Le/f_t panel: Confocal image of NIH 3T3 cells stained with antibodies to tubulin (red), stabilized microtubule (green) and a DNA staining dye (blue). Note that microtubules are stabilized at the leading edge of migrating cells.

Right panel: Confocal image of an NIH 3T3 cell expressing fluorescence-labeled tubulin (red) and a tubulin binding protein, EB1 (green). EB1 is localized at the tip of microtubules.
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Our graduate school has a long history dating back to 1873 with the establishment of a Pharmaceutical Department within the First University District Medical School, featuring two years of preparatory courses and three years of regular study. Since then, the school has cultivated Japan's leading researchers and instructors, producing extremely talented people in the fields of industry, health care, and government.

Drug development involves the processes of core research, non-clinical tests, clinical trials (studies), and more recently, drug management after their release in the market. In recent years, the term “drug discovery” has come to replace “drug development” in many cases. This is a relatively new term, first coined in 1990, but I feel that “drug discovery” has much more of a “scientific” nuance than “drug development”. Reflecting that, modern drug development involves not just the low molecular pharmaceuticals of the past, but also brand-new drugs based on the latest in scientific knowledge, including antibody drugs, nucleic-acid drugs, and regenerative medicines. Finding new drug-discovery goals has also become difficult even for world-class pharmaceutical firms, leading to a major rise in companies reaching out university research laboratories to search for the seeds to new discoveries.

It is said that “we cannot create innovative drugs without fundamental scientific discoveries”. Our graduate school pursues internationally top-level core research, including the discovery of new molecular functions/life phenomena, the invention of new reaction/synthesis techniques, and the development of new analytical technology, all with an aim to create new seeds in the field of core research in drug discovery. We also aim to make leading contributions to the fields of post-core research drug-discovery processes, including the cultivation of leading pharmacists in the medical field, the development of approval/screening and its methodology (regulatory science), and discoveries in post-release side-effect data and drug repositioning, through the timely establishment of endowed chairs and other actions centered around the Department of Pharmacy with pharmacist certification process.

Interdisciplinary study has become one keyword for the development of academics. This graduate school has applied itself to being open to core research topics in fields like organic chemistry, biochemistry, and physical chemistry, as well as applied sciences like pharmaceutics and regulatory science. The extremely high level of our research activity is clear when looking at the quality and quantity of published papers in international academic journals, the amount earned in grants-in-aid for scientific research and other competitive research grants, and the academic and other awards earned by our staff. It has become a popular department in recent years, seeing a very large number of applicants from the University of Tokyo’s College of Arts and Sciences, and based on adjusted scores from students in the Junior Division, we have gathered the most talented students at the University here. I believe the thrill of research lies in the rush we feel whenever we encounter unexpected experimental results. I want our department’s undergraduate students, graduate students, and young researchers to taste this experience for themselves, eventually growing into tomorrow’s leaders in Japanese science and technology. At the same time, in order to produce active players in industry and government, I feel it is integral to listen to people’s thoughts and discuss them in a group atmosphere. It is only through efforts like these that we gain a deeper understanding of each other, making it possible to see the way to more constructive policies in the future.

Going forward, I do not intend to allow the department to rest on its laurels, its current privileged state and its past glories. We will continue to make more contributions to core research, expand our pipelines to fields like industry and government, and provide service to Japan’s scientific, industrial, and governmental spheres.
### History

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1873</td>
<td>Department of Pharmaceutical Manufacturing was established in Daiichi-Daigaku-Ku Igakko (The First University District Medical School) in Kanda Izumicho, Tokyo.</td>
</tr>
<tr>
<td>1874</td>
<td>Daiichi-Daigaku-Ku Igakko was renamed as Tokyo-Igakko (Tokyo Medical School).</td>
</tr>
<tr>
<td>1876</td>
<td>Tokyo-Igakko was moved to Hongo, Tokyo.</td>
</tr>
<tr>
<td>1877</td>
<td>Tokyo Daigaku, The University of Tokyo was established. Tokyo-Igakko was renamed as the University of Tokyo Faculty of Medicine. The organization of pharmaceutical education began with the establishment of Pharmaceutical Institute (later Department of Pharmaceutical Manufacturing in the Faculty of Medicine). For the first 10 years, instruction was given by foreigners and in particular a Dutch chemist Dr. J. E. Eijkman. He left a large amount of fine work in the study of components of various domestic medicinal plants.</td>
</tr>
<tr>
<td>1886</td>
<td>The University of Tokyo was renamed as Imperial University and the name of the Department of Pharmaceutical Manufacturing in the Faculty of Medicine was changed to the Department of Pharmacy in the Imperial University Medical College. Japanese who had returned from studies in Germany took over the education of students, carried out valuable investigations of their own, and also established the ground for pharmaceutical organic chemistry in Japan.</td>
</tr>
<tr>
<td>1897</td>
<td>The Imperial University was renamed as Tokyo Imperial University.</td>
</tr>
<tr>
<td>1919</td>
<td>A faculty system was introduced and renaming the Department of Pharmacy in the Medical College as the Department of Pharmacy in the Faculty of Medicine, Tokyo Imperial University.</td>
</tr>
<tr>
<td>1947</td>
<td>Tokyo Imperial University was renamed as The University of Tokyo.</td>
</tr>
<tr>
<td>1949</td>
<td>The University of Tokyo was established under the new system (Junior division for the first two years and Senior Division for the 3rd and the 4th years).</td>
</tr>
<tr>
<td>1953</td>
<td>The Graduate School of Chemistry-related was established (Master’s Program in the field of Pharmaceutical Sciences).</td>
</tr>
<tr>
<td>1955</td>
<td>Doctoral Program in the field of Pharmaceutical Sciences was added.</td>
</tr>
<tr>
<td>1958</td>
<td>The Department of Pharmacy separated from the Faculty of Medicine and became an independent faculty as the Department of Pharmaceutical Sciences, the Faculty of Pharmaceutical Sciences.</td>
</tr>
<tr>
<td>1960</td>
<td>The Department of Pharmaceutical Technochemistry was established.</td>
</tr>
<tr>
<td>1965</td>
<td>The Graduate School of Pharmaceutical Sciences, The University of Tokyo was established. (Department of Pharmaceutical Sciences and Department of Pharmaceutical Technochemistry)</td>
</tr>
<tr>
<td>1966</td>
<td>The Research Institute for Chemical Hazards was established.</td>
</tr>
<tr>
<td>1973</td>
<td>The Experimental Station for Medicinal Plant Studies was established.</td>
</tr>
<tr>
<td>1976</td>
<td>The Research Institute for Chemical Hazards was abolished, and instead the Department of Pharmaceutical Life-Science was established.</td>
</tr>
<tr>
<td>1991</td>
<td>Two departments were unified into the Department of Pharmaceutical Sciences.</td>
</tr>
<tr>
<td>1997</td>
<td>The graduate school was reorganized along with the new system, &quot;Graduate School Priority System&quot; and reformed into three Departments, that is Pharmaceutical Chemistry, Pharmaceutical Biology, and Pharmaceutical Technology. Although the Faculty's emphasis of education is shifted from the Undergraduate Program to the Graduate Program, most of the faculty members also continue undergraduate education.</td>
</tr>
<tr>
<td>2000</td>
<td>Clinical Pharmacy Course was established in the Master’s Program.</td>
</tr>
<tr>
<td>2004</td>
<td>Pharmaceutical Sciences Research Building was constructed.</td>
</tr>
<tr>
<td>2006</td>
<td>Following the revision of the School Education Act, the Faculty of Pharmaceutical Sciences started a new program with Department of Pharmaceutical Sciences (4-year program) and Department of Pharmacy (6-year program).</td>
</tr>
<tr>
<td>2008</td>
<td>Department of Integrated Pharmaceutical Sciences was added to the Graduate School, which consists of total 4 departments.</td>
</tr>
<tr>
<td>2010</td>
<td>The former 4 departments in the Master’s Program were abolished and the Department of Pharmaceutical Sciences was established. Clinical Pharmacy Course was abolished.</td>
</tr>
<tr>
<td>2012</td>
<td>The former 4 departments in the Doctoral Program were abolished. Department of Pharmaceutical Sciences and Department of Pharmacy were established in the Doctoral Program. Dual Speciality Course on Pharmacist Education was established.</td>
</tr>
</tbody>
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### Facts & Figures

#### Number of Academic and Administrative Staff

<table>
<thead>
<tr>
<th></th>
<th>As of July 1, 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>162</td>
</tr>
<tr>
<td><strong>Academic Staff</strong></td>
<td></td>
</tr>
<tr>
<td>Professors</td>
<td>18</td>
</tr>
<tr>
<td>Associate professors</td>
<td>10</td>
</tr>
<tr>
<td>Lecturers</td>
<td>9</td>
</tr>
<tr>
<td>Assistant professors</td>
<td>25</td>
</tr>
<tr>
<td>Spec. appt. professors</td>
<td>1</td>
</tr>
<tr>
<td>Spec. appt. assoc. prof.</td>
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</tr>
<tr>
<td>Spec. appt. lecturers</td>
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<tr>
<td>Spec. appt. assist.prof.</td>
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</tr>
<tr>
<td><strong>Subtotal</strong></td>
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<tr>
<td><strong>Researcher</strong></td>
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<tr>
<td><strong>Subtotal</strong></td>
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<tr>
<td><strong>Administrative Staff</strong></td>
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<td>Office</td>
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<tr>
<td>Technical</td>
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<td><strong>Subtotal</strong></td>
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#### Number of Students

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<th>As of May 1, 2016</th>
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<tbody>
<tr>
<td><strong>Undergraduates</strong></td>
<td></td>
</tr>
<tr>
<td>3rd year</td>
<td>90 (2)</td>
</tr>
<tr>
<td>4th year</td>
<td>87 (1)</td>
</tr>
<tr>
<td>5th year</td>
<td>4 (0)</td>
</tr>
<tr>
<td>6th year</td>
<td>7 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>188 (30)</td>
</tr>
<tr>
<td><strong>Graduates</strong></td>
<td></td>
</tr>
<tr>
<td>Master’s Program</td>
<td>95 (8)</td>
</tr>
<tr>
<td>Doctoral Program/Pharmaceutical Sciences</td>
<td>101 (8)</td>
</tr>
<tr>
<td>Doctoral Program/Pharmacy</td>
<td>196 (16)</td>
</tr>
<tr>
<td>Total</td>
<td>392 (34)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>570 (63)</td>
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#### Number of Research Students, etc.

