Special Lectures

1SL1A March 27, 11 : 00–12 : 00, Room A

Logic of Life

Kurokawa, Kiyoshi (*Academic Fellow, National Graduate Institute for Policy Studies(GRIPS)*)

Homo sapience has come a long way reaching top of the animal kingdom of the Planet Earth. Physiology is a discipline to understand the function of our body. We inquire how our body and its organs and systems function. Advances of science and technical over last 100 years was utterly amazing, and allowed us to understand our inquiries to the levels of gene, molecule, cell, furthering understanding of 'Logic of Life.' As we gain more insights into our body systems, we tend to go deeper more as technology advances, testing each own's hypotheses. However, we must think of 'Logic of Life'from a variety of logical reasoning. One is our evolutionary history, ontogeny and phylogeny. In this regard, critical textbooks are very valuable, eg, Stephan Gould's theory of evolution, Schmidt Nielsen's 'Animal Physiology'. We could learn a great deal from different view−points and gain further insights into why we study 'Logic of Life'.

1SL2A March 27, 13 : 20–14 : 20, Room A

Challenge of molecular medicine in regulating the structure and the function of biological molecules : From GTP molecular switch to self and non−self recognition in immune response

Arai, Ken−ichi (*Professor Emeritus, University of Tokyo, Founding President, Asia Pacific International Molecular Biology Network(A−IMBN), President, SBI Biotech Ltd.*)

When I graduated from medical school in 1967, the concept that the gene is programmed with digital information was established in prokaryotes employing host parasite interaction of bacteria and the phage. I was impressed with the contribution of biochemistry and physiology in unraveling the biophysical basis of allosteric regulation of hemoglobin and electrophysiological basis of neuronal activity and emerging fields such as host−parasite relationship(bacteria, virus, fungi etc), regulation of endocrine system and the recognition and the memory of self & non−self in immune and neuronal systems are fascinating. However, digital molecular biology was not directly applicable to medical science at that time, and I realized a long journey to understand the molecular basis of body's function that will open the rational basis for diagnosis, therapy and prevention of many human diseases. I was fortunate to meet with my mentors, Dr. Yoshito Kaziro and Dr. Arthur Kornberg and worked with them at IMSUT and Stanford in DNA replication and the translation of genetic information to proteins. Also recombinant DNA technology developed at Stanford changed my way of thinking, and I was able to start and work with my colleagues at two biotech ventures(DNAX and SBIBT) to develop novel therapy based on the discovery of the molecular basis of immune recognition and the control of proliferation and differentiation of eukaryotic cells. Now, digital molecular biology and physiology are working together to shape up molecular medicine. Today, I will talk about the wandering of medical researcher for over 40 years from GTP molecular switch to self and non−self recognition in immune response.

1. GTP molecular switch in protein synthesis(IMSUT)and yeast mating pheromone signals(DNAX).
2. DNA replication in bacteria using phages and plasmids(Stanford, DNAX, IMSUT)and control of cell cycle (G1 to S)by CDC7 kinase(IMSUT).
3. Cytokine network(DNAX)and self & non−self recognition in innate & acquired immune responses(IMSUT, SBIBT).
4. Personalized medicine(gene & cell therapy)using stem cells(DNAX, IMSUT, SBIBT).

1SL3A March 27, 14 : 20–15 : 20, Room A

Physiology between "survival and death"

Okada, Yasunobu (*National Institute for Physiological Sciences, Okazaki, Japan*)

Physiology is defined as "Logic of Life". In physiological studies, thus, the causative mechanisms of normal physiological functions of living bodies are to be elucidated. In the case of human body, the brain became so highly developed to allow not only adjusting all the organs to maintain homeostasis but also communicating with other brains and humans. Physiological researches must integrate the results at every level, from molecules to cells, tissues, organs, entire organisms and social human-to-human interactions. Also, physiologists should elucidate genuine mechanisms under the "Law of Causality". To do so, changes in physiological functions must be observed under perturbations that are induced either artificially, in an invasive or non-invasive manner, or naturally in the pathophysiological processes eventually resulting in dysfunctions or death. In this context, we have been studying the mechanisms of induction of and rescue from cell death to establish "Physiology of Cell Death".

At the very beginning time, "*Physiologie*"(natural science) was divided into "Physiology" covering all life sciences and "Physics" covering all material sciences. As time advanced, many branches such as Anatomy, Pharmacology and Biochemistry sprouted off from classical Physiology. Nowadays, Molecular Biology and Brain Science have become major prosperous life sciences, and then Physiology seemingly looks dying. However, now we can integrate both molecular information and brain information into living human bodies under the law of causality, thereby reviving Physiology as "Integrative Physiology".

Keywords : classical physiology, death, survival, integrative physiology

2SL4A March 28, 11 : 00–12 : 00, Room A

A personal and Societal journey through physiology−perspectives on the role of physiology in medicine and 125 years of the American Physiological Society

Barrett, Kim E. (*Professor of Medicine and Dean of Graduate Studies, University of California, San Diego, President−Elect, American Physiological Society*)

It is an honor to address the Japanese Physiological Society on its 90th anniversary, and to bring congratulations on this important milestone from the American Physiological Society (APS). My presentation will be in two parts. In the first, I will present research from my laboratory, which studies the role of epithelial transport dysfunction in the pathogenesis of digestive disease states. Using both cell line and mouse models, we have uncovered pathophysiological correlates of infection with *Salmonella* that may underlie diarrheal symptoms, which previously were poorly understood. Infection of colonic epithelial cell lines with *Salmonella* results in an upregulation of capacity for chloride secretion. However, *in vivo*, these bacteria fail to increase chloride secretion, but rather profoundly suppress fluid and electrolyte absorption by altering the expression and/or localization of key colonic ion transporters including the chloride/bicarbonate exchanger, DRA, and the ENaC sodium channel. These effects are dependent on bacterial invasion, and may be accounted for by increased epithelial proliferation, with an accompanying immaturity of the surface cells normally responsible for electrolyte absorption. In the second part of the talk, I will sketch the history of the APS and describe some of our programs that make APS relevant and valuable to our diverse membership. In particular, I will comment on our publications, our sectional structure and associated involvement of the membership at-large in our meetings and society governance, and our educational programs that target trainees spanning from schoolchildren to early-stage investigators. These latter programs fulfill our mission to attract and support the next generation of physiology practitioners.

