CANCER RESEARCH INSTITUTE
# 金沢大学がん進展制御研究所概要目次

Cancer Research Institute Contents

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はじめに

Kanazawa University Cancer Research Institute was founded as the only cancer research institute of the Ministry of Education in 1967. Cancer Research Institute started with 8 departments including clinical section, and was later expanded to 10 departments. In 1997, the former departmental structure was replaced with a super-department structure and Center for the Development of Molecular-targeted Drugs was established. Since its establishment, our institute has been producing epoch-making achievements such as the discovery of proteinases, elucidation of function of chemokines, apoptosis, and angiogenic factors, and development of novel anti-cancer drugs.

Recently, in cancer research, more endeavors are required to translate the achievements in basic research to clinics. Thus, with the aim of overcoming unsolved clinical situations in cancer, such as metastasis and drug resistance, Cancer Research Institute was reorganized to establish 2 fundamental departments and 2 centers in 2006. In April 2010, when basic research groups moved to a new building in Kakuma Campus, we launched a novel research project, “Cell Sociology of Cancer”, where we are trying to elucidate cancer stem cell and tumor microenvironment, in order to conquer metastasis and drug resistance. Concurrently, with the intention of putting forward this project, our institute has been reorganized to establish 4 programs; “Cancer and Stem Cell Research Program”, “Cancer Microenvironment Research Program”, “Cancer Molecular Target Exploration Program”, and “Cancer Therapeutics Development Program”.

In order to fulfill Kanazawa University’s aim to serve as the stronghold of intellect in East Asia, our institute implemented research collaboration program since 2008. In July 2010, our institute was authorized by the Ministry of Education, Culture, Sports, Science and Technology of the Japanese government as the Joint Usage/Research Center on Metastasis and Drug Resistance and started the Joint Usage/Research Center Program in April 2011.

In Cancer Research Institute, researchers from a variety of fields including natural science, engineering, and clinical medicine have assembled to establish a cutting-edge research locus, to prevail over metastasis and drug resistance. With the authorization as the Joint Usage/Research Center, all members in the institute are endeavoring to widen collaboration with researchers in a wide variety of fields, to establish an international center of excellence on metastasis and drug resistance and to eventually promote research for conquering these conditions.

With the publication of the 2012 Kanazawa University Cancer Research Institute Outline, I would like to request your continuous support and understanding.

Naofumi MUKAIDA, M.D., Ph.D.
Director, Cancer Research Institute
### 結核研究所  
**Tuberculosis Research Institute**

- **1940.12.6**
  金沢医科大学に「結核の化学療法に関する研究」のため結核研究施設が設置された。
  
- **1942.3.20**
  金沢医科大学附属結核研究所となり「結核の予防及び治療に関する学理並びにその応用研究」を目的とする、薬理薬剤、細菌免疫及び化学の3研究部門に増設された。

- **1947.7.3**
  金沢市泉本町に診療部門が増設された。

- **1949.5.31**
  金沢大学医学部の結核研究所となった。

- **1963.3.18**
  薬理薬剤部門が薬理部門に、診療部門が臨床部門に研究部門名が変更された。

- **1963.4.1**
  病態生理部門が増設された。

- **1964.4.1**
  臨床部門の診療施設が結核研究所附属病院に改称された。

- **1967.3.**
  臨床部門及び附属病院が金沢市泉町に新築移転された。

### 医学部附属発癌研究施設  
**Cancer Research Facility, School of Medicine**

- **1961.4.1**
  医学部に「癌の基礎生物学的研究」のため附属発癌研究施設が新設され、研究部門は生化学部門が設置された。

- **1964.4.1**
  細胞学部門が増設された。

- **1966.4.5**
  分子免疫部門が増設された。

### がん研究所  
**Cancer Research Institute**

- **1967.6.1**
  「がんに関する学理及びその応用の研究」を目的に、結核研究所と医学部附属発癌研究施設が統合され金沢大学がん研究所となり、分子、ウイルス、細胞、免疫、免疫、病態生理、薬理、化学療法及び臨床の8研究部門が設置された。

- **1968.6.1**
  生物物理学部門が増設された。

- **1969.4.3**
  基礎研究所の研究棟が金沢市宝町に新築移転された。

- **1977.4.18**
  外科部門が増設され、臨床部門が内科部門に研究部門名が変更された。

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*tuberculosis research facility was established in school of medicine for the study of chemotherapy of tuberculosis.*

*tuberculosis research institute was established by expanding the facility. three departments, department of pharmacetics, department of microbial immunology and department of chemistry, opened for `the basic and applied research for the prevention and treatment of tuberculosis`.*

*department of medical examination and treatment opened in izumi-honmachi, kanazawa.*

*the tuberculosis research institute was attached kanazawa university.*

*two departments were renamed; department of pharmacetics to department of pharmacology, department of medical examination and treatment to department of clinic.*

*clinical facility of the department of clinic renamed as tuberculosis research institute hospital.*

*the department of clinic and the tuberculosis research institute hospital moved to yonezumi-machi, kanazawa.*

*cancer research facility was established in school of medicine for `the basic biological study of cancer`. department of biochemistry opened.*

*department of virology opened.*

*department of molecular immunology opened.*

*cancer research institute was established combining the tuberculosis research institute and the cancer research facility. the institute started with eight departments; molecular biology, virology, molecular immunology, immunology, pathophysiology, pharmacology, experimental therapeutics and clinic.*

*tuberculosis research institute hospital was renamed as cancer research institute hospital.*

*department of biophysics opened.*

*a new building for basic research departments moved to takara-machi, kanazawa.*

*department of surgery opened. department of clinic was renamed as department of internal medicine.*
1983. 3.30
附属病院に管理棟（軽量鉄骨）及び渡り廊下が築かれた。
An office building was built for the Cancer Research Institute Hospital.

1997. 4.1
10部門を3大部門（14研究分野）1センターに改組し、腫瘍分子科学、細胞制御、腫瘍制御の3大部門及び分子標的薬剤開発センターを置く。
Ten departments were reorganized to be consisted of three departments (14 divisions) and one center. Department of Molecular Oncology, Department of Molecular and Cellular Biology, Department of Basic and Clinical Oncology and Center for the Development of Molecular Target Drugs opened.

2001. 4.1
附属病院は医学部附属病院と統合された。
The Hospital was merged with the University Hospital.

2006. 4.1
3大部門14研究分野1センターを2大部門2センターに改組し、がん分子細胞制御研究部門。がん補償制御研究部門の2大部門及びがん幹細胞研究センター。分子標的がん診療研究開発センターを置く。
Three departments (14 divisions) and one center were reorganized to be consisted of two departments and two centers. Department of Molecular Cancer Cell Biology, Department of Cancer Biomedicine, Center for Cancer and Stem Cell Research and Molecular and Cellular Targeting Translational Oncology Center opened.

2010. 3.
基礎研究系の研究棟が金沢市角間町に新築移転された。
A new building for basic research departments moved to Kakuma-machi, Kanazawa.