<table>
<thead>
<tr>
<th></th>
<th></th>
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<th></th>
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<th></th>
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<tbody>
<tr>
<td>Undergraduate-level</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Graduate-level</td>
<td>11</td>
<td>8</td>
<td>3</td>
<td>9</td>
<td>9</td>
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<tr>
<td>Undergraduate auditor</td>
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<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
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<tr>
<td>Subtotal</td>
<td>13</td>
<td>10</td>
<td>5</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>Commissioned researcher</td>
<td>5</td>
<td>9</td>
<td>10</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Subtotal</td>
<td>5</td>
<td>9</td>
<td>10</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>18</td>
<td>19</td>
<td>15</td>
<td>22</td>
<td>23</td>
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</table>

#### Number of International Students

<table>
<thead>
<tr>
<th>Countries and Regions</th>
<th>Undergraduate</th>
<th>Graduate School</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Master’s</td>
<td>Doctoral</td>
<td>Research Student</td>
</tr>
<tr>
<td>China</td>
<td>2</td>
<td>13(2)</td>
<td>12(5)</td>
</tr>
<tr>
<td>Bangladesh</td>
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<td>1(1)</td>
<td></td>
</tr>
<tr>
<td>India</td>
<td></td>
<td>1(1)</td>
<td></td>
</tr>
<tr>
<td>Thailand</td>
<td></td>
<td>1(1)</td>
<td></td>
</tr>
<tr>
<td>Indonesia</td>
<td></td>
<td>1(1)</td>
<td></td>
</tr>
<tr>
<td>Philippines</td>
<td></td>
<td>1(1)</td>
<td></td>
</tr>
<tr>
<td>Korea</td>
<td>1</td>
<td>1(1)</td>
<td></td>
</tr>
<tr>
<td>Taiwan</td>
<td></td>
<td>1(1)</td>
<td></td>
</tr>
<tr>
<td>Nigeria</td>
<td></td>
<td>1(1)</td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td></td>
<td>1(1)</td>
<td></td>
</tr>
<tr>
<td>Sri Lanka</td>
<td></td>
<td>1(1)</td>
<td></td>
</tr>
<tr>
<td>Croatia</td>
<td></td>
<td>1(1)</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>3</td>
<td>16(3)</td>
<td>17(7)</td>
</tr>
</tbody>
</table>

#### Number of Doctoral Degree Holders

<table>
<thead>
<tr>
<th></th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
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<tbody>
<tr>
<td>Program Doctorate</td>
<td>59</td>
<td>56</td>
<td>51</td>
<td>39</td>
<td>54</td>
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<tr>
<td>Thesis Doctorate</td>
<td>23</td>
<td>18</td>
<td>15</td>
<td>14</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>82</td>
<td>75</td>
<td>65</td>
<td>53</td>
<td>72</td>
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<tr>
<td>As of May 1, 2016</td>
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#### Current Status of Graduates

<table>
<thead>
<tr>
<th>Academic Year</th>
<th>Undergraduate-level Graduates</th>
<th>Graduate School Graduates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Pharmaceutical Company</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemical industry companies</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Financial, insurance, &amp; trading companies</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Others</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Subtotal</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Seeking for further education (Graduate school)</td>
<td>80</td>
<td>4</td>
</tr>
<tr>
<td>Research student, other undergraduate course, etc.</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Study abroad</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>JSPS special researcher, etc.</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Subtotal</td>
<td>84</td>
<td>7</td>
</tr>
<tr>
<td>Total (Number graduating/completing program)</td>
<td>84</td>
<td>7</td>
</tr>
</tbody>
</table>

( ) International students

( ) Numbers indicate MEXT Scholarship Students
Following the revision of the School Education Act, the Faculty of Pharmaceutical Sciences got off to a new start in 2006 as a program with a 6-year maximum course term, all graduates of which are eligible to take the national qualifying examination for pharmacists. Out of consideration for the role of our 4-year program, unique to Japan, that has produced many outstanding pharmaceutical specialists, we have additionally established a graduate program in pharmaceutical sciences that allows graduates of the 4-year program to take courses in clinical pharmacy and practicums equivalent to those of the 6-year program, with a time limit of 12 years on completion of the program. Students completing this graduate program (the so-called 4 + 2 + 2 Program) will also be eligible to sit for the national qualifying exam for pharmacists.

With these parallel 6-year and 4-year programs, the University of Tokyo’s Faculty of Pharmaceutical Sciences not only provides traditional training in basic research for drug discovery but also offers some courses in advanced training for pharmacists. The Faculty next plans to establish in the Graduate School a Pharmaceutical Sciences program in 2012 corresponding to the second half of a doctoral course, along with a dual speciality course on pharmacist education that will make graduates of this program eligible to take the national qualifying exam for pharmacists.
Pharmaceutical Sciences Education Program

Following the revision of the School Education Act, the Faculty of Pharmaceutical Sciences got off to a new start in 2006 as a program with a 6-year maximum course term, all graduates of which are eligible to take the national qualifying examination for pharmacists. Out of consideration for the role of our 4-year program, unique to Japan, that has produced many outstanding pharmaceutical specialists, we have additionally established a graduate program in pharmaceutical sciences that allows graduates of the 4-year program to take courses in clinical pharmacy and practicums equivalent to those of the 6-year program, with a time limit of 12 years on completion of the program. Students completing this graduate program (the so-called 4 + 2 + a Program) will also be eligible to sit for the national qualifying examination for pharmacists.

With these parallel 6-year and 4-year programs, the Faculty of Pharmaceutical Sciences, the University of Tokyo not only provides traditional training in basic research for drug discovery but also offers some courses in advanced training for pharmacists. Doctoral program of the Graduate School of Pharmaceutical Sciences was reorganized in April, 2012. 4-year doctoral program (Department of Pharmacy) was newly established along with the existing 3-year doctoral program (Department of Pharmaceutical Sciences). Also, a Dual Speciality Course on Pharmacist Education was established in the 3-year program, and that will make graduates of this program eligible to take the national qualifying examination for pharmacists.
Department of Pharmaceutical Sciences

After graduating from the Department of Pharmaceutical Sciences with the four-year program, students can proceed to a two-year master's program, then to a three-year doctoral program. The size of the department is 90% (72 students) of the entire students of the faculty.

Even though a student is a graduate of the Department of Pharmaceutical Sciences, he/she will be able to receive the qualification of candidacy for the national examination for pharmacists as long as he/she entered the University in or before 2018 and has completed the required academic subjects as well as practical training. Although it is possible for students to complete most of the academic subjects by their fourth year, they will receive practical training during the doctoral program after the completion of master's program.

Department of Pharmacy

The Department of Pharmacy with the six-year program was established for students who entered the University during or after 2006. In response to the advancement of medical care, the purpose of the establishment of this department is to train and develop high-quality pharmacists. Besides conventional academic subjects, six-month practical hospital/pharmacy training is imposed on students. The size of the department is 10% (8 students) of the entire students of the faculty. Although the University of Tokyo does not focus on training pharmacists, it provides high-quality pharmacy education to a small number of students, aiming to create personnel who will be able to lead this field. At the Faculty of Pharmaceutical Sciences we collaborate with the University of Tokyo Hospital and local pharmacies, in an effort to smoothly implement practical training.

Furthermore, the four-year doctoral program was established in 2012, the year when students who entered the University in 2006 graduated. When students complete the College of Arts and Sciences and proceed to the Faculty of Pharmaceutical Sciences, they do not choose between the Department of Pharmaceutical Sciences and the Department of Pharmacy. They will choose one of those departments during their fourth year when they have fully understood the details of research conducted in the Faculty of Pharmaceutical Sciences/Graduate School of Pharmaceutical Sciences.

Faculty Curriculum

Lectures and practicums lie in the center of the education at the Faculty of Pharmaceutical Sciences. They are provided to students in order for them to acquire the broad knowledge and the perspectives of pharmacists, as well as to have a clear view when they decide which field of pharmacy they should enter as specialists. One can say that lectures provided to faculty students are the essence of pharmaceutical sciences. Furthermore, reflecting the diversity in research areas in the Faculty of Pharmaceutical Sciences, the pharmacy practicums encompass a wide range of training areas. It is efficiently designed in a way that students will be able to put organic chemistry, physical chemistry, biochemistry and clinical pharmacy into practice. When students enter into their fourth year, each student will be allocated to a class of his/her own choice and will have opportunities to get hands-on experience in the cutting-edge pharmacy through the participation in research projects.

Department of Pharmaceutical Sciences  80 credits
(Compulsory: 62 credits, Elective: 18 credits or more)

Department of Pharmacy  120 credits
(Compulsory: 109 credits, Elective: 11 credits or more)

2nd year: Autumn 1

<table>
<thead>
<tr>
<th>Course Title</th>
<th>Credits</th>
<th>Course Outline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiological Anatomy of Human Body</td>
<td>1</td>
<td>Students will learn the structures and functions of each organ (i.e., anatomy and physiology) as the basic knowledge for them to understand pharmacotherapy and pathophysiology.</td>
</tr>
<tr>
<td>Pharmaceutical Affairs Law and Patent Law</td>
<td>1</td>
<td>Students will learn the basics of the Patent Act and pharmacy-related laws and regulations.</td>
</tr>
<tr>
<td>Pharmacology 1</td>
<td>1</td>
<td>Students will learn the fundamentals of pharmacology in order to understand actions of drugs that affect the autonomic nervous system and the circulatory system.</td>
</tr>
</tbody>
</table>
Students will learn the fundamentals of molecular biology to understand the life sciences.

To achieve proper use of the pharmaceutical products, and contribute to the drug development, the lecture explains the pharmacokinetics, a theoretical scheme for quantitatively understanding the disposition of drugs in the body, and describes the factors that cause inter-individual variation in drug disposition and response.

Students will receive lectures and practicums regarding statistical methods and experimental methods used for drug evaluations.

Students will understand the immune system and the immune response to infections and allergies in the level of dynamic behaviors of tissues, cells and molecules.

Students will learn the fundamentals such as stereochemistry, structural chemistry, reduction and oxidation.

Students will acquire the physiochemical concept by understanding quantum chemistry and spectroscopy.

Lectures pertaining to the fundamentals, applications and biological effects of isotopes and radiation (which are indispensable for the fields of medicine and pharmaceutical sciences) will be given.

Lectures are aimed to allow students to understand important concept of thermodynamics, acquire the physicochemical perspectives and learn methods that are important in pharmaceutical sciences.

This course covers chemical equilibrium, qualitative and quantitative chemical analysis, and instrumental analysis.

Students will learn the fundamentals of cell biology to understand the life sciences.

The outline, history and the future vision of pharmaceutical sciences will be explained in an easy to understand manner, allowing students to think about the relationship between pharmaceutical sciences and society in terms of industry and medical care. Moreover, students will learn some of the latest studies in the field of pharmaceutical sciences.

Fundamental organic chemistry which contains Acid and Base, Nucleophilic Substitution and Elimination Reactions.

2nd year: Autumn 2

<table>
<thead>
<tr>
<th>Course Title</th>
<th>Credits</th>
<th>Course Outline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmaceutics</td>
<td>1</td>
<td>Students will learn dosage forms, design/manufacturing methods and usability evaluation methods, and drug delivery system.</td>
</tr>
<tr>
<td>Microbiology and Chemotherapy</td>
<td>1</td>
<td>The basic biochemical and genetic methods will be outlined using microorganisms such as E-coli as materials. Students will also learn the mechanisms of action of antibiotics.</td>
</tr>
<tr>
<td>Physical Chemistry III</td>
<td>1</td>
<td>Students will learn the hierarchy of protein structure, various intermolecular interactions, enzyme structures and the theory of enzyme reaction.</td>
</tr>
<tr>
<td>Pharmaceutical and Medical Businesses</td>
<td>1</td>
<td>Students will learn the basics of strategic management to understand what exactly company/research institute management means. The structure and characteristics of medical care/pharmaceutical industry will also be explained.</td>
</tr>
<tr>
<td>Pathology</td>
<td>1</td>
<td>Pathological changes of cells and tissues and classification and treatment of diseases will be explained.</td>
</tr>
<tr>
<td>Molecular Structural Bio-Sciences</td>
<td>1</td>
<td>The fundamentals and actual examples of structural analysis of biomaterials will be explained using the nuclear magnetic resonance method or the X-ray crystal structure analysis method.</td>
</tr>
<tr>
<td>Functional Biology</td>
<td>1</td>
<td>Students will learn the fundamental of higher-order function cell to understand life sciences.</td>
</tr>
</tbody>
</table>
### 3rd year: Spring 1

