

### **Summary**

In the 1st lecture, the lecturer will explain the fundamental matters of membrane physiology such as the mechanisms of resting membrane potential and action potential generation. In the 2nd lecture, the lecturer will explain the molecular diversity and the functioning mechanisms of ion channels and receptors. In the 3rd and 4th lectures, we will explain the basic concept and molecular mechanisms of the transepithelial transport and epithelial homeostasis as basic functions of the epithelium, which is responsible for physiological functions of various organs. In the 5th and 6th lectures, we will explain the basic concept of signal transduction, posttranslational modification of proteins and molecular basis for synapse organization. In the 7th, and 8th lectures, we will explain the relationship between the structure and function of soluble proteins and membrane proteins in cells. The structural analysis method will also be explained.

### **Achievement of the goal**

- (1) Students can explain the mechanisms of resting membrane potential and the action potential generation. Students can also exemplify the molecular diversity and the functioning mechanisms of ion channels and receptors.
- (2) Students can describe the basic mechanisms that drive epithelial fluid transport, and can explain the mechanism of the reabsorption of electrolytes, water, and nutrients in nephron segments in terms of transcellular and paracellular transport. Students can describe structure and function of the intestine. Students can explain molecular mechanism involved in intestinal stem cell proliferation and epithelial differentiation, which is required for maintaining intestinal homeostasis.
- (3) Students can explain the basic concept of signal transduction, posttranslational modification of proteins and molecular basis for synapse organization.
- (4) The relationship between the structure and function of soluble proteins and membrane proteins in cells can be explained with examples. Further, the structural analysis methods can be also explained.

## **Grading method**

Assignments based on the above achievement goals (1), (2), (3), and (4) will be presented, and students will be asked to answer any two of them in a report.

Students who submit reports by the deadline and are judged to have understood the main points will receive credit. Attendance of at least half of the class is required for credit.

## **Class Schedule**

1st lecture, April 23 (Fri)

"Introduction of cell physiology, mechanisms of membrane potential and generation of action potential"

Yoshihiro Kubo (Division of Biophysics & Neurobiology)

The lecture will start with the explanation of the basics of membrane physiology, including the ionic composition of intracellular and extracellular solutions, the electro-chemical potential and the equilibrium potential. Next, the mechanism of the determination of the resting potential will be explained. The lecturer will then explain the voltage- and time dependent activity of ion channels which was uncovered by voltage-clamp analysis, and show that the generation of action potential can be reconstituted based on the activity of Na<sup>+</sup> and K<sup>+</sup> channels.

2nd lecture, April 30 (Fri)

"Molecular diversity and mechanism of function of ion channels and receptors"

Yoshihiro Kubo (Division of Biophysics & Neurobiology)

The lecture will start with the overview of the researches after 1980 which undoubtedly proved the presence of ion channels/receptors by elucidating the molecular identity. Then, the molecular and functional diversity of ion channels/receptors will be explained. The lecturer will then explain the mechanisms and structural determinants of ion channel functions, focusing on the ionic selectivity and the voltage-dependent gating. Finally, various inherited diseases caused by genetic mutations of ion channel genes will be briefly introduced.

3rd lecture, May 14 (Fri)

"Mechanisms of epithelial fluid transport"

Mikio Furuse (Division of Cell Structure)

In this lecture, the structure of the epithelium and the epithelial fluid transport will be outlined as introduction. Next, the lecture will explain the basic mechanism by which major electrolytes and water are absorbed into or secreted from epithelial cells by the driving force of the sodium pump. In addition, the molecular mechanism of the paracellular transport, which has recently been clarified, will be described. Then, the mechanism of fluid transport in renal and small intestinal epithelia will be explained.

4th lecture, May 21 (Fri)

"Mechanisms of the maintenance of epithelial homeostasis"

Yasushi Izumi (Division of Cell Structure)

In this lecture, I will outline intestinal structure and function in mammals and *Drosophila*, and then introduce molecular mechanisms underlying their intestinal stem cell proliferation and epithelial differentiation, which is required for maintaining intestinal homeostasis. Further, I will talk about the effect of inflammation, aging, microbial infection on intestinal epithelial homeostasis.

5th lecture, May 28 (Fri)

"Signal transduction and posttranslational modification of proteins"

Masaki Fukata (Division of Membrane Physiology)

The lecture begins with the explanation of the basic concept of intracellular signal transduction. As representative examples, G-protein-coupled receptor (GPCR) pathways and receptor tyrosine kinase (RTK) pathways will be introduced. Next, the lecturer will explain posttranslational modification of proteins that dynamically regulate protein functions and cellular functions. Examples include phosphorylation, lipidation and ubiquitination.

6th lecture, June 4 (Fri)

"Molecular basis for synapse organization"

Yuko Fukata (Division of Membrane Physiology)

The lecturer will explain the structure, molecular basis and function of the synapse. This lecture introduces 1) the diversity and roles of synaptic cell-adhesion molecules, receptors and scaffolding proteins in synapse organization

and 2) the molecular basis of synaptic transmission and synaptic plasticity and the neurological disorders induced by synaptic dysfunction.

7th lecture, June 11 (Fri)

"Structural-function linkage and its structural analysis method of intracellular soluble proteins"

Kazuyoshi Murata (Division of Structure Biology)

In this lecture, I will explain the structures of intracellular soluble proteins such as proteasomes, spliceosomes, and ribosomes, whose detailed molecular structure dynamics and their functional relationships have been clarified in recent years. The latest structural analysis method that made these possible will be also described.

8th lecture, June 18 (Fri)

"Structural-function linkage and its structural analysis method of intracellular membrane proteins"

Kazuyoshi Murata (Division of Structure Biology)

In this lecture, I will explain the structures of intracellular membrane proteins such as ion channels, transporter, and GPCR, whose detailed molecular structure dynamics and their functional relationships have been clarified in recent years. The latest structural analysis method that made these possible will be also described.

### **Place**

Online (Zoom)

### **Language**

English

### **Reference books**

- (1) Ion channels of excitable membranes 3<sup>rd</sup> Edition (by Hille B), Sinauer, 2001
- (2) Mark F.Bear et al, 「Neuroscience: Exploring the Brain, Fourth edition」 : Lippincott Williams & Wilkins Inc.
- (3) Boron & Boulpaep "Medical Physiology 3<sup>rd</sup> Edition", Elsevier