, Ph.D.

Biostatistics and Mathematics
Columbus State University, Columbus, GA

Sreenivas Chandana, M.D., Ph.D.

Hematology & Oncology
Western Michigan University School of Medicine &
Michigan State University, Kalamazoo, MI

Kavitha Das, BDS, MPH, MS

Senior Scientist in Cardiology
Icahn School of Medicine at Mount Sinai
New York, NY

Ramasubbareddy Dhanireddy, M.D.

Pediatrics, Neonatology & Obstetrics
University of Tennessee Health Sciences Center
Memphis, TN

Suresh Karne, M.D., Ph.D.

Digestive Disease Center-Huntsville Hospital
University of Alabama - Huntsville Campus
Huntsville, AL

Pavan Kumar Panchavati

MD, MPH, FHM, FAFP, SFHM
Digestive Disease Center-Huntsville Hospital
University of Alabama - Huntsville Campus
Huntsville, AL

Kusum Punjabi, M.D., MBA, FACEP

Emergency Medicine
Robert Wood Johnson Medical School &
Rutgers University, New Brunswick, NJ

Soumya R. Neravetla, M.D., FACS

Cardiovascular & Thoracic Surgery
Mercy Health - Springfield Regional Medical Center
Springfield, OH

Manoj Shah, M.D.

Gastroenterology, Pediatrics and Nutrition
Loma Linda Univ. School of Medicine
Loma Linda, CA

Editorial Advisors

Vikas Khurana, M.D., MBA

Gastroenterology
Noble Medical Care, Upper Darby, PA

Vemuri S. Murthy, M.D., M.S., FAHA, FICS

Department of Emergency Medicine
University of Illinois at Chicago,
College of Medicine, Chicago, IL

Editorial Board Members

Amit Chakrabarty

M.D., M.S., FRCS, FICS
Center for Continence and Female Pelvic Health
Poplar Bluff Urology, Poplar Bluff, MI

Prasad S. Garimella, M.D., FAASM, FCCP

Pulmonary & Critical Care and Sleep Medicine
Philadelphia College of Osteopathic Medicine (Georgia Campus)
& Gwinnett Pulmonary Group, Duluth, GA

Mahadevappa Hunasikatti, M.D., FCCP

Pulmonary & Critical Care and Sleep Medicine
Respiratory/Sleep Devices Branch
FDA Center for Radiological Health, Silver Spring, MD
Internal Medicine, Fairfax Hospital, Falls Church, VA

Shailaja Pulisetty, M.D., CMD

Internal Medicine/Geriatric Medicine
Transactional team. Aetna, St. Louis, MO

Madhumitha Rajagopal, Ph.D., (M.D.)

Nephrology & Hypertension
Albert Einstein College of Medicine, New York, NY

Ravi Raghavan, M.D., MRCPATH

Pathology & Human Anatomy and Neurosurgery
Loma Linda Medical Center, and University of
California School of Medicine, Riverside, CA

**Malireddy S. Reddy
BVSc (DVM), M.S., Ph.D.**

Probiotics, Immune Modulation, Microbiota, Hospital
Acquired Infections and Pathogenesis of Bacterial Infections
International Media and Cultures, Inc., Denver, CO

Abhijit Roychowdhury, M.D.

Department of Radiology
Fayetteville VA Medical Center and
Campbell School of Osteopathic Medicine, NC

Gunjan J. Shukla, M.D.

Cardiovascular Medicine and Cardiac Electrophysiology,
New York Medical College School of Medicine, New York, NY
Good Samaritan Hospital, Westchester Health Network,
Westchester, NY

Kausik Umanath, M.D., M.S., FASN

Nephrology & Hypertension, and Clinical Research
Wayne State University School of Medicine, and
Henry Ford Health System, Detroit. MI

