SNUH SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

제4회 분당서울대학교병원 암센터 심포지움

'Building Bridges for Cancer Research and Treatment'

일자 2019년 7월 26일(금)

장소 분당서울대학교병원 1동 지하1층 대강당

PROGRAM

09:00–09:10	인사말	김형호 (분당서울대학교병원)	
	축 사	백롱민 (분당서울대학교병원)	
09:10–10:10	For the Next 10 Years	이재호 (분당서울대학교병원)	
09:10–09:30	Cancer Registry in SNUBH	이호영 (분당서울대학교병원)	2
09:30–09:50	Next Generation Biobank	조석기 (분당서울대학교병원)	4
09:50–10:10	Korean Cell Line Bank and Cancer Organoids	구자록 (서울대학교)	6
10:30–12:00	Plenary Session (1): Cutting Edges in Oncology	이근욱 (분당서울대학교병원)	
10:30–11:00	Recent Advancement of Immuno-Oncology	방영주 (서울대학교병원)	10
11:00–11:30	Translational Research in Immuno-Oncology	신의철 (KAIST)	12
11:30–12:00	Clinical Trials in JCOG	Masanori Terashima (Shizuoka Cancer Center, Japan)	14
13:00–14:30	Plenary Session (2): Beyond Precision Medicine	정진행 (분당서울대학교병원)	
13:00–13:45	Insights from Cancer Genome Sequencing Data	Peter J. Park (Harvard Univ. USA)	18
13:45–14:30	CRISPR/Cas-assisted Genetics and Cancer Modeling in Adult Stem Cell-based Organoids	구본경 (IMBA, Austria)	22
14:50–16:30	Live Surgery by Smart Surgeries™ Platform at SNUBH	김형호 (분당서울대학교병원)	
14:50–16:30	Laparoscopic Ultralow Anterior Resection with D3 Lymph Node Dissection (Total Mesorectal Excision and Autonomic Nerve Presevation)	강성범 (분당서울대병원 외과)	
14:50–16:30	Robotic Partial Nephrectomy For A Complex Mass	변석수 (분당서울대병원 비뇨기과)	
14:50–16:30	Laparoscopic Distal Pancreatectomy	윤유석 (분당서울대병원 외과)	
16:30 ~	맺음말	이근욱 (분당서울대학교병원)	

SNUH SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

For the Next 10 Years

좌장: 이재호 (분당서울대학교병원)

CURRICULUM VITAE

이 호 영
분당서울대학교병원 의료정보센터 핵의학과

학 력

1994~2000	서울대학교 의과대학 의학과
2002~2005	서울대학교 의과대학원 핵의학전공
2005~2010	서울대학교 의과대학원 분자종양전공

경 력

2000~2001	서울대학교병원 인턴
2001~2005	서울대학교병원 핵의학과 전공의
2005~2008	국립암센터 핵의학과 공중보건의
2008~2012	서울특별시보라매병원 핵의학과 조교수
2012~현재	분당서울대학교병원 핵의학과 부교수
2014~현재	서울대학교 의과대학 핵의학교실 부교수
2016~현재	분당서울대학교병원 의료정보센터 센터장

학회활동 및 수상내역

대한핵의학회
대한의료정보학회

Cancer Registry in SNUBH

Ho-Young Lee | SNUBH Bioinformatic Center

Currently, most of the hospital are using digital healthcare information system (HIS). Using the HIS means the data those are produced in the hospital are recorded and could be reused. These are possible due to the progression of IT technique. Therefore, the most of the medical records are change to data. Data based decision is necessary for clinical purpose and hospital management. How to use the data is important thesis.

In SNUBH, annually about 500 cases of lung cancer operation are performed. Also, there are many cases of cancer operation. We are planning to build our own cancer registration. On the process of the building the cancer registration, manual process is necessary in now. However, we hope to make automatic process to gather the important parameter from the data made during the hospital course of patients. By using automatic process, we could reduce the human error and the registration could have more reliability. Furthermore, the data are not made and managed by the each department, it will be managed by central team. In those central process, the outcome and data will have more reliability.