2SL5A March 28, 13 : 20–14 : 20, Room A

Fixing ryanodine receptor Ca^{2+} leak–a novel therapeutic strategy for contractile failure in heart and skeletal muscle

Marks, Andrew R.[1,2] ([1]*Departments of Physiology and Cellular Biophysics, Clyde and Helen Wu Center for Molecular Cardiology;* [2]*Departments of Medicine, College of Physicians and Surgeons of Columbia University, New York, USA*)

A critical component in regulating cardiac and skeletal muscle contractility is the release of Ca^{2+} via ryanodine receptor (RyR) Ca^{2+} release channels in the sarcoplasmic reticulum (SR). In heart failure and myopathies, the RyR channel has been found to be excessively phosphorylated, oxidized and nitrosylated and depleted of the RyR-stabilizing protein calstabin (FK506 binding protein 12/12.6). This remodeling of the RyR channel complex results in an intracellular SR Ca^{2+} leak and impaired contractility. Despite recent advances in heart failure treatment, there are still devastatingly high mortality rates with this disease. Moreover, pharmacological treatment for muscle weakness and myopathies is nearly nonexistent. A novel class of RyR-stabilizing drugs, Rycals™, which reduce Ca^{2+} leak by stabilizing the RyR channels due to preservation of the RyR-calstabin interaction, have recently been shown to improve contractile function in both heart and skeletal muscle. This opens up a novel therapeutic strategy for the treatment of contractile failure in disorders of cardiac and skeletal muscles.

Conflict of interest : A.R. Marks is a consultant for a start-up company, ARMGO Pharma Inc., that is targeting RyR channels to treat heart disease and to improve exercise capacity in muscle diseases.

3SL6B March 29, 13 : 20–14 : 20, Room B

Drug Discovery Research in Industry – Globalization and industry researchers –

Maruyama, Tetsuyuki (*General Manager, Pharmaceutical Research Division, Takeda Pharmaceutical Company Limited*)

Emerging markets, payer changes, patent cliffs, innovation hurdles and globalization are some of the hot topic words that are indicative of the rapidly changing state of the pharmaceutical industry. The reality of most of these hot topic words, especially globalization, is that they can mean vastly different things to different people, regions and organizations. Maruyama, Tetsuyuki will discuss in this session what globalization means to researchers and the challenges they face in operating in a global environment. He will also present his views on how Takeda is overcoming these challenges from a drug discovery perspective including how the researchers are encouraged to change their mindset to think differently to adapt to a global research environment.

3SL7B March 29, 14 : 20–15 : 20, Room B

The status quo of *The Journal of Physiological Sciences* is not sacred

Sakuma, Yasuo (*University of Tokyo Health Sciences, Tokyo, Japan*)

According to the Journal Citation Reports® published in the last June by Thomson Reuters, Impact Factor (IF) for *The Journal of Physiological Sciences (JPS)* attained 1.606 in 2011. This all-time high value is a result of a steady rise from 1.125 in 2009 and 1.356 in 2010. *JPS* owes this accomplishment to devoted authors who submit original manuscripts, diligent handling editors and referees, and an avid readership who cites published articles in the *JPS* regularly. The IF value is in the Q3 category of the Journal Ranking, the third among four ranks along with *Neuroscience Research, Journal of Pharmacological Sciences, Endocrine Journal*, some of the journals published for Japanese societies in the proximate field of physiology. When we look around, however, we found *American Journal of Physiology-Endocrinology and Metabolism, The Journal of Physiology, Pflüger's Archive* in the top Q1 category. Thus, the status quo of *JPS* is not sacred.

We have published 59 articles of 218 submissions in 2011, culminating in the acceptance rate of 28%. The mean time needed to make editorial decision was 2 months. Foreign authors constitute 72.5% of submission ; while 66.0% of accepted manuscripts had their origin in Japanese laboratories. It is apparent that we have to encourage foreign authors to submit their best results to the *JPS*. The published articles can be accessed via Springer Link, from institutions with subscriptions. Each council member is provided with a token to access electronic publications. Recent data show that 50-150 downloads from http : //www.springer.com/12576 in each day. By placing your e-mail address in this site, you can get the table of contents of every new issue.

Authors of outstanding publication in the *JPS* receive Irisawa Prize of The Physiological Society of Japan. We sincerely hope the members of the Society to encourage their colleagues and students to submit their best results to the *JPS* and also ask favor of the members to afford their precious time to laborious process of refereeing when asked by handling editors.

At the end of my tenure of the Editor-in-Chief of the *JPS*, I would like to quote an Editorial by my friend, Prof. Jeffrey D. Blaustein, the departing Editor-in-Chief of *Endocrinology* in which I also serve on the board. He wrote : "I write my final editorial for *Endocrinology* with some sadness and of course a touch of relief as I hand over my duties to incoming Editor-in-Chief"[1]. I totally agree his sentiment and feel the same way as I hand over the duty to Prof. Yoshihiro Ishikawa.

1. Blaustein JD (2012) Editorial : A bittersweet transition : Some final thoughts. Endocrinology 153 : 5689-5691