<table>
<thead>
<tr>
<th>Course Title</th>
<th>Credits</th>
<th>Course Outline</th>
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<tbody>
<tr>
<td>Pharmacology II</td>
<td>1</td>
<td>Students will understand drug actions that affect the central nervous system, endocrine system and immune system by learning the physical function and mental function.</td>
</tr>
<tr>
<td>Drug Informatics</td>
<td>1</td>
<td>Methods for constructing novel drug information effective in real-life medical care situations will be explained. These methods include methodology to standardize drug information and quantify drug reactions.</td>
</tr>
<tr>
<td>Clinical Pharmacology</td>
<td>1</td>
<td>Students will learn the fundamentals of pharmacotherapy and clinical development with the clinical perspectives from pathophysiology through pharmacokinetics, clinical pharmacology to clinical testing. Students will also learn diagnoses, treatment and clinical trials in real-life situations from experts in the departments of clinicopathology, internal medicine, surgery and radiology to understand the disease “cancer.”</td>
</tr>
<tr>
<td>Interactive Organic Chemistry</td>
<td>1</td>
<td>The fundamentals of organic chemistry by practicum and group discussion will be outlined and reviewed.</td>
</tr>
<tr>
<td>Laboratory Works of Pharmaceutical Sciences I</td>
<td>5</td>
<td>To acquire fundamental experimental operations, and experience basic organic reactions and some practical synthesis of organic compounds.</td>
</tr>
<tr>
<td>Laboratory Works of Pharmaceutical Sciences II</td>
<td>3</td>
<td>Basic experiments in bio-organic chemistry (extraction, isolation, identification and biosynthesis of natural organic compounds; the fundamentals and applications of the extinction method and the fluorescence method; learning high-speed liquid chromatography; drug metabolism reaction experiments; enzyme kinetics; visits to the Experimental Station for Medicinal Plant Studies)</td>
</tr>
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</table>

### 3rd year: Spring 2

<table>
<thead>
<tr>
<th>Course Title</th>
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</thead>
<tbody>
<tr>
<td>Organic Chemistry V</td>
<td>1</td>
<td>Students will learn the chemistry of natural organic compounds having biological activity, as well as the fundamentals of biosynthesis.</td>
</tr>
<tr>
<td>Biophysics</td>
<td>1</td>
<td>Students will learn about the hierarchic structure of an organism (from molecules to an individual) as well as each level of the hierarchy.</td>
</tr>
<tr>
<td>Health Chemistry</td>
<td>1</td>
<td>The impact of environmental materials toward organisms will be explained.</td>
</tr>
<tr>
<td>Organic Chemistry VI</td>
<td>1</td>
<td>This is a class for learning metabolism of medical drugs, fundamentals of drug development, chemistry of carbohydrates and synthetic polymers. Enzyme induction, polymorphism, metabolic reactions, enzymes, reaction mechanisms of P-450 will be explained in molecular level. The fundamentals of drug development such as molecular design, chemical libraries and lead compounds, and polymers such as carbohydrates and synthetic polymers will be also explained.</td>
</tr>
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</table>
3rd year: Autumn 1

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<thead>
<tr>
<th>Course Title</th>
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</thead>
<tbody>
<tr>
<td>Medicinal Chemistry II</td>
<td>1</td>
<td>Students will learn organic chemistry of biologically active substances and pharmaceutical molecules, as well as that of molecular design.</td>
</tr>
<tr>
<td>Toxicological Pharmacology</td>
<td>1</td>
<td>Scientific proof of drug safety will be explained from the molecular biological, cell biological, pathophysiological and sociological perspectives, mainly focusing on the stress response of organisms.</td>
</tr>
<tr>
<td>Medicinal Chemistry I</td>
<td>1</td>
<td>Lectures pertaining to advanced level of organic synthetic chemistry, transition metal chemistry, heterocyclic ring and natural product synthetic chemistry will be given.</td>
</tr>
<tr>
<td>Molecular Physiological Chemistry</td>
<td>1</td>
<td>The latest knowledge regarding extracellular signaling molecules such as hormones will be explained.</td>
</tr>
<tr>
<td>Special Lectures on Pharmaceutical Sciences I</td>
<td>1</td>
<td>Students will learn the ideal way of pharmaceutical sciences through bio/medical ethics.</td>
</tr>
<tr>
<td>Laboratory Works of Pharmaceutical Sciences IV</td>
<td>5</td>
<td>(1) Experiments in physiological chemistry: Regulation of blood sugar levels (physiological/metabolic experiments); proliferative response of culture cells (isotope experiments) (2) Experiments in molecular biology: Basic experiments in molecular biology using culture cells (3) Experiments in genetics: Basic experiments in molecular genetics using animal models (4) Experiments with microorganisms: Basic experiments with microorganisms and antibiotics; basic experiments on gene manipulation</td>
</tr>
<tr>
<td>Special Laboratory Works of Pharmaceutical Sciences I</td>
<td>1</td>
<td>Through the determination of genetic polymorphism of drug metabolizing enzymes, students will learn the significance and interpretation method of genetic polymorphism in consideration of future medical care. Furthermore, they will learn the appropriate process of research on human genome and genes, as well as the importance of compliance of ethical guidelines.</td>
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3rd year: Autumn 2

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<tr>
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<tbody>
<tr>
<td>Medicinal Chemistry III</td>
<td>1</td>
<td>In lectures on organic chemistry (which is essential for drug development), the fundamentals of organic reaction chemistry, and chemistry of biologically-active substances will be explained. The fundamentals of chemical biology especially about photo-functional molecules will be explained.</td>
</tr>
<tr>
<td>Biological Basis of Cancer</td>
<td>1</td>
<td>Lectures pertaining to biology of cancer, clinic and treatment of cancer especially pharmacotherapy will be given.</td>
</tr>
<tr>
<td>Natural Product Chemistry</td>
<td>1</td>
<td>Students will learn the origins, ingredients, evaluations and applications of natural drugs (primarily those described in the Pharmacopoeia of Japan) as well as plant biotechnology.</td>
</tr>
<tr>
<td>Metabolism and disease</td>
<td>1</td>
<td>Metabolism and various diseases caused by metabolic failure will be explained.</td>
</tr>
<tr>
<td>Laboratory Works of Pharmaceutical Sciences V</td>
<td>3</td>
<td>Basic experiments in pharmacology using whole animals and organs, observation of pathology specimens, histochemistry, analysis of the mechanism of cell signaling, genetic experiments using budding yeast</td>
</tr>
<tr>
<td>Special Lectures on Pharmaceutical Sciences II</td>
<td>1</td>
<td>Students will learn the ideal way of pharmaceutical sciences through voices of victims of harmful effects of drugs.</td>
</tr>
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</table>

4th year (Department of Pharmaceutical Sciences)

<table>
<thead>
<tr>
<th>Course Title</th>
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</thead>
<tbody>
<tr>
<td>Special Laboratory Works of Pharmaceutical Sciences</td>
<td>20</td>
<td>Students will be allocated to a laboratory in the Faculty of Pharmaceutical Sciences (including the Dept. of Pharmacy, the Univ. of Tokyo Hospital), and participate in frontline pharmaceutical research.</td>
</tr>
</tbody>
</table>
To understand basic and advanced chemical principles and concepts that is important for pharmaceutical sciences.

To understand X-ray crystallography, structural analysis by NMR, sensitive analysis by fluorometric and mass spectrometric method, biosynthesis of natural products, and chemical biology for drug development.

To learn the fundamentals of biopharmaceutical sciences, including biochemistry, molecular biology, cell biology, molecular genetics, and pathology.

To learn the fundamental knowledge in the fields of pharmacokinetics, pharmacology, pathology, drug informatics, regulatory science, pharmacobusiness, and pharmacoeconomy among clinical pharmaceutical sciences.

To learn the chemistry that are essential for carrying out cutting-edge pharmaceutical research related to the life sciences.

Explains the principles of X-ray crystallography, nuclear magnetic resonance imaging, single-molecule fluorescence imaging, and methods for high sensitivity analysis of biomolecules, and introduces methods for analyzing the structure and function of biomolecules and applications of those methods.

Courses are open every other year.

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<tbody>
<tr>
<td>Laboratory Works of Pharmaceutical Sciences VI</td>
<td>20</td>
<td>Students will be assigned to a laboratory in the Faculty of Pharmaceutical Sciences and participate in frontline pharmaceutical research. They will also independently conduct research and study for practical hospital/pharmacy training.</td>
</tr>
<tr>
<td>Practice for Clinical Pharmacy II</td>
<td>4</td>
<td>For practical hospital/pharmacy training, students will acquire basic knowledge, skills and attitude required for fulfilling pharmacists’ duties within the University, such as preparation and formulation of drugs and drug administration guidance.</td>
</tr>
<tr>
<td>Practice for Clinical Pharmacy III</td>
<td>10</td>
<td>In order to understand duties and responsibilities of hospital pharmacists and be able to participate in team approach to medical care, students will acquire basic knowledge, skills and attitude required for fulfilling pharmacists’ duties within the University, such as preparation and formulation of drugs and drug administration guidance.</td>
</tr>
<tr>
<td>Practice for Clinical Pharmacy IV</td>
<td>10</td>
<td>In order to understand social roles and responsibilities of pharmacies and be able to participate in medical care in their local communities, students will acquire basic knowledge and skills regarding, and attitude toward, pharmacy services under health insurance, drug supply and management, information provision, health examinations and relationship with medical institutes and local communities.</td>
</tr>
<tr>
<td>Special Laboratory Works of Pharmaceutical Sciences</td>
<td>20</td>
<td>Students will be allocated to a laboratory in the Faculty of Pharmaceutical Sciences (incl. Dept. of Pharmacy, the Univ. of Tokyo Hospital) and participate in frontline pharmaceutical research.</td>
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### Department of Pharmaceutical Sciences

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<tr>
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<tbody>
<tr>
<td>Special Lecture Cell Biology</td>
<td>2</td>
<td>Introduces the latest research trends in biopharmaceutical sciences from the perspective of cell biology</td>
</tr>
<tr>
<td>Special Lecture Molecular Biology</td>
<td>2</td>
<td>To understand living organisms according to the functions of genes and proteins and to learn the current molecular biology, including disease pathophysiology, while also learning the latest methods in genetics and biochemistry</td>
</tr>
<tr>
<td>Special Lecture Disease Biology</td>
<td>2</td>
<td>From a biological perspective, outlines the academic disciplines and the mechanisms leading to disease onset while focusing primarily on infection and immunity</td>
</tr>
<tr>
<td>Special Lecture Clinical Pharmaceutical Science</td>
<td>2</td>
<td>To learn cutting-edge medical and pharmaceutical research in an omnibus format</td>
</tr>
<tr>
<td>Special Lecture Social Pharmaceutical Science</td>
<td>2</td>
<td>To gain a deeper understanding of the relationship between pharmaceutics and society from a variety of different angles, including information, statistics, government policy, business management, the pharmaceutical industry, etc</td>
</tr>
<tr>
<td>Special Lecture English for Science</td>
<td>2</td>
<td>To train in both listening and speaking by learning topics related to pharmaceutical sciences in English</td>
</tr>
<tr>
<td>Special Lecture Pharmaceutical Regulatory Science</td>
<td>2</td>
<td>To learn regulatory frameworks and practical methodology for evaluating the effectiveness, safety, risks, and benefits of new pharmaceuticals</td>
</tr>
<tr>
<td>Special Lecture Clinical Science</td>
<td>2</td>
<td>This course aims on the systematic comprehension of pharmacotherapy and clinical development of drugs on the basis of pathophysiology of diseases; students will learn pharmacokinetics, clinical pharmacology and regulatory and ethical issues of clinical trials. This course also aims on the comprehension of the cancer as a disease; students will learn practical aspects of diagnosis, treatment and clinical trial from medical professionals in clinical pathology, internal medicines, surgical therapy, radiation therapy and others.</td>
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### Department of Pharmacy