To build up the process, active participation of many teams is necessary. Technically, natural language processing is useful. The registration is staring from oncology filed but it will also expand to the other acute and chronic disease, rare disease et al. After the clean database is built, those will be helpful not only for the academic activity of member in SNUBH, but also for the patients who will visit SNUBH.

CURRICULUM VITAE

조 석 기
분당서울대학교병원 흉부외과

학 력

1997	서울대학교 의과대학 의학과 졸업
2007	서울대학교 의과대학원 흉부외과학 석사
2011	서울대학교 의과대학원 흉부외과학 박사

경 력

2005~2007	분당서울대학교병원 흉부외과 전임의, 촉탁의
2007~2009	경북대학교병원 흉부외과 임상교수
2009~2011	경북대학교 의학전문대학원 흉부외과학교실 조교수
2011~2014	서울대학교 의과대학 흉부외과학교실 조교수
2013~2014	스탠포드대학병원 연수
2014~2019	서울대학교 의과대학 흉부외과학교실 부교수
2019~현재	서울대학교 의과대학 흉부외과학교실 교수
	분당서울대학교병원 흉부외과 전문의

학회활동 및 수상내역

대한흉부심장혈관외과학회 교육위원, 수련심사위원
대한흉부종양외과학회 학술위원
대한폐암학회 연구위원
세계폐암학회 회원

Next Generation Biobank

조 석 기 | 분당서울대학교병원 흉부외과

인체유래물은행 (이하 바이오뱅크)은 생명윤리법에 근거하여 인체유래물 또는 유전정보와 그에 관련된 역학정보, 임상정보 등을 수집, 보존하여 이를 직접 이용하거나 타인에게 제공하는 기관으로 보건복지부장관의 허가를 받은 곳을 말한다. 전통적인 의미의 바이오뱅크는 수술 또는 채혈 등으로 얻은 조직과 혈액을 표준화된 방법에 따라서 보관하고, 보관된 인체유래물과 임상정보를 결합하여 연구목적에 맞게 후향적으로 사용하는 것이 전부였다. 따라서 보관된 인체유래물 종류와 개수, 분양된 샘플과 이를 이용한 연구 건수 등이 1세대 바이오뱅크의 평가항목이었다.

최근에는 환자마다 다른 유전체정보, 임상정보, 생활 정보를 분석해 최적의 치료 방법을 제공하는 정밀의료 (precision medicine) 서비스가 전 세계적으로 확산되고 있다. 그에 따라 바이오뱅크에 대한 관심이 높아지고 있어 많은 의료기관에서 설립을 추진하고 있으며 기존의 바이오뱅크에서는 더 발전된 방향으로 진화되어 가고 있다. 국내 바이오뱅크 사업은 2008년부터 시작되었으며 현재 질병관리본부 산하에 국립중앙인체자원은행이 오송에 있고 전국 대학병원에 17개의 인체자원단위은행이 설치되어 있다.

차세대 바이오뱅크는 혈액과 조직 이외에 시컨싱데이터, PDX 등의 다양하고 방대 인체유래물 등을 효율적으로 관리할 수 있는 시스템, 환자의 임상, 영상, 병리결과 등을 포함하고 암환자의 치료병력, 재발, 생존 여부 등의 완벽한 임상 정보를 관리하는 시스템, 환자 동의 기반 연구윤리 시스템 등의 결합시스템으로 정의할 수 있다.