2010. 4.1
2大部門2センターを4プログラムに改組し、がん幹細胞研究プログラム。がん微小環境研究プログラム。がん分子標的探索プログラム及びがん分子標的療法開発プログラムを置く。
Two departments and two centers were reorganized to be consisted of four programs. Cancer and Stem Cell Research Program, Cancer Microenvironment Research Program, Cancer Molecular Target Exploration Program and Cancer Therapeutics Development Program opened.

2010. 7.
「がんの転移・薬剤耐性に関わる先端的共同研究拠点」として文部科学省より認定された。
Cancer Research Institute was authorized by the Ministry of Education, Culture, Sports, Science and Technology of the Japanese Government as the Joint Usage/Research Center on Metastasis and Drug Resistance.

■がん進展制御研究所 Cancer Research Institute

2011. 4.1
がん研究所は、がん進展制御研究所に改称された。共同利用・共同研究拠点として活動を開始した。
The name of Cancer Research Institute in Japanese was changed. The Joint Usage/Research Center Program started.
## 歴代所長

### Successive Directors

<table>
<thead>
<tr>
<th>年度</th>
<th>姓名</th>
<th>取締研究所長</th>
</tr>
</thead>
<tbody>
<tr>
<td>1942.4.8-1954.3.31</td>
<td>石坂伸吉</td>
<td>ISHIHARA, Shinji (Director of Tuberculosis Research Institute)</td>
</tr>
<tr>
<td>1954.4.1-1954.6.30</td>
<td>戸田正三</td>
<td>TADA, Shozo (Director of Tuberculosis Research Institute)</td>
</tr>
<tr>
<td>1954.7.1-1958.6.30</td>
<td>周本健一郎</td>
<td>OKAMOTO, Hajime (Director of Tuberculosis Research Institute)</td>
</tr>
<tr>
<td>1958.7.1-1961.6.30</td>
<td>養下正道</td>
<td>KAKISHITA, Masanori (Director of Tuberculosis Research Institute)</td>
</tr>
<tr>
<td>1961.7.1-1962.6.30</td>
<td>藤本信一郎</td>
<td>SAITO, Koshiro (Director of Tuberculosis Research Institute)</td>
</tr>
<tr>
<td>1962.7.1-1966.6.30</td>
<td>石崎有信</td>
<td>ISHIHARA, Akinobu (Director of Tuberculosis Research Institute)</td>
</tr>
<tr>
<td>1966.7.1-1967.5.31</td>
<td>伊藤亮</td>
<td>ITOU, Ryo (Director of Cancer Research Institute)</td>
</tr>
<tr>
<td>1967.6.1-1967.8.31</td>
<td>周本健一郎</td>
<td>OKAMOTO, Hajime (Director of Cancer Research Institute)</td>
</tr>
<tr>
<td>1968.1.1-1971.3.31</td>
<td>石川正二郎</td>
<td>KOSHIKAWA, Toshiharu (Director of Cancer Research Institute)</td>
</tr>
<tr>
<td>1971.4.1-1975.1.30</td>
<td>伊藤亮</td>
<td>ITOU, Ryo (Director of Cancer Research Institute)</td>
</tr>
<tr>
<td>1975.1.31-1978.4.1</td>
<td>石川正二郎</td>
<td>KOSHIKAWA, Toshiharu (Director of Cancer Research Institute)</td>
</tr>
<tr>
<td>1978.4.2-1982.4.1</td>
<td>横村三郎</td>
<td>KUMAZAWA, Saburo (Director of Cancer Research Institute)</td>
</tr>
<tr>
<td>1982.4.2-1984.4.1</td>
<td>沼田正一郎</td>
<td>KURATA, Yorichi (Director of Cancer Research Institute)</td>
</tr>
<tr>
<td>1984.4.2-1986.3.31</td>
<td>渡田真治</td>
<td>HATANO, Motochi (Director of Cancer Research Institute)</td>
</tr>
<tr>
<td>1986.4.1-1990.3.30</td>
<td>石田哲行</td>
<td>MIGITA, Shunzuke (Director of Cancer Research Institute)</td>
</tr>
<tr>
<td>1989.4.1-1993.3.31</td>
<td>岡村正典</td>
<td>KAMEYAMA, Tadahito (Director of Cancer Research Institute)</td>
</tr>
<tr>
<td>1993.4.1-1997.3.31</td>
<td>高橋守信</td>
<td>TAKAHASHI, Morinobu (Director of Cancer Research Institute)</td>
</tr>
<tr>
<td>1997.4.1-2001.3.31</td>
<td>磐伊正義</td>
<td>MAUZEN, Masayoshi (Director of Cancer Research Institute)</td>
</tr>
<tr>
<td>2001.4.1-2005.3.31</td>
<td>山本健一</td>
<td>YAMAOKA, Ken-ichi (Director of Cancer Research Institute)</td>
</tr>
<tr>
<td>2005.4.1-2009.3.31</td>
<td>佐藤博</td>
<td>SATO, Hiroshi (Director of Cancer Research Institute)</td>
</tr>
<tr>
<td>2009.4.1-2011.3.31</td>
<td>田村直史</td>
<td>MUKAIDA, Naofumi (Director of Cancer Research Institute)</td>
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### Successive Directors of the Institute Hospital

<table>
<thead>
<tr>
<th>年度</th>
<th>姓名</th>
<th>取締研究所長</th>
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<tbody>
<tr>
<td>1964.4.1-1965.7.31</td>
<td>水上哲次</td>
<td>MIZUMOTO, Tatsuki (Director of Tuberculosis Research Institute)</td>
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<tr>
<td>1965.8.1-1966.2.1</td>
<td>石崎有信</td>
<td>ISHIHARA, Akinobu (Director of Tuberculosis Research Institute)</td>
</tr>
<tr>
<td>1966.2.1-1967.6.1</td>
<td>岡本孝</td>
<td>KURAKANE, Kyuichi (Director of Tuberculosis Research Institute)</td>
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<tr>
<td>1967.6.1-1982.4.20</td>
<td>岡本孝</td>
<td>KURAKANE, Kyuichi (Director of Cancer Research Institute)</td>
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<td>1982.4.20-1983.1.31</td>
<td>磐伊正義</td>
<td>MAUZEN, Masayoshi (Director of Cancer Research Institute)</td>
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<tr>
<td>1983.2.1-1991.1.31</td>
<td>磐伊正義</td>
<td>MAUZEN, Masayoshi (Director of Cancer Research Institute)</td>
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<tr>
<td>1991.2.1-1993.1.31</td>
<td>坂口香織</td>
<td>SAWABU, Norito (Director of Cancer Research Institute)</td>
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<tr>
<td>1993.2.1-1997.1.31</td>
<td>坂口香織</td>
<td>SAWABU, Norito (Director of Cancer Research Institute)</td>
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<td>1997.2.1-2000.1.31</td>
<td>坂口香織</td>
<td>SAWABU, Norito (Director of Cancer Research Institute)</td>
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### 附設研究センター