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<thead>
<tr>
<th>Course Title</th>
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</thead>
<tbody>
<tr>
<td>Practical Studies for Clinical Pharmacy</td>
<td>4</td>
<td>To acquire the practical methodology, awareness of the issues, and independence to respond to the needs of society in sophisticated medical environments</td>
</tr>
<tr>
<td>Practical Studies for Social Pharmacy</td>
<td>4</td>
<td>To acquire the practical methodology, awareness of the issues, and independence to respond to the needs of society in medical administration environments</td>
</tr>
<tr>
<td>Practical Studies for Drug Discovery</td>
<td>4</td>
<td>To acquire the practical methodology, awareness of the issues, and independence to respond to the needs of society in drug discovery environments</td>
</tr>
<tr>
<td>Special Studies for Pharmacy</td>
<td>20</td>
<td>To learn—through practice, seminars, and individualized laboratory research activities—comprehensive methodology pertaining to the interaction of molecules and organisms for the purpose of discovering and appropriately using pharmaceuticals</td>
</tr>
</tbody>
</table>
Laboratory of
Organic and Medicinal Chemistry

Synthesis of novel intelligent molecules which link chemical structures to biological functions in organic and medicinal chemistry

Research Topics

1. Synthesis of new compounds exhibiting characteristic structural features and properties, finally relevant to biological functions.
2. New reactions to functionalize aromatic compounds based on designed superelectrophiles
3. Design and synthesis of intelligent molecules, which will have impacts on functions of membrane proteins
4. Computational modeling and simulations of organic and macromolecular systems

Our aims of researches emphasize on design and synthesis of structurally novel organic molecules, which are characteristic in terms of structural (bonding) features and intrinsic functions such as chemical reactivities and biological functions. Designs of such novel molecules are based on our finding new chemistry including ground-state stable non-planar amide peptides and nitrosamines, and structures of multiply positively charged molecules. We study nitrogen-pyramidal amides and related nitrosamines, i.e., molecules that take nonplanar structures, different from the common planar amides. We apply this chemistry to construction of molecules of highly ordered structures such as helix peptide mimetics stable in water. We also develop new chemistry involving dication or trication molecules and apply them as superelectrophiles to synthesize a variety of novel multifunctionalized aromatic compounds, which are pharmaceutically relevant. We are also creating chemical molecules, which will be useful to controlling biological events of membrane proteins such as ion channels, neurotransmitters and G-protein-coupled receptors. These molecules also contribute to understanding the physiological functions of these membrane proteins. We combine all the experimental projects with computational chemistry, which will lead to deep understanding of the underlying chemistry.

Chemical modulation of functions of membrane proteins
Laboratory of Synthetic Medicinal Chemistry

Prof. M. Inoue

Assist. Prof. M. Nagatomo
Assist. Prof. H. Itoh
Project Assist. Prof. K. Hagiwara

http://www.f.u-tokyo.ac.jp/~inoue/e_index.html


Total synthesis and functional analysis of biologically active natural products

Research Topics

1. Development of new synthetic methodologies for total synthesis
2. Total synthesis of highly oxygenated polycyclic natural products
3. Total synthesis and functional analysis of ion channel-forming molecules
4. Total synthesis and functional analysis of antimicrobial molecules
5. Synthesis of new artificial molecules by modification of natural products templates

Natural products have been tremendously important in biology and human medicine because of their power to modulate signal transductions of biological system. Since the removal of sub-structures of the natural products often leads to significant losses of their activity, total chemical syntheses of their entire structures with a precision at an atomic level are necessary to provide sufficient amounts of material required for biological and medical applications. Architecturally complex natural products with molecular weight over 1000 are capable of highly specific interactions with their target proteins. Therefore, they are powerful agents for selectively controlling intricate biological systems. The goal of our research program is efficient, practical and flexible syntheses of gigantic natural molecules, which include highly oxygenated polycyclic natural products as well as ion channel-forming peptides. At the core of this research program is the development of new strategies for assembling architecturally complex natural products in a concise fashion. These synthetic developments would enable unified synthesis of new artificial analogs by modification of natural products templates. The new synthetic methods for the natural products and the synthetic analogs will allow us to tailor and enhance their drug like properties, to gain control over diverse signal transductions thereby offering new research methods for the study of life science.
The main theme of our research is the development of revolutionary catalyses facilitating new drug design and synthesis. In this direction, we would like to promote human health based on the catalysis development. Chemical synthesis in 21st century should be clean, robust, and concise, no matter how complex the target molecules are. The “ideal synthesis” will be only possible by new catalytic methodologies. Moreover, new catalyses will expand the diversity of readily available building blocks, leading to structurally novel artificial drug design. Sustainability based on new catalysis is another direction of our research. Specifically, we are interested in catalytic activations of small molecules such as H₂ and O₂.

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Laboratory of Natural Products Chemistry

We establish the mechanisms of natural product biosynthesis as a science in their own right, to construct a rational system for the production of new and useful substances.

**Research Topics**

1. The biosynthesis and bioengineering of medicinal natural products (genome mining, engineered biosynthesis)
2. The enzyme biocatalysts (structure-function analysis, enzyme engineering, mechanistic studies)
3. The search for bioactive substances and isolation/structure determination

Natural organic compounds, prominent among which are antibiotics such as penicillin, are gifts from nature, and the benefits they have bestowed upon humankind as sources for the pharmaceuticals, etc., that maintain health is inestimable. In our laboratory, we study the process of biosynthesis of natural organic compounds produced by plants and microorganisms, using not only the foundation discipline of organic chemistry, but also incorporating the methods of biochemistry and molecular biology in an effort to understand the enzymes that catalyze each biosynthesis reaction and the functions and control mechanisms of the genes that govern their expression at the molecular level. In addition, we are expanding our research into “biosynthesis engineering,” by which rational systems for the biological production of new and useful substances can be designed and constructed, based on the mechanisms of biosynthesis that have been brought to light. We also are carrying out research on the mechanisms by which the bioactivity of natural products is expressed, while at the same time searching for natural products that are active in intracellular signaling.

![Concept of "biosynthesis engineering," by which non-natural compounds are generated](image1)

![Synthetic biology of complex natural products](image2)
Understanding of chemical phenomena at the atomic and electron levels and creation of a new science of materials through flexible construction of molecules

Research Topics

1. Development of advanced molecular transformation methods supporting materials science and life sciences (methodology development/synthetic chemistry)
2. Periodic table-traversing chemistry that transcends the frameworks of organic chemistry, inorganic chemistry, and metallic chemistry (elements chemistry)
3. Elucidation of the structural chemistry of intermediates and transitional states (physical chemistry, spectroscopy, theoretical calculation)
4. Design and production of materials founded on synthetic chemistry, spectroscopy, and computational chemistry (materials science/life sciences)

Our laboratory focuses on understanding the properties and phenomena of substances by “language of chemistry” such as molecules, atoms, and electrons (Seeing/Knowing); on developing reactions that manipulate the bonds between atoms completely in control (Designing); and on producing functional materials (Producing).

In our laboratory, we strive to develop technologies for the precise chemical conversion of tiny, tiny molecules less than 1 billionth of a meter in size (nanometer scale; nm). Thanks to recent advances in spectroscopy and theoretical calculation, it is getting possible to accurately predict and reproduce snapshots of the state of the electrons that form materials, as well as of reactions between molecules.

With the 3 methods, namely, synthetic chemistry, spectroscopy, and theoretical calculation as the pillars of our science, we expand upon elements chemistry in an interdisciplinary manner as we meet the challenges of elucidating life phenomena and creating a new materials science.
"Chemical Biology" and "Chemical Medicine" in order to promote life science research and to develop novel medical tools

**Research Topics**

1. Fundamental photophysical and photochemical research to establish rational design principle for novel chemical tools
2. Theoretical design, synthesis and biological application of novel chemical tools, including sensor molecules and signal perturbation techniques for cellular signaling molecules, such as Ca^{2+} ion, reactive oxygen species, or various enzymes
3. Development of chemical tools, e.g., MRI probe and fluorescent probe, for diagnostic imaging and their in vivo application
4. Clinical use of our newly developed fluorescence probes for rapid imaging of tumor with human clinical fresh specimens
5. Research on drug discovery: Searching for novel lead compounds that control disease-related proteins, and development of high-quality screening systems

Our laboratory conducts research on the analysis and perturbation of dynamic living systems, using chemistry as a powerful tool. One of the important goals in modern life sciences is to elucidate the dynamic behaviors of biomolecules in situ in the living cells/organisms. So far, our laboratory has succeeded in developing bioimaging probes/other chemical tools including signal perturbation methodology and high quality screening systems by applying the probe design strategies that we established. Likewise, we utilize our probe design principle to establish chemical tools for clinical use, including a tumor-specific intraoperative fluorescence imaging methodology. On top of that, we are now conducting dozens of pilot clinical trial projects by utilizing above mentioned chemical tools with external collaborators in domestic hospital and abroad.

The above-described areas of research have attracted enormous attention in recent years under the name of “Chemical Biology”, and we believe that they will open up new horizons in life sciences.


We measure the functions of biomolecules at the level of a single molecule to elucidate vital functions

**Research Topics**

1. Research on the principles of action by which biomolecular machines such as molecular chaperonin and ribosomes operate
2. Single-molecule fluorescence imaging of intracellular mRNA processing and transport
3. Development of micro nanodevices for analyzing the functions and interactions of biomolecules

In order to understand living organisms, it is necessary to conduct research at a variety of different levels. The lowest level is that at which biomolecules such as proteins and DNA work. When these come together, biological supramolecules, cells, organs, and the like are created, while at the higher end, individual organisms, societies, and ecosystems are constituted. We focus on the level of the smallest unit, the “biomolecule,” together with the level of the “cell,” at which life functions are first expressed, to find answers to questions like “By what mechanisms do biomolecules function?” and “When they aggregate, what kinds of systems do they construct?” Concretely speaking, we bind a fluorescent dye to a single biomolecule and observe it with a sensitive fluorescence microscope. Some biomolecules can exhibit their functions even at the level of the single molecule. For example, the motor protein known as kinesin moves on rail proteins called microtubules. Humankind does not at this point in time possess the technology for creating this kind of molecular machine, but we believe that humankind will be able to make this kind of molecular machine in the near future through research on the motor protein. On the other hand, self-assembly of a variety of different biomolecules creates complex systems which differ greatly from manmade ones. By researching such biological systems, we close in on the mysteries of life.
Laboratory of Physical Chemistry

We develop original NMR methods for elucidating protein functions based on dynamical structure information

Research Topics

1. Elucidation of the functional dynamics of membrane proteins
2. Reconstitution of membrane proteins into lipid bilayer condition with tailored stable isotope labeling for in situ NMR analyses.
3. Analyses of protein-protein interactions involving intracellular signaling
4. Development of new NMR methods for analyzing the structure and dynamics of high molecular weight proteins
5. Real-time observation of the intracellular biological events using the in-cell NMR method

Membrane proteins play fundamental roles in many biological processes, and are recognized as the principal target proteins for drug development. Recently, accumulating evidence has suggested that membrane proteins are structurally dynamic, and exist in an intrinsic conformational equilibrium, such as between the active and inactive conformations.

We use NMR for obtaining dynamic structural information about the membrane proteins under physiological conditions. We have analyzed the relationships between the dynamical structures and the functions for biologically important membrane proteins: GPCRs, ion channels, and adhesion molecules (Figure 2). To achieve this goal, we are developing new methodologies, including the reconstitution of membrane proteins within lipid bilayer conditions, a sophisticated stable isotope labeling techniques, and NMR methods for analyzing the structure and dynamics of high molecular weight proteins.