CURRICULUM VITAE

구 자 록
서울대학교 의과대학 의과학과

학 력

1992,1994	학사, 석사 서울대학교
1998	박사, 서울대학교 대학원 (수의병리학, 종양세포생물학, 암유전체학)
	학위논문 : 인체대장암세포주의 세포학적 및 분자생물학적 특성분석

경 력

1994~2001	서울대학교 암연구센터, 연구원, 선임연구원
2001~현재	조교수, 부교수, 교수, 서울대학교 의과대학 의학과/대학원 의과학과
2002~현재	세계지적재산권기구(WIPO) 승인 한국세포주연구재단
	(국제특허미생물기탁기관) 이사
2002~2015	한국연구재단 연구소재은행, 국가목적형소재은행 한국세포주은행 연구과제 책임자
2008~현재	서울대학교 암연구소 연구지원부장, 연구부장
2013~2014	미국 NIH/NHGRI/GMBB 방문연구원
2017~현재	과학기술정보통신부지정 생명연구자원기탁등록보존기관
	서울대학교 한국세포주은행 책임자

연구주제

1) Establishment and characterization of human cell lines and organoids
2) Cancer genomics and anticancer drug screening in cancer cell lines and organoids
3) Biobanking and biorepositories of cell lines and organoids

Korean Cell Line Bank and Cancer Organoids

구 자 록 | 서울대학교 의과대학

An organoid is a miniaturized and simplified version of an organ produced in vitro in three dimensions that shows realistic micro-anatomy. Organoids as well as cell lines are important because they provide a consistent renewable source of cell material for study. Organoids like as cell lines can be also established from original tumor tissues, metastatic tumor tissues, PDX, ascites, pleural effusions or circulating tumor cells of cancer patients.

Cancer cells that are grown in organoid culture system retain cell-cell and cell-matrix interactions that more closely resemble those of the original tumor compared with cells grown in two dimensions on plastic. Utilizing organoid culture system, high-throughput drug screening from patient-derived tumor samples offers a unique opportunity to identify effective cancer drugs for individual patients.

Over 450 human cancer organoids derived from colorectal, pancreatic, breast, gastric, ovarian cancers, hepatocellular carcinoma and renal cell carcinomas have been established since 2016 in our laboratory. The characteristics of these human cancer organoids have been analyzed (DNA fingerprinting analysis, mycoplasma contamination test, cell viability test for anticancer drugs and NGS (WES and RNA seq.) for detections of mutations and expressions of genes. We have been conducting anticancer drug screening assay on these cancer organoids and also these human cancer organoids will be available in the future thorough the KCLB (Korean Cell Line Bank, https://cellbank.snu.ac.kr).

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Plenary Session (1): Cutting Edges in Oncology

좌장: 이근욱 (분당서울대학교병원)

CURRICULUM VITAE

방영주
서울대학교 의과대학 내과 (종양내과)

학 력

1979	서울대 의대 졸업
1989	서울대 대학원 박사

경 력

1986~현재	서울대 의대 교수
2000~2006	서울대 암연구소 소장
2009~2017	서울대병원 임상시험센터 센터장
2010~2014	서울대 의대 내과학교실 주임교수
2013~2017	서울대병원 의생명연구원 원장

학회활동 및 수상내역

2006~2008	대한항암요법연구회 회장
2008~2010	한국임상암학회 이사장
2012~2014	대한암학회 이사장
2009.12.8	보건산업기술대상 대상 (대통령상)
2012.6.13	Kobayashi Foundation Award
2012.10.24	지식창조대상 (장관상)
2017.3.21	홍조근정훈장
2018.3.21	아산의학상
2018.11.9	김노경상

Recent Advances in Immuno-Oncology

Yung-Jue Bang | Division of Medical Oncology, Seoul National University Hospital, Seoul

Recent advances in immuno-oncology (IO) are transforming the practice of medical oncology. The impact of IO has been largely centered on the immune checkpoint inhibitors such as anti-CTLA4 or anti-PD-1/PD-L1 antibodies, which are used across 23 different tumor types. These agents can induce durable clinical responses. New checkpoint modulators targeting LAG3, TIM-3, TIGIT, OX-40, or GITR are being explored as an opportunity to overcome the challenges of current checkpoint inhibitors. Other important IO classes are bispecific antibodies, cytokine therapy, oncolytic viruses and CAR-T technologies. Currently, more than 8,000 IO trials are ongoing, largely focused on checkpoint modulators and combinations with other IO agents, targeted agents, and chemotherapies.