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<tr>
<th>研究センター</th>
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<tr>
<td>2006.4.1-2009.3.31</td>
<td>向田直史</td>
<td>MUKAIDA, Naofumi (Director of Cancer Research Institute)</td>
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<tr>
<td>2009.4.1-2010.3.31</td>
<td>坂口香織</td>
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### 名誉教授

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<tr>
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<tr>
<td>石野光男</td>
<td>TAKAHASHI, Morinobu (Director of Cancer Research Institute)</td>
</tr>
<tr>
<td>勝利</td>
<td>MINAMOTO, Toshiharu (Director of Cancer Research Institute)</td>
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## 附設分子標的がん医療研究開発センター

### Molecular and Cellular Targeting Translational Oncology Center

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<th>年度</th>
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<tr>
<td>2006.4.1-2010.3.31</td>
<td>塚之木茂</td>
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組織
Organization

がん従来制御
研究所
Cancer Research Institute

所長
(Director)

プログラム
Program

がん幹細胞研究プログラム
Cancer and Stem Cell Research Program

がん微小環境研究プログラム
Cancer Microenvironment Research Program

がん分子標的探索プログラム
Cancer Molecular Target Exploration Program

がん分子標的医薬開発プログラム
Cancer Therapeutics Development Program

中央実験施設
Central Research Resource Branch

組織
Organization

がん治療制御
研究所
Cancer Research Institute

所長
(Director)

プログラム
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Cancer and Stem Cell Research Program

がん微小環境研究プログラム
Cancer Microenvironment Research Program

がん分子標的探索プログラム
Cancer Molecular Target Exploration Program

がん分子標的医薬開発プログラム
Cancer Therapeutics Development Program

中央実験施設
Central Research Resource Branch

職員数
Number of Staff

平成24年7月1日現在

教授
Professors
准教授
Associate Professors
講師
Lecturers
助教
Assistant Professors
計
Total
特任教授
Professors
合計
Grand Total

12
7
0
20
39
2
41

会計
Accounting

一般事務
General Affairs

研究協力
Research Cooperative Affairs

中央施設
Central Facilities

共同利用施設
Central Facilities

事務部長
Director
課長
Chief
副課長
Vice-Chief
がん幹細胞研究プログラム

Cancer and Stem Cell Research Program

■ 遺伝子・染色体構築研究分野 Division of Molecular Genetics

教授 平尾 敦
Professor HIRAO, Atsushi

助教 田所 優子
Assistant Professor TADOKORO, Yuko

助教 星野 孝之
Assistant Professor HOSHII, Takayuki

助教 大田 久美子
Assistant Professor OHTA, Kumiko

■ 腫瘤遺伝学研究分野 Division of Genetics

教授 大島 正伸
Professor GSHIMA, Masanobu

助教 大島 淑子
Assistant Professor GSHIMA, Hiroko

助教 石川 智夫
Assistant Professor ISHIKAWA, Tomo-o

助手 劉井 国子
Assistant NAOI, Kuniko
■ 腫瘍分子生物学研究分野  Division of Oncology and Molecular Biology

教授 高橋 智聡  
Professor TAKAHASHI, Chiaki

助教 木戸 歌治  
Assistant Professor KIDO, Yukiharu

助教 SHAMMA AWAD  
Assistant Professor

■ がん幹細胞探索プロジェクト  Exploratory Project on Cancer Stem Cells

准教授 仲 一仁  
Associate Professor NAKA, Kazuhiro
Stem cells are defined as cells that have the ability to perpetuate through self-renewal, and develop into mature cells of a particular tissue through differentiation. Appropriate controls of stem cell functions are critical for maintaining tissue homeostasis. We have revealed that genes that are involved in longevity, including FOXO and mTOR pathways, contribute to the maintenance of stem cell self-renewal capacity. Thus, signaling pathways for control of intracellular metabolism may play a critical role in stem cell regulation.

Recent evidence has demonstrated that in tumors only a minority of cancer cells has the capacity to proliferate extensively and form new tumors. These tumor-initiating cells, which are called cancer stem cells, are thought as a novel target for cancer therapy. The investigation of distinct and parallel roles in normal stem cells and cancer stem cells will contribute to the design of cancer therapy without damaging normal tissues.
Aim and Projects on going

Accumulating evidence has indicated that cooperation of oncogenic mutations and host reactions are responsible for tumorigenesis. To elucidate the genetic mechanisms of tumorigenesis, we constructed mouse models and examined histopathogenesis of gastric tumors.

1) Wnt signaling and PGE2 pathway are important for gastric tumorigenesis. We constructed mouse model, in which both Wnt and PGE2 pathways are activated in the gastric mucosa, and found that transgenic mice develop gastric cancer (Oshima H, et al, Gastroenterology, 2006).

2) Infection-associated inflammation plays a role in gastric tumorigenesis. Using in vitro and in vivo systems, we have found that TNF-α from activated macrophages promotes Wnt signaling in surrounding gastric cancer cells, which further contribute to tumorigenesis. Wnt promotion may be one of important mechanisms of inflammation in gastric tumorigenesis (Oguma K et al, EMBO J, 2008).

3) Using primary cultured cells from mouse gastric cancer, we have shown that tumor cells activate bone marrow-derived cells to be myofibroblasts that play a role in tumor angiogenesis (Guo X, et al, JBC, 2008).

4) Sox17 represses Wnt signaling and downregulated in gastric and colon cancer, suggesting that Sox17 is a tumor suppressor. Importantly, we found that Sox17 expression is strongly induced at early stage of tumorigenesis. It is thus possible that Sox17 plays a role in tumor development (Du YC, et al, Gastroenterology, 2009).
ヒトがんにおける臨床的エビデンスが豊富なかがん遺伝子・がん抑制遺伝子を変異させたマウス・細胞を中心に、シンプルで分子生物学的・遺伝学的な解析をしたがんのin vivo・in vitroがんモデル系を組み立て、発がん・転移・薬剤耐性・かん幹細胞を克服する突起2を新たなパラメータを提案する。具体的な取り組みは以下。

1) 数多くの増殖シグナルのアダプター分子となるRB蛋白質(pRB)の不活化化は、多くのがんがんの悪性進展過程において観察される。pRBは、従来知られた細胞周期や細胞分化の制御だけではなく、細胞老化、DNA損傷応答、DNA修復、さらには核分裂、ミトコンドリア機能あるいはサイトカイン分泌の制御作用によっても腫瘍発症や悪性度を規定することを見出していた。

2) かん細胞は正常細胞から派生するが、原因に異なる。それは、好気的糖酵解、熟虫合成の元々であり、前者をp53,後者をpRBが制御している。その他、RanやMyc等のかがん遺伝子も代謝調節に関与する。様々なかがんシグナルにより誘導されるメタボリック・リプログラミングが、かん細胞の悪性化に与える影響とその機構を探索する。

3) 悪性進展機構の深い理解に基づき、かん幹細胞が示すと想定される様々な挙動の中核の一部を安定的に表現するin vitroがん幹細胞モデル系を組み立て、かん幹細胞の発現に関与する遺伝子の探索および新しいかがん標的薬の開発に応用する。

図1
RB蛋白質に集まる様々なシグナルとRB蛋白質から発せられる様々なシグナル。RB蛋白質の多様な働きを説明する。E2Fファミリーが最も有名な領域であるが、その他のにも、多様な機能が予測される。

図2
がん抑制遺伝子の複合的変異によって誘導される幹細胞様のかがん細胞集団の強大な増殖能力。

We innovate **in vivo** and **in vitro** cancer model systems that can be readily analyzed by genetic and molecular biology techniques. This aims to find pathways critical for carcinogenesis, metastasis, drug resistance, and stem cell-like behaviors in cancer cells. Below are ongoing projects in our laboratory.