Figure 1: NMR spectrometers in our group

Figure 2: The functional dynamics of membrane proteins revealed in our group. (A) The efficacy of GPCR ligands, (B) The gating mechanism of potassium channel(KcsA), (C) The cell rolling mechanism mediated by CD44
Laboratory of
Protein Structural Biology

Determining three-dimensional structures of proteins and nucleic acids, and elucidating their functions in living cells

Research Topics

1. Structural biology of proteins and nucleic acids using X-ray crystallography and small angle X-ray scattering
2. Structure and function relationship of proteins and nucleic acids
3. Structures of immune-system proteins and their complexes
4. Structures of nuclear proteins and their complexes
5. Structures of proteins in signal transduction and their complexes

Structural biology seeks to provide a complete and coherent picture of biological phenomena at the molecular and atomic level. Our laboratory aims at achieving a comprehensive understanding of structure/function relationships of key cellular components and processes, and roles in living cells. In the elucidation of three-dimensional structures, X-ray crystallography is extensively used since this method provides us with detailed structural information on the biological functions and roles. We also take an interdisciplinary approach, combined with methods of biophysics, biochemistry, molecular biology, genetic and protein engineering, and small angle X-ray scattering. With these structural biological approaches, we can obtain the information on three-dimensional structures that are required for drug design and discovery.

We are now carrying out structural biological researches into immune-system proteins, nuclear proteins and proteins in signal transduction.
Laboratory of Health Chemistry

Exploration of new functions for biomembranes and their constituent lipids

Research Topics

1. Molecular mechanism of lipid biosynthesis and homeostasis
2. Molecular mechanism of membrane dynamics (e.g., endo/exocytosis)
3. Identification of new bioactive lipids and elucidation of their functions
4. Elucidation of functions of membrane lipids using C. elegans genetics

Biomembranes serve as barriers that segregate cells from the external environment. They also produce intracellular organelles, and are essential for cellular functions. The Laboratory of Health Chemistry aims to elucidate the physiological functions of lipids, essential constituents of biomembranes. Over 1,000 lipid species exist in biomembranes, and the appropriate balance among them is assumed to be fundamental to stability, activity, and localization of proteins, and regulation of gene expression. We focus on major components of cellular lipids, called phospholipids, and are trying to identify proteins involved in their biosynthesis and homeostasis. We also study the functions of lipids in the dynamic behavior of biomembranes, such as endo/exocytosis.

Various bioactive lipids are formed from membrane phospholipids, and affect a range of biological phenomena and diseases. Our study also focuses on “inflammatory response” which is the underlying condition of lifestyle-related diseases. To better understand the molecular mechanisms underlying inflammation, we are trying to comprehensively clarify when, where and how much lipid mediators are formed in the inflammatory sites using LC-ESI-MS/MS-based lipidomics system.
Laboratory of
Physiological Chemistry

G protein-mediated signaling networks and their physiological significance

Research Topics

1. Identification and characterization of novel families of small G proteins
2. Molecular mechanisms of endocytic pathway regulated by small G proteins
3. Molecular mechanisms of the nutrient sensing mediated by small G proteins
4. Mechanism of protein exit from the endoplasmic reticulum regulated by G proteins

Our laboratory is interested in the molecular mechanisms of signal transduction that underlie human physiology. Abnormal regulation of cellular signaling is often found in human diseases. Pharmaceutical drugs usually work to offset, alleviate, compensate and correct such deranged transduction of signals. Thus, understanding the molecular principles of signal transduction would greatly help to develop new drugs. We take a broad range of experimental techniques that utilize biochemistry, molecular biology, cell biology and molecular genetics. Our research has centered around GTP-binding proteins, so called “G proteins.” We wish to expand and deepen our understanding of signaling networks involving G proteins and their physiological significance.

Laboratory of Molecular Biology

We investigate mechanisms regulating cell fate determination during development and homeostasis with an emphasis on neural stem cells and signal transduction.

Research Topics

1. Mechanisms regulating neural stem cell fate during brain development and in the adult brain
   - Roles of Polycomb group proteins and other chromatin modifiers in neural stem/progenitor cell fate during neocortical development
   - Signaling pathways that regulate the fate commitment and differentiation of neural stem/progenitor cells
   - Mechanisms that regulate the generation and maintenance of adult neural stem cells

2. Investigation of chromatin-level regulators of neuronal differentiation/maturation and activation

3. Dissection of signaling pathways regulating cell migration and metastasis

4. Dissection of signaling pathways regulating cell death and innate immunity

Our bodies have hundreds of cell types that each have distinct jobs, but they all contain the same genetic information. Our lab asks how the distinct fates of cells during development and homeostasis are determined by both cell-intrinsic programs and by environmental inputs.

Our first research goal is to understand the molecular basis of brain development with an emphasis on the regulation of neural stem/progenitor cell fate. Our second goal is to understand the intracellular signal transduction pathways that regulate cell proliferation, survival/death and migration, and the involvement of these pathways in tumorigenesis.

Please visit our HP for details.
Laboratory of Genetics

Prof. M. Miura
Assoc. Prof.
Y. Yamaguchi
Project Assist. Prof.
T. Katsuyama

http://www.f.u-tokyo.ac.jp/~genetics/index_e.html

Research of cell and tissue communications for establishment and maintenance of cell society

Research Topics

1. Regulation and function of cell death in development, growth, and regeneration
2. Regulation of cell number and size of tissue via programmed cell death mechanism
3. Roles of dying cells as a signal center
4. Metabolic regulation of development, growth, aging and tissue regeneration
5. Molecular mechanisms of hibernation

Programmed cell death functions in dynamic tissue formation or remodeling. We have revealed that in the embryonic development, or aging process, caspases are activated by physiological stresses and exert regulatory functions. We aim to reveal how cell society is constructed and maintained during development, growth, and aging process with a particular focus on understanding the regulatory mechanisms and functions of cell death. From the perspective of cell sociology, we are also studying the unique biological phenomena such as tissue regeneration and hibernation. We believe that our research would stimulate and encourage students and researchers to have the breadth of vision for life science research and provide new insights into the molecular logic underlying the formation and maintenance of cell society.
Laboratory of Cell Signaling

From signal transduction to drug discovery

**Research Topics**

1. Signal transduction and functions of ASK family proteins
2. Exploration of novel signaling molecules involved in cell death and stress responses
3. Molecular mechanisms of pathogenesis induced by dysfunction of stress signaling

The Laboratory of Cell Signaling has been focusing on analyses of the intracellular signal transduction, through which we seek to elucidate molecular basis of human diseases and identify novel drug targets. Our current research mainly focuses on the pathophysiological roles of stress responsive signals in various diseases such as cancers, immune disorders, cardiovascular diseases and neurodegenerative diseases. In addition to molecular genetic tools such as mice, flies and worms as well as basic experimental techniques from molecular cloning to protein biochemistry, we always incorporate novel analytic technologies such as mass spectrometry-based proteomic analysis and genome-wide RNAi screening systems into our research exploring “target molecules and molecular mechanisms”. By taking advantage of such experimental approaches, we aim to open up new fields in pharmaceutical sciences with paying attention to whole body physiology, diseases and drug discovery.
Laboratory of Protein Metabolism

Shedding light on the various biological phenomena controlled by proteolysis

**Research Topics**

1. The action mechanism of the proteasome, a multisubunit macromolecular complex responsible for regulated protein degradation in eukaryotic cells
2. Proteasome dysfunction in human diseases and aging
3. The mechanism of T-cell selection by the thymus-specific proteasome
4. The mechanism for the disposal of abnormal proteins by the ubiquitin-proteasome system

Laboratory of Protein Metabolism explores the regulatory mechanism of cellular functions by the ubiquitin-proteasome system, which is the major proteolytic machinery in eukaryotic cells. The lab’s main interest is the proteasome, which is an elaborate proteolytic enzyme that degrades ubiquitinated proteins and is a key regulator of physiological events. The questions we are interested in are, how is the proteasome regulated, how does it assemble, and how is it involved in human diseases. To this end, we make use of experimental techniques including biochemistry, molecular biology, cell biology, genetic engineering of the mouse, fly genetics, and yeast genetics. In recent years, there has been accumulating evidence indicating a close relationship between the ubiquitin-proteasome system and human diseases such as cancer, neurodegenerative diseases, immune disorders, and aging. The goal of our research activities is to provide new molecular bases for the development of drugs for such diseases.
Laboratory of
Immunology and Microbiology

Prof. S. Hori

Assoc. Prof. C. Kaito
Assist. Prof. A. Nakajima
Assist. Prof. R. Murakami

http://www.f.u-tokyo.ac.jp/~bisei/

Understanding the principles of immunological tolerance and homeostasis

Research Topics

1. Mechanisms of immunological tolerance and homeostasis
2. Mechanisms of regulatory T cell development and function
3. Molecular mechanism of bacterial virulence

The immune system has evolved the ability to distinguish "self" from "non-self" to maintain homeostasis of the body. The immunological "self" is established in an adaptive and acquired manner through continuous interactions with changing internal as well as external environments. The ultimate goal of this laboratory is to elucidate, throughout multiple layers, from molecules, cells, cell populations, tissues, to individuals, the principles that govern the development of such immunological "self" and its transformation during diseases. Towards this end, we focus on a cell-extrinsic, dominant control mechanism of the immune system that depends on a subpopulation of T lymphocytes called regulatory T (Treg) cells. As one approach, we elucidate how mutations in the Foxp3 gene, encoding a transcription factor critical for Treg cell development and function, lead to a breakdown of immunological tolerance and homeostasis.

Fig. 1: Disintegration of immunological "self" underlies a variety of diseases

Fig. 2: Foxp3-expressing regulatory T (Treg) cells are indispensable for immunological tolerance and homeostasis
Elucidation of the mechanisms determining pharmacokinetic properties of drugs that contributes to drug design, and safe and effective utilization of drugs

**Research Topics**

1. Prediction of pharmacokinetic properties and responses of drugs based on in vitro experiments: analysis of the effect of genetic polymorphisms and drug-drug interactions
2. Elucidation of transporters determining the elimination pathway of drugs, and drug transport systems at the blood-brain barrier
3. Elucidation of mechanisms for the membrane trafficking of transporters
4. Development of transporter-based drug delivery systems (DDS)
5. Elucidation of mechanisms of drug-induced toxicity
6. Elucidation of genetic and epigenetic regulation of drug transporters

Pharmacological and adverse effects of drugs depend on their pharmacokinetic properties, which determine their exposure to the targets. Our laboratory aims to establish methods for quantitative and theoretical prediction of pharmacokinetic properties of new chemical entities in humans based on the molecular mechanisms. In particular, we investigate the impact of transporters on the elimination of drugs from the liver and kidney, the distribution of drugs into their target organs e.g., the brain, and drug absorption in the small intestine, in order to develop drug screening systems and to elucidate the mechanisms of drug-drug interaction, and interindividual variation in pharmacokinetics of drugs. We have also started research on the regulation of membrane trafficking of the transporters using low molecular weight compounds to cure transporter related-diseases. Research achievements in this laboratory contribute to predicting and evaluating rational pharmacokinetic properties in drug development, drug review and regulation, and in clinical use, and to developing medical therapy for transporter related-diseases.


An example of a drug successfully designed to minimize interindividual variation in pharmacokinetics by considering transporter characteristics.
Laboratory of Chemical Pharmacology

Pharmacological approach toward the brain: from molecule to animal

Research Topics

1. Study on neuronal networks involved in learning and emotion using neuronal activity genetic markers
2. Study on brain network operation using functional imaging of multicellular activity
3. Studying on neuronal network formation during development

Pharmacology includes two aspects: 1) to analyze the biological action of drugs and 2) to search the strategies for developing treatments for diseases. We conduct our pharmacological research by taking advantage of state-of-the-art technologies and a wide range of knowledge from molecule to animal.

We focus on the roles of the cerebral limbic system and cerebral cortex, in particular, the hippocampus and amygdala, which are involved in learning, memory, and emotion.