CURRICULUM VITAE

신의철
카이스트 의과학대학원

학 력

1990~1996	연세대학교 의과대학 의학사 (M.D.)
1996~1998	연세대학교 대학원 의학석사 (미생물학/면역학)
1998~2001	연세대학교 대학원 의학박사 (Ph.D., 미생물학/면역학)

경 력

2002~2007	미국 NIH, NIDDK, Postdoctoral Fellow
2007~현재	KAIST 의과학대학원 조교수, 부교수, 교수
2018~현재	연세의대 의생명과학부 겸임교수
2019~현재	한국과학기술한림원 의약학부 정회원

학회활동 및 수상내역

2011~2012	대한면역학회 백신연구회 회장
2013~현재	대한면역학회 편집부위원장
2014~2017	대한백신학회 학술이사
2018~현재	대한바이러스학회 학술이사
2019~현재	대한면역학회 면역항암연구회 회장

Translational Research in Immuno-Oncology

Eui-Cheol Shin | Laboratory of Immunology and Infectious Diseases, Graduate School of Medical Science and Engineering, Korea Advanced Institute of Science and Technology (KAIST), Daejeon, Republic of Korea

During immune responses, antigen-specific T cells are regulated by various mechanisms including inhibitory receptors and regulatory T cells to avoid excessive and persistent immune responses. These regulatory mechanisms, called 'immune checkpoint', suppress T cell responses particularly in chronic viral infection and cancer, in which viral antigens or tumor antigens persist for a longtime, and lead to T cell exhaustion in patients with chronic viral infection or cancer. Among them, cytotoxic T lymphocyte-associated protein 4 (CTLA-4) and programmed cell death 1 (PD-1) are the most well-known receptors and have been targeted for drug development. As a result, anti-CTLA-4 and anti-PD-1 (or anti-PD-L1) blocking antibodies were developed for cancer treatment and known as 'immune checkpoint inhibitors'. However, anti-CTLA-4 and anti-PD-1 (or anti-PD-L1) blocking antibodies fail to control tumors in a significant proportion of cancer patients. Therefore, it is an important question how the coverage of immune checkpoint inhibitors can be extended to the majority of cancer patients who do not have control or regression of their cancer. In this lecture, strategies to improve treatment responses of anti-PD-1 will be discussed, including novel immuno-modulators and biomarkers predicting treatment responses.

CURRICULUM VITAE

Masanori Terashima
Division of Gastric Surgery, Shizuoka Cancer Center

Education

1983	M.D., cum laude, Iwate Medical University
1987	Ph.D. (Dr. of Medical Science), Iwate Medical University

Career

1987–1994	Member of Medical Staff, Department of Surgery 1, Iwate Medical University
1994	Assistant Professor, Department of Surgery 1, Iwate Medical University
1994–1995	Research Fellow, Division of Cancer Pharmacology, Dana-Farber Cancer Institute, MA
1994–2002	Assistant Professor, Department of Surgery 1, Iwate Medical University
2002–2007	Associate Professor, Department of Surgery 1, Fukushima Medical University
2007–2008	Director, Clinical Cancer Center, Fukushima Medical University
2008–	Chief, Division of Gastric Surgery, Shizuoka Cancer Center
2016–	Chairman, Stomach Cancer Study Group, Japan Clinical Oncology Group

Study and Research

1) Surgical therapy for gastrointestinal malignancies especially for gastric cancer

2) Surgical oncology of human gastrointestinal malignancies

Clinical Trials in JCOG

Masanori Terashima | Division of Gastric Surgery, Shizuoka Cancer Center, Japan

Japan Clinical Oncology Group (JCOG) is a largest Japanese cooperative group, and is funded primarily by the National Cancer Centre Research and Development Fund. Stomach Cancer Study Group is established at 1984 and one of the largest study group in JCOG. We have conducted many trials for the treatment of gastric cancer. Among them, I would like to introduce surgical trials and trials for perioperative treatment.