1) The RB tumor suppressor gene product has been implicated in control of cell cycle and terminal differentiation. However, we propose pRB plays many more roles during tumor progression beyond such functions. We focus on pRB functions in chromatin instability, DNA damage response, cellular senescence, mevalonate pathway, lipid metabolism, mitochondrial function, chromatin remodeling and stem cell-like behaviors in cancer cells.

2) Analysis of oncogenic signals that induce malignant behaviors in cancer cells through metabolic reprogramming.

3) Development of **in vivo** & **in vitro** cancer stem cell models in an aim to develop novel drugs or chemicals that specifically target hypothetical cancer stem cells.
がん幹細胞探索プロジェクト

Exploratory Project on Cancer Stem Cells

近年、一部のがんで、がん細胞を生み出すとされる「がん幹細胞」の存在が報告されており、がん剤治療後の根治を欠いたがん幹細胞は再発を引き起こす原因になると考えられている。例えば、慢性骨髄性白血病(CML)患者の治療にはメチル転化メタセルなどのチロシンキナーゼ阻害薬(TKI)が用いられているが、TKI抵抗性のCML幹細胞の残存はCMLの再発の原因となる。

私たちはCMLのマウスモデルを用いて、CML幹細胞を増殖し、CML幹細胞のTKI抵抗性にフォーカスした転写因子FOXOが重要な役割を担っていることを見出した(図1)。また、このFOXOはがん微小環境細胞が作り出すTGF-βによって活性化されており、CML幹細胞を移植したマウスにTGF-β阻害薬を投与するとTKI抵抗性のCML幹細胞を抑制できることを見出した。従って、TGF-β-FOXOシグナルはTKI抵抗性のCML幹細胞の治療薬を開発するための重要なターゲットであると考えられる(図2)。

現在、TGF-β-FOXOシグナルによるCML幹細胞のTKI抵抗性メカニズムの解明と、このメカニズムをターゲットにする新しいCML治療薬の開発を目指した研究を実施している。

図1 ■ CML幹細胞のTKI抵抗性制御におけるフォーカス転写因子FOXOの役割

野生型(Foxo3a+/+)、およびFoxo3aマックスアウト(Foxo3a+)マウス由来のCML幹細胞を移植したマウスにチロシンキナーゼ阻害薬(TKI)の投与を行った。その結果、CML幹細胞におけるFOXO遺伝子の欠損はTKI投与後のCMLの再発を軽減することが明らかとなった。従って、FOXOはCML幹細胞のTKI抵抗性の制御に必須の役割を担う。

Fig.1 ■ FOXO plays an essential role for the tyrosine kinase inhibitor (TKI) resistance of CML stem cells

Mice transplanted with wild-type (Foxo3a+/+) or Foxo3a-deficient (Foxo3a−/−) CML stem cells received TKI. FOXO deficiency promoted the survival of CML-affected mice after administration of TKI, indicating that FOXO is responsible for the maintenance of TKI-resistant CML stem cells.

図2 ■ TGF-β-FOXOシグナルによるCML幹細胞のTKI抵抗性制御メカニズム

CML幹細胞(CML stem cells)は分化したCML細胞(CML cells)の供給源となる。CML幹細胞はTKIに対して抵抗性を示し、根絃を欠いたCML幹細胞はCMLの再発の原因となる。FOXOはCML幹細胞のTKI抵抗性の制御に関与している。また、CML幹細胞のFOXOはがん幹細胞の選択出るTGF-βによって活性化される。従って、TGF-β-FOXOシグナルはTKI抵抗性のCML幹細胞を治療するための重要なターゲットとなる。

Fig.2 ■ TGF-β-FOXO signaling pathway maintains TKI-resistant CML stem cells

We have recently reported that FOXO is crucial for the TKI resistance of CML stem cells. Furthermore, TGF-β originate from the microenvironment regulates FOXO activity in CML stem cells. The goal of our research is development of novel agents that can specifically suppress the effects of these TGF-β-FOXO signaling pathway, and thereby provide a novel avenue for curative CML patient therapy.
がん微小環境研究プログラム
Cancer Microenvironment Research Program

■ 細胞機能統御研究分野　Division of Molecular Virology and Oncology

教授 佐藤 博
Professor SATO, Hiroshi

准教授 滝野 隆久
Associate Professor TAKINO, Takahisa

■ 分子生体応答研究分野　Division of Molecular Bioregulation

教授 向田 喜史
Professor MUKAIDA, Naofumi

助教 馬場 智久
Assistant Professor BABA, Tomohisa
■ 免疫炎症制御研究分野 Division of Immunology and Molecular Biology

教授 須田 貴司
Professor SUDA, Takashi

助教 今村 隆
Assistant Professor IMAMURA, Ryu

助教 木下 健
Assistant Professor KINOSHITA, Takeshi

■ 腫瘍動態制御研究分野 Division of Tumor Dynamics and Regulation

教授 松本 邦夫
Professor MATSUMOTO, Kunio

助教 中村 隆弘
Assistant Professor NAKAMURA, Takahiro

助教 酒井 克也
Assistant Professor SAKAI, Katsuya
Aim and Projects on going

Accumulation of mutation in oncogenes and tumor suppressor genes in normal cells results in malignant tumors. Malignant tumors invade into tissues and finally metastasize to distant organs. The goal of our project is to elucidate the molecular mechanism of tumor metastasis and develop diagnostic and therapeutic application.

Tumor invasion into tissue requires degradation of tissue basement membrane. We discovered a protease which is the key enzyme for tumor metastasis, and named it as MT1-MMP (Nature, 1994). Accumulating evidences indicate that MT1-MMP plays important roles in not only tumor invasion but also regulation of tumor growth and migration.