Our experimental techniques cover from genetics, biochemistry, and cell biology to electrophysiology, histochemistry, and behavioral pharmacology. Recent technical advances have allowed us to investigate the neuronal network dynamics on far larger scales than hitherto. Functional multineuron calcium imaging reveals the dynamics of network activity with single cell/synapse resolution (Upper Figure), through which we elucidate the structural and functional relationship that generates spatiotemporally organized spike patterns. We also address the mechanisms of learning and memory using in situ mapping learning-relevant neuronal circuits with immediate early genes with cellular and temporal resolution (Lower Figure).

We believe that these novel approaches open up a new avenue for our mesoscopic understandings of network function and malfunction associated with depression, stress-relevant disease, and epilepsy.
Laboratory of Neuropathology and Neuroscience

From understanding the molecular pathogenesis of neurodegenerative and psychiatric diseases to development of therapeutics and novel basic science

**Research Topics**

1. Understanding the molecular mechanisms of intramembrane proteolysis by γ-secretase
2. Research on Aβ metabolism (production, secretion and clearance) and its regulatory mechanisms
3. Elucidation of pathophysiological functions of risk factors for Alzheimer diseases
4. Molecular mechanisms of aberrant vesicular trafficking and diseases
5. Biological and pathological roles of synaptic adhesion molecule and its metabolism
6. Elucidation of pathological roles of glial cells towards development of glial cells-targeting drugs

Aim of our laboratory is that understanding the molecular pathogenesis of neurodegenerative and psychiatric diseases to develop novel approaches to therapeutic, prevention and diagnosis. Also, we are pursuing novel basic science by understanding the molecular basis of diseases. Especially, we are studying Alzheimer disease, autism spectrum disorder and schizophrenia to identify the pathological mechanisms and therapeutic targets of these diseases at molecular levels. To understand the disease condition, we have to realize the basic mechanisms of cells and living organisms, and vice versa. We believe that this disorder-to-normal cycle in research is a basis of modern disease and basic biology, and bolsters both scientific areas by novel knowledge and technology. From this standpoint, we proceed disease-oriented molecular and cellular research in a multidisciplinary manner by mutual collaborations with organic chemists, structural biologists, physicians and pharmaceutical companies.
Laboratory of Pharmaceutical Regulatory Science

Establishing scientific drug evaluation

Research Topics

1. Advancing methods for rational drug evaluation
2. Analyzing drug development behaviors and policies
3. Evaluating drug regulation and guidelines
4. Developing systems to implement the above policies and guidelines

The goal of our research is to establish scientific principles and methods in drug evaluation with societal perspectives in mind. Pharmaceutical research and development (R&D), clinical development in particular, regulatory review and approval of new drugs, and post marketing activities are our research interests. We provide evidence on R&D efficiency, performance and outcomes of regulations, and public health impact through rigorous analysis based on economic models. Conflicts in global pharmaceutical R&D, including recent launch delay of new drugs in Japan and so-called ethnic differences, are always high on our agenda. Aside from the research activities, we also make efforts to develop human resources in both private and public sectors with up-to-date knowledge, ethics, and philosophy, and rationale in drug evaluation. We offer lectures for graduate and undergraduate students, and a half-year training course for industry and regulatory professionals. We aim to secure transparency and social responsibility on drug regulation through our research and educational programs.


Laboratory of
Medicinal Plant Chemistry
(Experimental Station for Medicinal Plant Studies)

An overall analysis is made of the old-yet-new drugs known as “medicinal plants” (crude drugs) to develop new ways of using them (utilizing the resources in the Experimental Station for Medicinal Plant Studies)

**Research Topics**

1. The cultivation of medicinal plants and tissue cultures
2. The production of useful secondary metabolites, using plant tissue culture technology
3. Chemistry and biosynthesis of plant-derived biologically active substances

Since prehistoric times, plants have been the principal material used as drugs by humankind. Many have fallen by the wayside through a long process of trial and error (human experiments), and the ones that remain can be considered the crude drugs of the present day. In recent years, the percentage of all drugs accounted for by antibiotics and biologics has increased, but the importance of plant-derived pharmaceuticals is by no means diminished and has led to the discovery of new drugs such as Taxol and vinblastine. Thus, the study of medicinal plants is by no means completed, and is continuing to evolve.

The Experimental Station for Medicinal Plant Studies, formally established in 1973, is located adjacent to the Kemigawa Athletic Ground. The saplings transplanted there back then have grown large and now form a dense enclosure of trees around the garden.

At the research lab in Hongo, we conduct research on the production of useful secondary metabolites using plant tissue culture technologies (from the induction of culture cells to the production of substances). Some of the research topics we are currently pursuing are the biosynthesis of diterpene constituents from Gymnosperm plant cultured cells, the production and biosynthesis of diterpene alkaloids using cultured tissue of monkshood, the production and biosynthesis of phenylethanoids using cultured cells of olive, and the production of biologically active constituents of Egyptian medicinal plants by means of plant tissue culture technologies.

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The sweetener glycyrrhizin is contained in the roots and stolons of Glycyrrhiza uralensis Fisher

*Aconitum japonicum* cultured root
Laboratory of
Bioorganic Chemistry
(Institute of Molecular and Cellular Biosciences)

Discovery and production of bioresponse modifiers
directed toward an understanding of life phenomena

Research Topics

1. Discovery and production of molecules that control the spatio-temporally dependent expression and function of proteins
2. Medicinal chemistry of nuclear receptor ligands
3. Design and synthesis of bioresponse modifiers that control the topology and dynamism of proteins
4. Developing new methods of drug discovery, using the multifunctional thalidomide as a template
5. Developing novel strategies for improving aqueous solubility of drug candidates by their molecular modification

The aims of this laboratory are to discover and produce new bioresponse modifiers based on medicinal and synthetic organic chemistry, and to use them to gain an understanding of life phenomena. Many life phenomena are controlled by the expression, localization, and degradation of proteins. Thus far, research on chemical control of the expression of proteins has succeeded in discovering and producing various nuclear receptor ligands. At the same time, functional molecules that regulate life phenomena through modification of proteolysis have been designed and produced. By a method differing from siRNA, it has become possible to destroy target proteins at any time, and this is expected to serve as a new technique for the functional analysis of proteins within cells. [PROTEIN KNOCKDOWN APPROACH]

In addition, we are designing and synthesizing molecules that control the folding process of proteins. [PHARMACOLOGICAL CHAPERONES] These are compounds that control dynamic structure-based function of proteins, and they will open up new domains in medicinal chemistry of bioresponse modifiers. We are also producing bioresponse modifiers using multifunctional thalidomide as a drug discovery template.


Elucidating the intracellular signaling involved in disease development, with the goal of drug discovery

Research Topics

1. Transcription factor NF-κB activation signal mediated by TRAF family
2. Signal transmission by ubiquitination
3. Malignant progression of cancer and signaling
4. Bone metabolism disorders and signaling
5. Autoimmune diseases and signaling

The themes pursued in our laboratory are related to “cancer”, “immunity”, and “bones”, since TRAF6 and NF-κB, which we are interested in, are profoundly involved in tumorigenesis, immune regulation, and bone metabolism. Upon cytokine stimulation, TRAF6 acts as E3 ubiquitin ligase to generate Lys-63-linked polyubiquitin chains, which do not induce proteasomal degradation rather act as platforms for formation of active signal complexes leading to the activation of NF-κB. A number of serious human diseases are caused by various kinds abnormalities in bone metabolism and immunodeficiencies. We were able to reproduce diseases similar to these human diseases in TRAF6- or NF-κB-deficient mice, indicating that TRAF6/NF-κB signals are essential for normal bone formation and the establishment of immunity. Abnormal activation of NF-κB also plays a critical role in the onset and progression of leukaemias and many other cancers. We are trying to elucidate how dysregulation of the TRAF6/NF-κB signals leads to malignant transformation and serious diseases related to immune regulation, and bone metabolism at the molecular level and conducting numerous experiments on gene transfer into cultured cells, aiming to put the results to use in drug discovery and the diagnosis and treatment of diseases.

TRAF6 generates Lys-63-linked polyubiquitin chains, which act as the scaffolding for interactions of various proteins to form signal complexes to transmit signals. As a result, NF-κB and MAPKs become activated, which induces and regulates many important biological processes.

X-ray images of a normal mouse (left) and TRAF6 knockout mouse (right). The TRAF6 knockout mouse displays osteopetrosis because TRAF6 is required for formation of osteoclasts, which absorb bones. Dysregulation of osteoclastogenesis is involved in the progression of rheumatoid arthritis, osteoporosis, and bone metastasis of cancer cells.
Laboratory of

Clinical Pharmacokinetics
(The University of Tokyo Hospital)

Systems-pharmacological studies for drug development in the next-generation

Research Topics

1. Therapies for lifestyle-related diseases based on the comprehensive understanding of molecular mechanisms that control the transport of endogenous small molecules

2. Therapies for bone metabolism diseases based on the comprehensive understanding of the dynamic control mechanisms of signal molecules involved in bone resorption and formation

3. Quantitative understanding of the pharmacological and toxicological effects of molecular targeted anti-cancer drugs to establish clinical applications and new drug discovery techniques

4. Large-scale omics analysis to establish methods of preventing and treating adverse drug reactions based on the quantitative understanding of underlying molecular mechanisms

5. Clinical pharmacokinetics based on detailed quantification of related molecular functions

It has been recognized very well that we need to describe / predict the functions of cells, tissues and organisms from the function of each constituent molecule in a quantitative manner in order to understand the life activities. Although we have used such approach in analyzing and predicting the drug disposition in humans, it is quite important for us to expand the concept to the analysis of pharmacological / toxicological actions of drugs in humans. We are using such “systems-pharmacological” methods to solve many kinds of problems that remain great challenges in drug discovery, such as how to identify the most effective target molecules among numerous candidates, and how to comprehensively predict the adverse drug reactions in humans.
Endowed Laboratory of Pharmaco-Business Innovation

Developing a professional who Understand Both Life Sciences and Business

Research Topics

1. Studies on industry dynamics in pharmaceutical/life science domain: Analysis of factors driving the reorganization of the industry

2. Studies on strategy and management issues in pharmaceutical/life science domain: Finding solutions for management issues of companies, universities, and medical institutions

3. Studies on industrial policy in pharmaceutical/life science domain: Making recommendations on social infrastructure for the development of the industry

While Japan aims at sustainable development for the future as a world leader in science and technology, pharmaceutical/life science domain occupies an important position in the national strategy. On the other hand, in a globalizing pharmaceutical industry, the presence of Japan as a market has relatively been declining little by little.

Under such circumstances, the objective of PBI course is to contribute to a sustainable development of the Japanese pharmaceutical industry by 1) conducting multilateral research on managerial issues of rapidly evolving pharmaceutical/life science industry for its long-term growth, such as those related to innovation, public health, global competition and harmonization, 2) fostering a new generation of industrial leaders capable of taking advantages of the new opportunities that are being created, and 3) developing a social infrastructure for drug discoveries including regulations.
Endowed Laboratory of
Drug Lifetime Management

Drug lifetime management for development of excellent drugs, proper use of drugs, and evolution of drugs

Research Topics

1. Development and practice of methodologies for the collection, evaluation, analysis, and distribution of drug post-marketing information
2. Creation of programs for promoting proper use and evolution of drugs in community healthcare
3. Development of new features in the community pharmacy to practice the above-mentioned 2
4. Specification, standardization, and digitization of drug information, and their clinical applications
5. Quantitative prediction of the effects of biodisturbance factors on pharmacokinetics and drug effects

Our university’s Faculty of Pharmaceutical Sciences bears the social mission of promoting drug discovery and the proper use and evolution of drugs while improving the quality of drug therapies. To these ends, this course in Drug lifetime management pursues various research to ensure that the developed drugs can amply exhibit their effects and lead a substantial “drug life.”