Most pivotal surgical trial was JCOG9502 in which the efficacy of paraaortic lymph node dissection (PAND) was evaluated. Unfortunately, we failed to demonstrate the superiority of PAND. Similarly, we failed to demonstrate the superiority of left-thoraco abdominal approach over abdominal trans-hiatal approach in tumors with esophageal invasion (JCOG9502). In JCOG 0110, we successfully demonstrated the non-inferiority of spleen preservation to splenectomy in gastric cancer located at upper third of the stomach. In JCOG 1001, we also failed to demonstrate the superiority of omento-bursectomy over omentectomy alone. From these RCTs, we learned that survival benefit cannot be obtained from highly invasive procedures with high morbidity. So, the paradigm had been changed to minimally invasive surgery (MIS). As a MIS trial, we conducted randomized phase III trial for cStage I (JCOG0912). In this trial we successfully demonstrated the non-inferiority of laparoscopic distal gastrectomy (LDG) to open distal gastrectomy. In addition, we also demonstrated the safety of laparoscopic total gastrectomy (LTG) in JCOG1401. Form these results, LDG and LTG will be recommended as a standard treatment for cStage I cancer. We are now carrying out a phase II trial to evaluate the safety of LTG with splenic hilar lymph node dissection (JCOG1809) and planning a phase III trial evaluating the superiority of robotic gastrectomy over laparoscopic gastrectomy.

In trials for perioperative chemotherapy, we conducted several phase II trials of neoadjuvant chemotherapy (NAC) for extensive nodal disease and type 4 and large type 3 cancer. From these results, we conducted phase III trial to confirm the efficacy of NAC for type 4 and large type 3 in JCOG0501. Unfortunately, we failed to demonstrate the superiority of NAC. We are now conducting NAC for cStage III cancer in JCOG1509. The results of other trials will be demonstrated and discussed.

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Plenary Session (2): Beyond Precision Medicine

좌장: 정진행 (분당서울대학교병원)

CURRICULUM VITAE

Peter Jungsoo Park
Professor of Biomedical Informatics, Harvard Medical School

Education

AB/SM (applied mathematics), Harvard; PhD (applied mathematics), Caltech

Career

Postdoctoral fellow (1999–2001), Instructor (2001–2005), Assistant Professor (2006–2010), Associate Professor (2010–2016), Professor (2016–), Harvard Medical School. Other appointments: Director, Bioinformatics and Integrative Genomics PhD program; Co-leader, Cancer Data Science Program, Harvard/Dana-Farber Cancer Center; Harvard Stem Cell Institute; Division of Genetics, Brigham and Women's Hospital.

Study and Research

The goal of my computational genomics laboratory is to understand genetic and epigenetic mechanisms related to disease processes using high-throughput sequencing data. We have developed bioinformatic algorithms for analyzing various types of genomic data. These include methods for detection of structural variants from whole-genome sequencing data, such as copy number variants, complex rearrangements, transposable element insertion, and microsatellite instability. We have made major contributions to consortium projects such as The Cancer Genome Atlas (TCGA), Encyclopedia of DNA Elements (ENCODE), Brain Somatic Mosaicism Network, and 4D Nucleome.

Recent publications

1) Cortés-Ciriano I, Lee JJK, Xi R, Jain D, Jung YL, Yang L, Gordenin D, Klimczak LJ, Zhang CZ, Pellman DS, Park PJ. (2019) Comprehensive analysis of chromothripsis in 2,658 human cancers using whole-genome sequencing. Nat Genet, in press.