Fig. 1 Induction of MT1-MMP and Invasive Growth by Oncogenic Transformation of Normal Epithelial Cells

Normal epithelial MDCK cells were transformed with oncogene (erbB2), and showed tumor phenotype including MT1-MMP expression. Normal cells grow to form cysts in collagen gel, but transformed cells which express MT1-MMP show invasive growth. Tumor invasive growth is suppressed by the addition of MMP inhibitor BB94. Normal MDCK cells form branching tubules upon addition of HGF, which is also suppressed by BB94.

Fig. 2 Cell Migration and MT1-MMP

HT1080 cells were cultured on collagen, which express MT1-MMP, and were stained for paxillin to visualize focal adhesion and actin. Addition of MT1-MMP inhibitor BB94 altered the localization of focal adhesion, reduced cell polarity and suppressed cell migration. MT1-MMP enhances motility signal by stimulating turnover of focal adhesion.
分子生体応答研究分野

Aims, Ongoing Projects, and Recent Achievements
Inflammatory responses occur upon tissue injuries, to reduce tissue damage. If inflammatory responses are exaggerated and prolonged as observed in chronic infection with Helicobacter pylori, tissue injuries continue, leading sometimes to carcinogenesis.

By interacting with tumor cells, stroma cells and leukocytes can produce various bioactive substances including chemokines. The produced molecules can affect tumor progression and metastasis. We are elucidating the interaction between tumor cells and stroma cells and obtained the following results recently.

1) By using mice deficient in chemokine-related genes, we are showing that chemokines can contribute to tumor development and progression by exerting various activities.

2) We revealed that the expression of a serine/threonine kinase, Pim-3, was aberrantly enhanced in malignant lesions of liver and pancreas. Moreover, aberrantly expressed Pim-3 can inactivate a proapoptotic molecule, Bad by phosphorylating its serine residue, and eventually prevent apoptosis of tumor cells. Thus, Pim-3 may be a good molecular target for cancer treatment.
Each cell composing our body has an ability to kill itself when necessary. Apoptosis is a common type of such functional and active cell death. To prevent oncogenesis, cells often die by apoptosis when their genes were severely damaged.

On the other hand, we have demonstrated that a neutralizing antibody against Fas ligand (FasL), an apoptosis-inducing protein, has therapeutic potential in animal models of inflammatory diseases including hepatitis. Furthermore, using this antibody, we successfully prevented hepatic cancer development in an animal model of chronic hepatitis. Currently, we are exploring the signal transduction pathway of FasL, which is a potential target of drugs therapeutic for inflammatory diseases and/or preventive for cancer associating with chronic inflammation.

Recent studies have revealed that besides FasL, many other proteins have roles in both apoptosis and inflammation. We are exploring the function of such proteins, which could be important players in biodefense and cancer.

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Recently studies have revealed that besides FasL, many other proteins have roles in both apoptosis and inflammation. We are exploring the function of such proteins, which could be important players in biodefense and cancer.
細胞増殖因子は極微量ながら細胞の増殖・分化や細胞死、さらに逃走や3-D形態形成など多彩な細胞機能を調節するタンパク質である。HGF（hepatocyte growth factor:肝細胞増殖因子）は、当初、肝細胞の増殖促進を指標として発見された増殖因子であり、Metチロシンキナーゼを受容体として生理活性を発揮する。HGFは上皮間質相互作用を介した器官の形態形成、成長においては肝臓をはじめとする組織・臓器の再生を担う一方、かん細胞のダイナミックな姿態、すなわち浸調・転移に関与している。私達の研究室ではHGFとMet受容体を中心として組織再生（肝再生）や薬剤耐性の獲得におけるHGF-Met系の意義、HGF-Met障害分子の創製と制御の基礎研究などを行っている。かんは“never healing wound (傷が治まらないような傷)”と捉えられる。多くのかんはダイナミックな組織の修復・再生を担う生物学的仕組みを巧みに使って勢力拡大・成長や浸調・転移、薬剤耐性（抗性）を起こす。私達は生化学・分子生物学を基盤として、HGF-Met系を分子標的とするかんの研究や再生制御の研究など原創的な研究成果を発表したいと考えている。

Hepatocyte growth factor (HGF) was originally discovered as a mitogenic protein for mature hepatocytes. HGF exerts various biological activities, including cell proliferation, 3-D morphogenesis, migration, and anti-apoptosis in diverse biological processes. The receptor for HGF is Met tyrosine kinase. HGF plays critical roles in dynamic morphogenesis and regeneration of various tissues such as the liver. In cancer tissues, however, aberrant activation of the Met/HGF receptor is tightly associated with malignant progression of cancer, i.e., 3-D invasion, metastasis, angiogenesis, and drug resistance. Thus HGF-Met system is emerging hot target in the molecular targeted therapy of cancer. Our research projects include 1) regulation of tumor invasion-metastasis via HGF-Met pathway, 2) aberrant Met activation and drug resistance in cancer cells, 3) discovery of HGF-Met inhibitory molecules (NK4 and small synthetic) and anti-cancer approach with HGF-Met inhibitors, and 4) significance of suppressive mechanisms for the HGF-dependent Met activation in 3-D epithelial morphogenesis and tissue regeneration. HGF-Met system makes a way for dynamic 3-D reconstruction of tissues via epithelial-mesenchymal interactions for regeneration of wounded tissues, whereas it is utilized for acquisition of malignancy of cancers. The similar that "cancer is never-healing wound" seems pertinent from the aspect of HGF-Met.

図1 形態形成やがん浸調・転移におけるHGF
HGFはMetチロシンキナーゼを受容体とし、正常組織の上皮3-D形態形成や組織再生を担う一方、かん組織においては肝細胞の3-D浸調や薬剤耐性を促す。HGF-Met系受容体は再生制御をつながる一方、HGF-Met系障害は転移・薬剤耐性を解薫するがん治療法開発につながる。

図2 3-D形態形成とHGF-Met関連分子による浸調阻止
HGFは乳頭腫や胃腺腫を含む上皮細胞の3-D形態形成を誘導する上、HGFは細胞の形態のは3-D positionによって異なる、3-D position依存的Met活性性の仕組みが形態形成や浸調の仕組みの解明につながる。一方、HGF-Met系に対する薬剤の関連分子はがん細胞の3-D浸調を抑制する（下）。HGF-Met系の抗癌性分子はがん転移・薬剤耐性を抑制することを示される。私達はHGF-Met系関連分子の研究も進めている。
がん分子標的探索プログラム
Cancer Molecular Target Exploration Program

■ ゲノム分子病態研究分野 Division of Molecular Pathology

教授 山本 健一
Professor YAMAMOTO, Ken-ichi

助教 林 嘉之
Assistant Professor HAYASHI, Naoyuki

助教 小林 昌彦
Assistant Professor KOBAYASHI, Masahiko

■ シグナル伝達研究分野 Division of Molecular Cell Signaling

教授 喜岡 克次
Professor YOSHIOKA, Katsuji

助教 佐藤 時香
Assistant Professor SATO, Tokiharu
■腫瘍制御研究分野 Division of Translational and Clinical Oncology