The research topics of this course are that (1) the proper collection of drug information (DI), (2) evaluation/analysis of DI based on pharmacokinetics and pharmacodynamics and quantitative prediction of changes in pharmacokinetics and drug effect due to various risk factors, (3) Qualitative evaluation and analysis of the individual cases, (4) Creation of archive based on the optimal specification/standardization/digitization of DI, and (5) their proper provision to the clinical field. Concretely speaking, the content of our research is to seize drug post-marketing problems (including trouble and needs related with drugs), to make a proposal, to the pharmaceutical field, for evolving drugs and their information in order to solve the problems, and to feedback them to the clinical field.
Maximizing and evaluating true "value" of various medical interventions, not only its impact for health care budgets but for health outcomes, to maintain and improve public health care system.

**Research Topics**

1. Health Technology Assessment (HTA)
2. Health economic analyses for drugs / medical devises
3. Surveys on public healthcare system / reimbursement system
4. Research on QOL (Quality of Life) instruments

Medical expenses are growing by the year, and present health-insurance system is at a crossroads. In order to utilize pharmaceuticals appropriately within a limited budget (what we call the “rational use of pharmaceuticals”), we have to evaluate efficiencies of various drugs. When we evaluate efficiency, we need to measure both clinical evidence, which endpoints are efficacy and safety, and economic evidence, of which the primary index is economy. In this course, we carry out economic evaluations of drugs that are either under development or already marketed (drugs for rheumatoid arthritis, cancer, smoking cessation therapy, hypertension, etc.)

It is important for us to set various perspectives, including regulatory administration, (pharmaceutical) industries, medical institutions, and patients, when we take economic evaluations. In this course, from societal perspective that includes all of above-mentioned perspectives, we explore the appropriate role of pharmaceuticals in health services.

After researching methodologies for evaluating them, conducting actual analyses, and analyzing policy, etc., we endeavor to recycle our findings back into society through policy proposals and the like.

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Molecular basis of intracellular membrane traffic and its pathophysiological relevance

**Research Topics**

1. Molecular basis of vectorial endosomal membrane traffic
2. The role of recycling endosomes in physiology and pathophysiology
3. Screening of low molecular weight compounds that regulate intracellular membrane traffic

Eukaryotic cells have elaborate internal connections of organelles to synthesize proteins and lipids, to release secreted proteins, to take up nutrients, and to degrade internalized molecules. Membrane proteins and lipids move from organelle to organelle using membrane-bound vesicles. Defects in this transport system, called “membrane traffic”, have been associated with a number of human diseases, including cancer and diabetes. Recent studies reveal that many pathogens, such as bacteria and viruses, exploit membrane traffic to invade and proliferate in host cells. Therefore, understanding of how membrane traffic is regulated in cells at molecular level is essential to cure diseases and to cope with pathogens.

We have shown that recycling endosomes (REs) serve as intersections of a number of essential membrane traffic, such as recycling-, exocytotic-, and retrograde-pathways, and sort proteins and lipids to the correct destinations. We identify critical molecules that manipulate the membrane traffic through REs, such as evectin-2, and now translate our cellular insights into pathophysiological applications.

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**Figure 1:** Intracellular transport of cholera toxin B-subunit (CTxB)
Fluorescent-labeled CTxB (in red) was taken up by COS-1 cells, and monitored its delivery for the indicated times. After a 15-min chase, CTxB reached REs that are spatially encircled by the Golgi (GM130 in green). After a 75-min chase, CTxB reached the Golgi. Scale bar, 10 μm

**Figure 2:** Evecrin-2 is essential for CTxB delivery to the Golgi
In cells depleted of evecrin-2, the traffic from REs to the Golgi was significantly impaired. Even after a 90-min chase, CTxB was entrapped at REs. Scale bar, 10 μm
In 1869, Meiji government decided to adopt German medicine and asked the minister of the North German Federation to send 2 instructors. In 1871, Müller (chief Army physician/staff surgeon) and Hoffman (Navy physician/staff internist) arrived in Japan and assumed their duties at the University East Building (Tôkô) in Shitaya Izumibashi (precursor of the Faculty of Medicine, University of Tokyo).

Müller and Hoffman, who were under the direct supervision of the Meiji Minister of Education, had absolute authority over medical education in Japan. A new curriculum was established with 3 preparatory years (changed to 2 the following year) and a 5-year main program.

Müller and Hoffman regarded “pharmaceutical sciences” as an independent branch of the natural sciences that was closely related to medicine, and they proposed the establishment of a pharmaceutical institute. This took shape in 1873 as the Department of Pharmaceutical Manufacturing, established in The First University District Medical School. Müller returned to Germany in 1875. In October of 1895, upon the third anniversary of his death, a bust of Müller was erected to honor him as a benefactor of Japanese medicine and pharmaceutical sciences.

Dr. Shimoyama was born in Owari Inuyama in 1853. In 1873, after transferring to the Department of Pharmaceutical Manufacturing, The First University District Medical School (the precursor of the Faculty of Pharmaceutical Sciences, University of Tokyo), he graduated in 1878. He gave the “address in reply” at the first degree-conferring ceremony held by the Faculty of Medicine.

In 1886, Dr. Shimoyama received the Doktor der Philosophie degree from Strasburg University in Germany and in 1899, he became the first person in Japan to be awarded a Doctor of Pharmaceutical Sciences degree.

Dr. Shimoyama became a professor of the Department of Pharmacy in the Faculty of Medicine in 1887, and a professor of a laboratory of Pharmacognosy, the Department of Pharmacy in 1893. While devoting great efforts to education and research, he also helped to cultivate successors through the establishment of the Pharmaceutical Society of Tokyo (the present Pharmaceutical Society of Japan) and the creation of a privately funded medicinal herb garden (Zekô Yakuen), etc.

Dr. Shimoyama died suddenly in February of 1912 while still in service as an educator. In remembrance of him, a bronze statue was erected beside the Pharmaceutical Sciences Building in 1913.

Education Center for Clinical Pharmacy

The center has been established in June, 2012. The purpose of the establishment is to enhance the educational research structure in those new educational programs, especially 6-year undergraduate program (Department of Pharmacy) and 4-year doctoral program (Department of Pharmacy).

**Research Topics**

1. Development of educational program for practice for clinical pharmacy
2. Development of educational program of clinical pharmacy
3. Development of postgraduate educational program for training leading pharmacists

**Dr. Leopold Müller**

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Dr. Leopold Müller (1824 - 1893)

**Dr. Junichiro Shimoyama**

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Dr. Junichiro Shimoyama (1853 - 1912)
After Graduating from Graduate School of Pharmaceutical Sciences

Graduates of Faculty of Pharmaceutical Sciences, who have acquired a comprehensive fundamental understanding and applied knowledge of the field, receive extremely high respect, resulting in relative easiness to find a job. Over 90 percent of graduates choose to move forward to Graduate School of Pharmaceutical Sciences, the University of Tokyo. An increasing number of applications from the University of Tokyo, other universities, and foreign universities take an annual entrance exam in August.

We have seen more and more of a social trend that prefers an individual with a researcher background and research experience higher than a Master's level. Our graduates who completed either undergraduate or graduate courses find positions in a wide array of fields, such as pharmaceuticals, chemical, and food related companies, universities, as well as government agencies. Half of graduate students opt for the doctoral course. After acquiring a PhD., they find vast opportunities not only in the academic field, such as universities and public research agencies, but in researching departments of companies, as leaders of projects.

B.S. Graduates

Department of Pharmaceutical Sciences

- Graduated School of Pharmaceutical Sciences, The University of Tokyo (Master's Program): 91.4%
- Other advanced degrees in different schools: 3.7%
- Government agencies and private enterprises: 6.9%
- Others: 0.0%

Department of Pharmacy

- Graduated School of Pharmaceutical Sciences, The University of Tokyo (Doctoral Program): 87.5%
- Other advanced degrees in different schools: 12.5%
- Government agencies and private enterprises: 10.0%
- Others: 0.0%

M.S. Graduates

- Graduated School of Pharmaceutical Sciences, The University of Tokyo (Doctoral Program): 56.9%
- Other advanced degrees in different schools: 34.3%
- Government agencies and private enterprises: 6.1%
- Others: 6.1%

PhD. Graduates

- JSPS Research Fellow: 25.9%
- Research labs of private enterprises: 23.5%
- Universities, government agencies, public research labs, and overseas postdoctoral research fellow: 18.9%
- Others: 13.7%

- Graduated School of Pharmaceutical Sciences, The University of Tokyo (Master's Program): 33.7%
- Other advanced degrees in different schools: 21.1%
- Government agencies and private enterprises: 20.0%
- Others: 11.1%
**Undergraduate**

First-year students receive liberal arts education at the Komaba campus. There are roughly 80 first-year students at the Faculty of Pharmaceutical Sciences, and this is one of the smallest faculties at the University of Tokyo. New students form close friendships in no time after starting their first year. They attend lectures and engage in pharmaceutical training, all the while maintaining close relationships with faculty members. Lectures encompass a broad range of academic fields closely related to real life medicine, such as organic chemistry, physical chemistry, biochemistry, molecular biology, and biomedical science. Assistant professors and graduate students as teaching assistants also take part in the pharmaceutical training classes.

Second-year students, after receiving an unofficial decision on their admittance to the Faculty of Pharmaceutical Sciences in the fall, begin to attend lectures on specialized topics on Mondays, Wednesdays, and Thursdays at the Hongo campus.

In the third year, students sit in on lectures in the morning and engage in pharmaceutical training in the afternoon. Lectures become more specialized, and during training sessions students work in groups of two to four.

Fourth-year students work in the laboratory of their choice, and they begin to focus less on classes and more on their senior research project. Students are allowed to work on their research not only at the laboratories within the Faculty of Pharmaceutical Sciences, but also at the cooperating laboratories at the Graduate School of Pharmaceutical Sciences. These laboratories are at the Institute of Medical Science, the Institute of Molecular and Cellular Biosciences, and the Department of Pharmacy of the University of Tokyo Hospital.

Students beginning their enrollment after 2006 must choose either the four-year course of the Department of Pharmaceutical Sciences or the six-year course of the Department of Pharmacy following the selection of the laboratory of their choice in their fourth year. Students who choose the Department of Pharmaceutical Sciences must complete a year-long senior research project in order to complete their degree. Those who decide on the Department of Pharmacy begin to work in the laboratory of their choice while they receive laboratory training for clinical pharmacy. At the end of the fourth year, students are expected to go through the first Pharmaceutical Common Achievement Tests for clinical pharmacy. In the fifth year, students receive laboratory training for clinical pharmacy, and work in pharmaceutical science laboratories. In the sixth year, students dedicate their time to working on their senior research project until graduation.

Each laboratory and related laboratories (Institutes) of the Graduate School of Pharmaceutical Sciences and the Department of Pharmacy of the University of Tokyo Hospital conducts leading research in their specialized areas of focus. Those who become graduate students at this department join the ranks of an extremely talented and world-renowned group of researchers. A hard, but rewarding life awaits. Students at the start of their graduate studies begin their research career by attending seminars and conducting experiments in world-renowned laboratories which are equipped with state-of-the-art facilities. It is common for graduate students to present the results of their research at conferences, research meetings, and symposiums, both domestic and abroad. Furthermore, students, during the course of their studies, are expected to publish their research in internationally known top-class academic journals.