Editorial Interns

TBD

Evolution of Peer-Review Process

- The earliest known concept of peer-review can be traced to 500 BCE in ancient Greece.
- The earliest documented peer-review process can be found in *Ethics of Physicians* by a Syrian author dating back to 900 AD.
- The first known editorial pre-publication peer-review goes back to 1665 by Henry Oldenburg, first editor of *Philosophical Transactions* of the London Royal Society.
- The modern peer-review process was not established until after the World War II. In 1936, Albert Einstein was offended when the editor of *The Physical Review* sent his manuscript to an external reviewer without his permission. Einstein withdrew his manuscript from the journal.
- *Science* and *The Journal of the American Medical Association (JAMA)* started to use external reviewers in 1950s and 1960s.
- *The Lancet* started using peer-review by referees in the field only in 1976. Until that time editorial board members of The Lancet decided on the manuscripts submitted.
- Today, peer-review process by external reviewers is the gold standard of scientific publications.

Sushruta Medical News is a Publication of the AAPI

©American Association of Physicians of Indian Origin (AAPI)

600 Enterprise Dr., Suite 108, Oak Brook, IL 60523

<https://www.aapiusa.org/>

The views expressed by the authors do not necessarily reflect those of the AAPI.



Pioneers in Medicine and Healthcare

James P. Allison, Ph.D.

**Regental Professor and Chair, Department of Immunology
Executive Director of the Immunotherapy Platform
MD Anderson Cancer Center, Houston, Texas**

Co-Winner of Nobel Prize in Medicine or Physiology 2018

Contributed by: Bellamkonda K. Kishore, M.D.

***The only right way to do science... is to not do experiments that give you an answer that's consistent to what you ought to get. But to do THE KILLER EXPERIMENT that can only be right if you're right.
– Jim Allison***

Cancer is a deadly disease known to humans for a long time. Tumors were found in fossilized bones and Egyptian mummies. Breast tumors have been documented in Egyptian papyrus dating back to 1500 BC. Despite the unprecedented scientific and technological breakthroughs that occurred in 20th century, we were not able to conquer cancer. In 1975 when Köhler and Milstein, two German scientists invented hybridoma technology for production of monoclonal antibodies that can be programmed like guided missiles to interact with or attack specific cell surface antigens, cancer biologists celebrated that they were very close to kill the cancer cells. However, within 10 to 15 years, it became clear that cancer cells cannot be easily targeted by monoclonal antibodies, as they keep changing their cell surface antigens often. A sense of disappointment reigned among cancer cell biologists. There were even satirical statements that immunology did not help to develop cancer therapy, but cancer biology aided in the development of immunology.

But that status quo changed and there was a ray of hope when James P. Allison, Ph.D., a Texas scientist showed that immunology can help fight cancer when it is directed to activate T cells. More than 20 years later, when his groundbreaking findings became solidly established, Dr. Allison was awarded Nobel Prize in Medicine or Physiology in 2018 along with Tasuku Honjo, M.D. "for their discovery of cancer therapy by inhibition of negative immune regulation." According to the Nobel Committee press release, *James P. Allison studied a known protein that functions as a brake on the immune system. He realized the potential of releasing the brake and thereby unleashing our immune cells to attack tumors. He then developed this concept into a brand new approach for treating patients.*

The impactful discovery of Dr. Allison is demonstration that CD28 is the major costimulatory molecule that allows full activation of native T cells and prevents anergy in T cell clones. He showed that CTLA-4 inhibits T-cell activation by opposing CD28-mediated costimulation, and hence blockade of CTLA-4 could enhance T cell responses, which in turn leads to tumor cell rejection in animal models. These groundbreaking discoveries paved the way for immune checkpoint blockade therapy for cancer, leading to the development of ipilimumab, an antibody to human CTLA-4 approved by the FDA. Although immune checkpoint inhibitors (ICIs) are very potent tools in the treatment of a variety of cancers by virtue of their ability to activate T cells, nevertheless, caution should be exercised as their use has been associated with immune-related adverse events, including cytokine release syndrome (CRS). Nevertheless, judicious use of ICIs in cancers is a very valuable tool in saving lives.

Dr. James Allison's Nobel Lecture 2018

<https://www.youtube.com/watch?v=0kuh7G9CP9Y>