教授 源 利成
Professor
MINAMOTO, Toshinari

准教授 川上 和之
Associate Professor
KAWAKAMI, Kazuyuki

■機能ゲノミクス研究分野 Division of Functional Genomics

教授 鈴木 健之
Professor
SUZUKI, Takeshi

助教 石村 貴彦
Assistant Professor
ISHIMURA, Akihiko
DNA damage is a constant threat to eukaryotic cells and defective response to this threat increases genetic instability, ultimately leading to cancer. The goal of our research is to clarify how cells recognize DNA damage and transduce signals to cell cycle checkpoint control, DNA repair and apoptosis machineries. To achieve this goal, we are currently studying the activation and functions of ATM (a gene mutated in ataxia telangiectasia) family in cellular response to DNA damage, using knockout cells. We are also studying how c-Abl family, BRCA1 and Chk2 are activated and what roles these factors play in the response.
Abnormal activation of intracellular signaling pathways often leads to tumors. The goal of our project is to elucidate the functions of MAP kinase (MAPK) cascades in vivo, which are major intracellular signaling pathways, and the molecular mechanisms of how the specificity of MAPK cascades is maintained.
Research Direction and Activities

The mission of the division centers on laboratory and clinical research to develop the novel strategies and modalities for diagnosis and treatment of cancer in the gastrointestinal and respiratory tracts. Research projects are based on molecular and cellular characteristics of individual tumor types that are relevant to metastatic potential, recurrence and outcome. Our current efforts are focused on:

1. Molecular mechanism underlying oncogenic signaling networks
   (1) Deregulated Wnt/β-catenin signaling
   (2) Glycogen synthase kinase 3β (GSK3β)-mediated signaling

2. Development of tailored chemotherapy by pharmacogenetics

3. Translational research of DNA methylation markers

4. Establishment of tissue material resources of human gastrointestinal cancer

We are intending to translate as much the achievements created from these studies as possible to the fields responsible for diagnosis and treatment of cancer patients in clinical setting.

Glycogen synthase kinase 3β (GSK3β) supports and promotes tumor cells' survival and proliferation, and protects them from apoptosis in cancers developed in the major digestive organs, the results warrant proposing this kinase as a novel target in cancer treatment (PCT/JP 2006/300160).

RNA trans-factor CRD-BP is a previously unrecognized transcription target of β-catenin/Tcf complex, and stabilizes mRNA of β-TrCP (β-transducin repeats-containing protein), NF-κB and c-Myc. CRD-BP is a novel cancer target that integrates multiple oncogenic signaling pathways.

Thymidylate synthase (TS) is a target of fluoropyrimidines including 5-FU. TS has unique gene polymorphisms (VNTR and SNP) in the 5'-UTR. Frequent LOH has been found in TS locus. The polymorphisms and LOH status are linked with TS gene expression and can be of clinical use for tailored chemotherapy.

Both promoter hypermethylation and global hypomethylation occur simultaneously in cancer. The profile of the DNA methylation is characteristic as molecular signature in individual cancer, linked with patients' outcome. Tailored medicine (prevention, diagnosis, and therapy) can be developed using the methylation markers.
A detailed knowledge of the genes and signaling pathways mutated in cancer will be required to develop the novel target-based cancer therapeutics. However, the heterogeneity and complexity of genomic alterations in most human cancers hamper straightforward identification of cancer-causing mutations. We use the retrovirus-infected mice as model systems for identifying new cancer genes efficiently. Retroviruses induce tumors through activation of proto-oncogenes or inactivation of tumor suppressor genes as a consequence of retroviral integrations into host genome. Thus the viral integration sites provide powerful genetic tags for cancer gene identification. We are exploring the novel molecular targets for cancer treatment based on functional characterization of the cancer genes isolated by high-throughput screens using retroviral insertional mutagenesis. Once these genes are identified, we use gene knockout and transgenic mice to understand how these genes function in tumorigenesis, and to develop new animal models for human cancer. Our current projects are as follows.

1) Isolation of novel cancer genes using retroviral insertional mutagenesis in mice with genomic instability
2) Involvement of histone methyltransferases and demethylases in the initiation and progression of cancer
3) The role of three families of enzymes in DNA demethylation pathway on cancer development
4) Functional analysis of the novel cancer genes using conditional knockout mice

Division of Functional Genomics

Fig.1 Efficient isolation of candidate tumor suppressor genes using retrovirus-infected Bloom syndrome model mice

Bloom syndrome is a recessive genetic disorder associated with genomic instability that causes affected people to be prone to cancer. The tumors derived from virus-infected Blm mice are more likely to carry viral integrations in both alleles of tumor suppressor genes through their genomic instability.

Fig.2 Most of the genes that encode histone methyltransferases and demethylases are shown to be the targets of retroviral insertional mutagenesis in mice

Histone modifications have important roles in regulating gene expression and genome function by establishing global chromatin environments. The methylation of four lysine (K) residues on the tail of histone H3 (K4, K9, K27 and K36) is regulated by a large number of histone methyltransferases and demethylases. Among them, most of the genes (shown in red) were identified as the targets of retroviral integrations, which indicated their important roles in oncogenesis.
がん分子標的医療開発プログラム
Cancer Therapeutics Development Program

■腫瘍内科研究分野  Division of Medical Oncology

教授 矢野 聖二

Professor YANO, Seiji

准教授 安本 和生

Associate Professor YASUMOTO, Kazuo

講師 大坪公士郎

Lecturer OHTSUBO, Koushiro

講師 山田 忠明

Lecturer YAMADA, Tadaaki

助教 山下 要

Assistant Professor YAMASHITA, Kaname

助教 毛利 久繼

Assistant Professor MOURI, Hisatsugu

助教 竹本 伸司

Assistant Professor TAKEUCHI, Shinji

助教 衣笠 寛倫

Assistant Professor EBISU, Hiromichi

特任助手 北 賢二

Assistant KITA, Kanzo
肺腺癌は、わが国の癌死亡原因の第一位である。その要因としては容易に多発が転移を来すことと、薬剤抵抗性を示すことがあげられる。本研究分野では、肝細胞增殖因子 (HGF)が分子標的薬であるゲフィチニブやエルロチニブの耐性を誘導することを明らかにした。また、手術で摘出した腫瘍組織を用いて薬剤感受性因子解析をおこない、再発時に最適の薬剤で治療をする個別化医学を目指し研究を進めている。一方、がん転移の分子機序解析には臨床を反映した動物モデルが必要不可欠である。我々は、ヒト肺癌細胞株を用い再現性の高い転移モデルを作製（多臓器、脳、肺、骨、がん性胸水）に確立し、種々の分子標的薬の転移効果を検証している。さらに、独自の同所移植モデルを用いたトランスレーショナルリサーチを展開し、難治性固形癌である胸膜中皮腫や肺癌、胃癌に対しても新規分子標的治療の開発を目指している。

図1 HGFによるゲフィチニブ耐性の分子機構

Lung cancer is the leading cause of malignancy-related death in Japan. High mortality of lung cancer is due to low susceptibility to anti-cancer drugs and high metastatic potential.