The members of the Faculty of Pharmaceutical Sciences and the Graduate School of Pharmaceutical Sciences, including faculty members, office staffers, graduate students, and undergraduate students form close-knit friendships, and this is not just because it is a relatively small department. The department hosts a slew of social events that include but are not limited to sports events, a boat race, general meetings of the University of Tokyo Pharmaceutical Association, and activities with international students and researchers. These events contribute to the growth of friendships and close bonds outside of academic life. The close bonds of the students and researchers in this department foster collaboration, and this leads to a wider spectrum of academic insights and new developments in research.
**Postgraduate**

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**Campus Social Events**

The members of the Faculty of Pharmaceutical Sciences and the Graduate School of Pharmaceutical Sciences, including faculty members, office staff, graduate students, and undergraduate students form close-knit friendships, and this is not just because it is a relatively small department. The department hosts a slew of social events that include but are not limited to sports events, a boat race, general meetings of the University of Tokyo Pharmaceutical Association, and activities with international students and researchers. These events contribute to the growth of friendships and close bonds outside of academic life. The close bonds of the students and researchers in this department foster collaboration, and this leads to a wider spectrum of academic insights and new developments in research.
Before Japan, I was in the faculty of medicine in Indonesia. I once aspired to become a physician, but I had a change of heart. Going to Japan one month after the Tohoku earthquake in 2011 was definitely a controversial idea to some. As a MEXT Scholarship student for undergraduate studies, I went despite not knowing the culture or the language, because I had a hunch that this would open the door to more international opportunities.

As I was still interested in health care but wanted to view it in a bigger scope, I chose pharmaceutical science and was assigned to the Laboratory of Pharmaceutical Regulatory Science under Prof. Ono. To my surprise, the professor, seniors and even the secretaries were very encouraging. They were there for me to discuss my research, and because of all of them, I could get published in a journal within one year of my undergraduate study. I also had a great half-year internship via my senior at a top research institute in Japan, investigating the world’s health policy for the Ministry of Labor, Health and Welfare. Even now, I am still grateful for the opportunity to know them, and I wish them all the best in their endeavors.

Besides the laboratory, the International Student Advising Room (ISAR) is doing everything to make sure you settle in well. They organize many annual events to get to know other students, provide Japanese classes, and assist you in everything from educational matters to living in Japan. With the support from the laboratory and ISAR, I believe any student will have a fruitful experience in this school, both academically and socially.

Currently, I am interested in design thinking, and pursuing my career in a private consultancy in Singapore after working in Tokyo. I want to explore idea-building and the international market before I get back to health care again. Looking back, I was glad that I went to Japan. The rigorous education, opportunities to other countries, and the international friends that I came across throughout my study are priceless. Now, I am glad that I had a change of heart.

The Graduate School of Pharmaceutical Sciences in the University of Tokyo, which attracts many students like myself who plan to make contributions to human health, is a friendly and vibrant department famous for its high academic standards, excellent atmosphere, and great environment for study and research.

In 2012, I was lucky to be enrolled in the Laboratory of Synthetic Organic Chemistry, which has ten students from different countries. We can communicate everything with each other in English fluently, and thus, we can tell that Kanai’s lab is a big international family. Under the kind, patient and professional supervision of Kanai-sensei and with the help of Japanese students and international students, I not only learned a lot about organometallic and medicinal chemistry, but also learned how to start a project and run a lab.

To help us adapt to the life in Japan, a series of unique events, including parties and educational trips, were frequently held by Kanai’s lab and the International Student Advising Room (ISAR). These events helped us better understand Japanese culture and communicate with Japanese students. All these activities made my life in Japan much more convenient and unforgettable. With the friendly and professional help from ISAR, lead by lecturer Kikuchi, I didn’t need to spend too much time dealing with trivial things in life. As a result, I could fully focus on my research and enjoy the life in Japan. What’s more, the three years I spent in Tokyo were really fantastic and enjoyable, despite my little knowledge about Japanese language. Last but not least, during my time in the University of Tokyo, I became a father as well—my son and daughter were born successively at that time. Therefore, I hope that they can also study in the University of Tokyo someday.

Due to my organometallic chemistry achievements made in the University of Tokyo, I got a professor position in Lanzhou University after being awarded a PhD degree in 2015. One year later, I successfully earned support from the national “Thousand Talents” youth program, one of the greatest honors for young scientists in my country. In the future, I want to devote all my time to the development of medical chemistry and continue to challenge the most difficult of topics, as I have done in the University of Tokyo. At the same time, since I enjoyed the research atmosphere in the University of Tokyo so much, I am exerting my utmost efforts to promote academic communication between China, Japan, and other countries. It is my dream to become a contributor to the development of both science and human society.
I joined the Department of Pharmacy (six-year program) of the Faculty of Pharmaceutical Sciences, and since graduation, I have been working as a pharmacist at the University of Tokyo Hospital’s Pharmaceutical Department.

After completing coursework at the Department of Pharmacy and passing clinical (OSCE) and written (CBT) examinations, students can spend the five months between the end of their fourth year and the summer of their fifth in hospital/pharmacy training, each lasting two-and-a-half months. Even if you do not pursue pharmacist work in the future, I think experiencing this glimpse at clinical work is both important and quite fun. My internship at the University of Tokyo Hospital allowed me to not only leverage the pharmacotherapy I learned in my university coursework; it also gave me a full overview of medical treatment that covered the entire body, including electrolytes and nutrition. The pharmacy training, held at a pharmacy near the University, was a great opportunity, giving me a real insight into the position of public-insurance compounding pharmacies in regional treatment.

In the laboratory I belonged to between my fourth and sixth year, I worked on the theme of “antidepressant migration into the fetus during pregnancy.” I devised a unique compartment model for pregnancy, connecting the mother and placenta to the fetus, and proposed a method of predicting density levels within the blood of the fetus. The fundamental pharmacokinetics I learned through this is still coming in very handy in my current work.

I say this because in on-the-field medicine, you often have to make decisions on the direction of treatment with little information to go on. Are pregnant women and newborn children included in clinical trials during the pharmaceutical development process? If you want to give a new anti-cancer drug to a patient undergoing dialysis, is a suitable dosage included in the documentation? Does data exist on interactions between every combination of drugs available in the world? The answer to all these questions is no. To make appropriate decisions in these situations where you only have limited amounts of information, you need to use the principles of pharmaceutics, starting with pharmacology and pharmacokinetics, to logically predict what may happen. At times like these, I feel that the fundamental education and logical thinking skills I learned in my years at the Faculty of Pharmaceutical Sciences help me out enormously, and I’m glad for it.

No matter which laboratory you join and which field you proceed into, I hope you will learn a great deal during your academic years with your friends, and I hope you will have a lot of fun along the way. I wish all of you great success in your life at the Faculty.

After joining the Faculty of Pharmaceutical Sciences, I conducted research at the Laboratory of Molecular Pharmacokinetics. Upon completing my doctoral course, I joined the company that I currently work for. I do not work as a researcher; instead, I am involved with the development of pharmaceutical products at the clinical phase (the phase where clinical trials are conducted and marketing applications are submitted for approval), planning the clinical development strategy/clinical study design and analyzing results. Since trials provide only a limited amount of data, it becomes necessary to think scientifically about the results obtained, considering what we can safely claim and what risks remain. What would be the most suitable dosage/regimen for people in different regions? Is it safe to prescribe to elderly patients? Is it all right for patients to take it along with other medications they’ve been taking? Those are the questions I think about as I conduct my day-to-day work.

The attraction of the Faculty of Pharmaceutical Sciences is the ability to study a wide range of fundamental and practical sciences, including organic chemistry, physical chemistry, and life science. For me as a student, with only a vague idea that I wanted to work in medical field somehow, being able to experience assorted studies in medicine and drug discovery was extremely helpful, since it allowed me to choose a research lab with a grasp of what fields I had an aptitude for. Every lab, no matter what the field, is filled with world-class professors—joining any one of them allows you to gain specialization, as well as the ability to think logically and plan/carry out a research project by yourself (as well as the ability to lead junior colleagues).

The work I am involved in right now naturally requires a broad scientific knowledge, but I feel that the abilities I gained during my time at the Faculty to carry out a project by myself and think logically about matters help me out more in my daily work.

The Faculty asks for a high level of performance and I had to deal with a lot of difficulty, but I think the abilities I gained through that experience—the ability to make it in modern society—would help me in any field I decided to pursue after graduation. Many Faculty graduates are exercising their abilities in fields outside of research, and I hope that everyone joining the Faculty avoids fixating too much on their perceived potential and remains active in a wide variety of fields.
Japanese Language Class

The Japanese Language Class provides an opportunity to learn Japanese language to international students, researchers and their spouses. It also deals with a broad range of topics on Japanese society, culture, history, etc. There are a variety of courses offered from elementary to advanced level.

International Student Advising Room

The International Student Advising Room (ISAR), established in 1994, provides a variety of services to support international students and researchers. http://www.f.u-tokyo.ac.jp/~israr/en/isar/index.html

ISAR offers:

• Advisory assistance and a counseling service
• Information for prospective international students
• Event planning
• Inter-university academic exchange program
• Information services

Lecturer M. Kikuchi
International Student Adviser

International Activities

International Training Program to Establish World Premier Research Center of the Pharmaceutical Sciences

University of Cambridge, University of Oxford, University of Bonn, LMU Munich

Academic Exchange Agreements between Universities

**USA**
The University of Texas M. D. Anderson Cancer Center

**Sweden**
The Sahlgrenska Academy, University of Göthenburg

**Germany**
Research Training Group 1873
The University of Bonn

**P.R.China**
Shenyang Pharmaceutical University

**Republic of Korea**
School of Pharmacy, Sungkyunkwan University

**Thailand**
Chulalongkorn University

**The Netherlands**
Leiden University

**Sweden**
Uppsala University
Experimental Station for Medicinal Plant Studies

Hanamigawa-ku, Chiba-shi, Chiba

The Experimental Station for Medicinal Plant Studies is located about 30 km east of the Hongo Campus. Its 6,123 m² plant specimen garden includes the medicinal plants that are considered important for the students’ education. This garden serves a variety of purposes, including maintenance of plant lineages; research on plant breeding and cultivation; collection and cultivation of medicinal plants native to Japan as well as introduced from overseas; research on medicinal plant ingredients from the standpoints of chemistry, pharmacology, biosynthesis, plant physiology, and pharmacognosy; and research on the medicinal plant cultivation and maintenance. The grounds of the Experimental Station also encompass a greenhouse, administration building, and laboratory building. At present, about 250 varieties of plants are under cultivation. Each year, 3rd-year students receive practical training in the plant specimen garden during the summer session. In 1982, the laboratory for medicinal plant studies was set up within the building in Hongo Campus and have continued research until now.

The University Museum, The University of Tokyo (Hongo Campus) houses a Pharmaceutical Sciences Division on its first floor, where a large number of specimens – mainly crude drugs and medicinal plants – are stored and managed. In October 2004, the first rooftop herb garden, with an area of approximately 100 m², was created on the rooftop of the auditorium of Pharmaceutical Sciences Research Building for enabling the students to come into close contact with medicinal plants. Several dozen varieties of medicinal plants are cultivated in light soil with a depth of about 60 cm, equipped with an automatic irrigation system.

Pharmaceutical Sciences Library

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(As of March, 2016)
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Facilities

Hongo Campus

Pharmaceutical Sciences Building

Graduate School of Pharmaceutical Sciences
Faculty of Pharmaceutical Sciences

Pharmaceutical Sciences Research Building
Left panel: Confocal image of NIH 3T3 cells stained with antibodies to tubulin (red), stabilized microtubule (green) and a DNA staining dye (blue). Note that microtubules are stabilized at the leading edge of migrating cells.

Right panel: Confocal image of an NIH 3T3 cell expressing fluorescence-labeled tubulin (red) and a tubulin binding protein, EB1 (green). EB1 is localized at the tip of microtubules.