We recently discovered a novel mechanism by which hepatocyte growth factor (HGF) induces resistance to gefitinib and erlotinib in lung cancer. We examine the expression of drug sensitivity-related genes using surgically resected lung cancer specimens for personalized medicine.

Since clinically relevant animal models are essential for elucidating the molecular pathogenesis of cancer metastasis, we have established reproducible mouse models representing multi-organ metastasis, brain metastasis, lung metastasis, bone metastasis, or malignant pleural effusion, using human lung cancer cell lines. We are elucidating anti-metastatic effects of several molecular targeted drugs in these models.

Furthermore, we established orthotopic implantation models of malignant pleural mesothelioma and gastric cancer. The goal of our translational research with these animal models is the establishment of novel molecular targeted therapeutics for solid tumors, such as malignant pleural mesothelioma, pancreatic cancer and gastric cancer.

図2 薬剤感受性因子の解析による肺癌の個別化医療

手術で摘出した組織を用い、薬剤感受性因子解析の結果にとづき最適の薬剤を選択

腫瘍内科研究分野

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中央実験施設
Central Research Resource Branch

■ 中央実験施設 Central Research Resource Branch

准教授 黒木 和之
Associate Professor
KUROKI, Kazuyuki

准教授 遠藤 良夫
Associate Professor
ENDO, Yoshio

准教授 久野 耕嗣
Associate Professor
KUNO, Kouji

助 教 天野 重義
Assistant Professor
AMANO, Shigetoyo
主な研究課題は次の通りである。
1) 核酸代謝検査から、分化の感受性に決定因子の解明
2) 5-アミノレプシン酸(5-ALA)を用いる光線療法の臨床応用
3) ADAMTS-1プロテーゼの発現における機能の解析
4) ボウル系の免疫能について

Main projects of this branch are as follows.
1) A study on the determinant of chemosensitivity to antitumor nucleosides in cancers
2) Antitumor effects of photodynamic diagnosis and therapy using 5-aminolevulinic acid in cancers
3) Molecular biology of hepatitis B viruses
4) Roles of ADAMTS-1 in organ functions
5) Phagocytic capacity of ascidian hemocytes

図1 ■ ヒト胃がん細胞の腹膜播種の検出
(A) ヌードマウスの腹腔内に2×10^6個の細胞を導入後、(B) 21日目に5-ALAを腹腔内投与し、(C) 6時間後にLED照射装置(405nm)を用い腹腔内の転移癌細胞の検出を行った。

Fig.1 ■ Detection of disseminated MKN-45 cells in peritoneal cavity of nude mice by ALA-PDD
(A) Highly metastatic MKN-45 P cells were inoculated i.p. into nude mice. (B) 5-Aminolevulinic acid was injected i.p. and mice were exposed to blue LED light (405nm). (C) Disseminated cells in peritoneal cavity were easily detected under blue light.

図2 ■ ADAMTS-1遺伝子欠損マウスの腎臓、卵巣におけ
る異常。
(A) 久野らが同定したADAMTS-1プロテーゼのドメイン構造。(B) ADAMTS-1遺伝子欠損マウスは、腎孟尿構造を破壊した腎損傷を示すが、ADAMTS-1遺伝子欠損マウスの腎臓では、核異常が観察され(C)、卵巣線維組織を失った異形成卵巣が著明するなど卵巣発育過程に異常が認められる(D)。

Fig.2 ■ Renal and ovarian anomalies in ADAMTS-1 null mice.
(A) Structure of the ADAMTS-1 protease. ADAMTS-1 null mice displayed renal anomalies, which resemble ureteropelvic junction (UPJ) obstruction (B). The ovulatory ability was significantly impaired in ADAMTS-1 null mice (C). ADAMTS-1 null ovaries also included a number of unusual follicles without granulosa cell layers (D).

図3 ■ B型肝炎ウイルスの感染機構
B型肝炎ウイルスの感染機構を知るため、ダックB型肝炎ウイルス(DHBV)をモデルに、DHBV表面質と結合する宿主特異的抗体を探索している。その結果、このウイルスのレセプターである新発カールポキシペプチダーゼ gp 180 を発見したが、感染成立にはさらに第二の増生因子が必要であることがわかった。

Fig.3 ■ Infection mechanism of hepatitis B viruses.
To understand the nature of the uptake pathway for hepadnaviruses, we have begun the search for the host proteins that interacts to envelope proteins of the duck hepatitis B virus (DHBV) as a model of these viruses. After our finding of novel carboxypeptidase gp 180, which is now regarded as a host receptor, recent experiments suggest that second host component may be required with gp 180 to fully reconstitute viral entry.
Central Facilities

- **Automated Cell Sorter (自動細胞解析分取装置)**

Normal or cancer cells consist of heterogeneous cell-populations. The BD FACS Aria, which was purchased in 2005, allows the isolation of defined cell subset(s) from heterogeneous mixtures. Cells can be sorted according to size, granularity, surface markers and DNA content. An advantage of using the FACS Aria is that cells can be sorted at rates up to 10,000 cells/second in a sterile environment enabling the recovered cells to be cultured. This is also applicable to transfected cells, where only a small proportion of the cells may express the antigen of interest. The FACS Aria has been used for a variety of experiments in stem cell biology, immunology, developmental biology, and cancer biology.

- **Experimental Small Animal CT Scanner**

The LaTheta™ CT scanner is designed for small animals and intended especially for the in-vivo and ex-vivo animal research. Its extremely sensitive detector allows working with low energy x-ray source, making possible longitudinal studies. This CT scanner has been used to monitor tumour growth and metastasis.
DNAシーケンサー  DNA Sequencer

DNAシーケンサーはクリーン化された遺伝子のDNA塩基配列を自動的に決定する装置で、従来の方法と異なり放射性物質を全く使用せず、4種類の蛍光標識物質のレーザーによる検出で塩基を判別するもので、配列の自動読み取り、データの解析装置を内蔵しています。AB3100Avantおよび3730ジェネティックアナライザは4チャンネルのキャビラリー電気泳動により同時に4サンプルを高速で分析可能です。各種のヒト遺伝子、マウス遺伝子の塩基配列の決定に頻繁に利用されています。

The DNA Sequencer determines the cloned DNA's base sequence automatically, unlike the old method, it uses no radioactive substances. The method used here is to distinguish the base by laser from 4 varieties of fluorescence activated substances, in addition, it is also equipped to read the sequences automatically, and analyze the data. It is frequently used to determine the base sequences of the different human and mouse genes.

共焦点レーザースキャン顕微鏡  Confocal Laser Scanning Microscopy

共焦点レーザー顕微鏡 (Carl Zeiss LSM 510) は、分光された蛍光をスリットにより任意の検出波長に設定することが可能で、多重染色を行う際の駆動波長の干渉を最小限に抑えることができます。Ar (458/477/488/514nm) とHeNe (543・633nm) レーザーを搭載しています。共焦点レーザー顕微鏡は、現代の細胞生物学には不可欠であるため、多くの研究者に頻繁に利用されています。

The confocal laser scanning microscope (Carl Zeiss LSM 510) can set the spectrum fluorescence to arbitrary detection wave length by the slit. The interference with the fluorescent wave length can be suppressed to the minimum. Therefore, this microscope resolves spectrally overlapping emissions under multiple staining. Ar (458/477/488/514nm) and the HeNe (543・633nm) laser are installed in this microscope. Many researchers are using this microscope frequently, since it is indispensable for current cell biology.
## 基礎統計
### Foundation Statistics

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Settlement of accounts for Each Year (Subsidy from the National Government)  in thousand yen

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### 土地・建物
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### 教育活動
Educational Activities

#### 大学院生・研究学生
Graduate Students and Research Students

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#### 交流協定校
Partner Universities and Facilities

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各種シンポジウム開催状況
Research Activities

1. 共同利用・共同研究拠点認定記念シンポジウム
Joint Usage/Research Center Symposium

目的：共同利用・共同研究拠点認定記念シンポジウムを開催する。

日時：平成23年4月21日（木）15:00～17:00
場所：開催場所

来場者数：140人

プログラム：
①「分子標的治療時代の肝臓・胃の動物」
鈴木 前生（公益財団法人がん研究会がん研究所長）
②「幹細胞治療の研究」
平尾 敦（金沢大学がん進展制御研究所）
③「レチノブラストマ遺伝子研究から見えるがん進展制御」
　高橋 智聡（金沢大学がん進展制御研究所）

2. 金沢国際がん生物学シンポジウム
International Symposium on Tumor Biology in Kanazawa

目的：がん及びがん関連分野の基礎及び臨床研究の国際的な交流を促進することを目的としている。

日時：平成23年5月25日（水）9:00～18:20
平成23年5月26日（木）9:00～17:20
場所：開催場所

来場者数：743名（2日間延べ）

プログラム：
①セッションⅠ：
免疫・アレルギー・炎症の分子生物学
小安 重夫（慶應義塾大学医学部）
②セッションⅡ：遺伝子治療学
吉村 崇（名古屋大学大学院生命農学研究科）
平山 順（東京医科大学歯学部医学系研究所）
③セッションⅢ：メタボリック症候群の分子生物学
松内 篤正（東京医科薬科大学医学系研究所）
異藤 廣（自然科学研究機構生物学研究所）
④セッションⅣ：再生医学とエピジェネティクス
鳥見 洋一（京都大学ウイルス研究所）
古関 哲彦（理化学研究所免疫・アレルギー科学総合研究センター）
⑤セッションⅤ：Leading Edge I
後藤由季子（東京大学分子細胞生物学研究所）
高橋 広（東京医科薬科大学医学系研究所）
瀬木 理（東京大学総合研究学園）
⑥セッションⅥ：Leading Edge II
中山 武（九州大学生物科学研究所）
長英二（公益財団法人がん研究会がん研究所）
水島 昇（東京医科薬科大学医学系研究所）
3. 県民公開セミナー
Open Seminar on the people of a prefecture

目的：がんに関する研究成果を公表するとともに、
地域住民の医療・健康の向上に貢献する。

日時：平成23年11月6日㈮ 13:30～16:30
場所：金沢大学医学類十全講堂

来場者数：約400人

プログラム：みんなで考えよう がん医療の課題～がん予防・早期発見・難治がん克服・がんと共に生きる～

総合司会：鳥場 貴子（ニュースキャスター）

第Ⅰ部
特別講演「がんを克服した母に寄り添った私の体験から」
　仁科 仁美（女優）

第Ⅱ部 パネルディスカッション がん医療の課題
①がんの予防（子宮頸がんワクチン、禁煙、食事）
　 笹川 勝之 (金沢医科大学病院産婦人科)
　 西 耕一 (石川県立中央病院呼吸器内科) 外
②がんの早期発見（乳がん、前立腺がん）
　 北川 和秀 (金沢大学附属病院泌尿器科)
　 井口 雅史 (金沢大学附属病院腎臓科) 外
③難治がんの克服
　 矢野 聖二 (金沢大学がん進展制御研究所腫瘍内科) 外

４．金沢大学がん進展制御研究所・富山大学和漢薬学総合研究所交流セミナー
Kanazawa University Cancer Research Institute/Toyama University Institute of Natural Medicine Joint Seminar

目的：本研究所及び和漢薬学総合研究所がそれぞれの共同利用・共同研究拠点としてお互いの特色を生かしセミナーを通じて研究交流を深めることで、がん研究と和漢薬研究の先導的共同研究の発展を目指す。

日時：平成24年11月18日㈮ 9:30～12:30
場所：富山大学和漢薬学総合研究所・民族薬物資料館

来場者数：約70名

プログラム：
①炎症反応により誘導されるがん進展機構
　 大島 正伸 (金沢大学がん進展制御研究所・教授)
②生薬活用の二面性：漢方薬資源と創薬資源
　 小松かつ子 (富山大学和漢薬学総合研究所・教授)
③和漢薬DBに関して
　 田中 隆 (富山大学和漢薬学総合研究所・准教授)
所在地
Campus Locations

Campus Locations

●金沢駅からのアクセス（北陸鉄道バス利用の場合）Access from Kanazawa Station by bus (Hokurutetsudo Bus)

■宝町キャンパス
Kakuma Campus
（金沢大学自然研究）バス下車まで 所要約34分
To bus stop ‘Kanazawa Univ. shobutsuen-mae’ about 34 min.
金沢駅東口出入口→金沢大学（東門）行
Kanazawa Station East Exit → ①２（Kanazawa Univ. （Kakuma））

■宝町キャンパス（操業制御研究分野、腫瘍内科研究分野）
Takara-machi Campus | Division of Translational and Clinical Oncology, Division of Medical Oncology
1.金沢駅東口出入口→金沢大学生前→③2 （Tobusyako） etc
Kanazawa Station East Exit ① → ②3（Kakuma Campus）
金沢駅東口出入口→④4（Tobusyako） etc
Kanazawa Station East Exit ② → ③4
Kanazawa Station West Exit ④ → ④5

金沢大学がん進展制御研究所概要

編集 金沢大学がん進展制御研究所
所在地 〒920-1192 金沢市宝町
Kakuma-machi, Kanazawa, 920-1192
〒920-0934 金沢市宝町13番1号
（腫瘍制御研究分野、腫瘍内科研究分野）
13-1, Takara-machi, Kanazawa, 920-0934
(Division of Translational and Clinical Oncology, Division of Medical Oncology)
TEL (076) 234-4527
FAX (076) 234-4527
URL: http://www.kanazawa-u.ac.jp/~ganken/
MAIL: y-somui@adm.kanazawa-u.ac.jp