2) Gulhan DC, Lee JJK, Melloni GEM, Cortés-Ciriano I, Park PJ. (2019) Detecting the mutational signature of homologous recombination deficiency in clinical samples. Nat Genet, 51:912-919.
3) Bohrson CL, Barton AR, Lodato MA, Rodin RE, Luquette LJ, Viswanadham VV, Gulhan DC, Cortés-Ciriano I, Sherman MA, Kwon M, Coulter ME, Galor A, Walsh CA, Park PJ. (2019) Linked-read analysis identifies mutations in single-cell DNA-sequencing data. Nat Genet, 51:749-754
4) Lodato MA*, Rodin RE*, Bohrson CL*, Coulter ME*, Barton AR*, Kwon M*, Sherman MA, Vitzthum CM, Luquette LJ, Yandava C, Yang P, Chittenden TW, Hatem NE, Ryu SC, Woodworth MB, Park PJ**, Walsh CA**. (2018) Aging and neurodegeneration are associated with increased mutations in single human neurons. Science, 359:555-559.

Insights from Cancer Genome Sequencing Data

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[Part 1: Predicting patients who are likely to respond to PARP inhibitors]

Different mutational processes operative in cancer leave distinct 'signatures' in the DNA. Mutational signature analysis is an attempt to deconvolve the mutational patterns from genome sequencing data to better identify the factors that give rise to cancer. Whereas previous work required a large amount of signal as found in exome and genome sequencing data, our new method (SigMA) enables accurate detection of mutational signatures from gene panels. I will describe the methodology behind SigMA and how it can be used to identify patients with deficiency in the homologous recombination DNA repair pathway who should be considered for treatment with PARP inhibitors.

[Part 2: Characterization of chromothripsis events]

Chromothripsis is a mutational phenomenon involving massive, clustered genomic rearrangements that occurs in cancer and other diseases. We analyzed whole-genome sequencing data from >2,600 tumors to find that chromothripsis events are much more pervasive than previously suggested, with a frequency of >50% in several cancer types. Whereas canonical chromothripsis profiles display oscillations between two copy number states, a considerable fraction of the events involves multiple chromosomes as well as additional structural alterations. In addition to non-homologous end-joining, we detect signatures of replicative processes and templated insertions; chromothripsis contributes to oncogene amplification as well as to inactivation of genes such as mismatch-repair related genes. These findings show that chromothripsis is a major process driving genome evolution in human cancer.

MEMO

CURRICULUM VITAE

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Education

2002.03~2006.02	Ph.D., Div. of Mol. and Lif. Sci., POSTECH, Republic of Korea (Advisor: Prof. Young-Yun Kong)
2000.03~2002.02	M.S. Div. of Mol. and Lif. Sci., POSTECH, Republic of Korea
1996.03~2000.02	B.S. Dept. of Lif. Sci., POSTECH, Republic of Korea

Career

2017.10~Present	Group Leader, IMBA, Vienna, Austria
2013.04~2017.11	Group Leader, Cambridge Stem Cell Institute, Univ. of Cambridge
2009.03~2013.04	Postdoctoral fellow, Hubrecht Institute, KNAW, the Netherlands (Mentor: Prof. Hans Clevers)
2006.03~2009.02	Postdoctoral fellow, Pohang University of Science and Technology (POSTECH) and Seoul National University (Mentor: Prof. Young-Yun Kong)

CRISPR/Cas-assisted Genetics in Intestinal Organoids

Bon-Kyoung Koo | IMBA - Institute of Molecular Biotechnology of Austrian Academy of Sciences

The identification of LGR5+ intestinal stem cells helped us to understand various aspects of adult stem cells and led to the establishment of primary 3D intestinal organoid culture system from mouse and human tissues. This novel culture system faithfully recapitulates various aspects of the intestinal epithelium *in vitro* with remarkable long-term expansion capacity and genetic stability. Thus, the model is recognised as a suitable *in vitro* model system for genetic studies. To exploit all the potential of this culture, protocols have been fully optimised for primary establishment, maintenance, cryopreservation, plasmid transfection and viral transduction. A number of examples will be shown to introduce how to apply CRISPR technology and organoid models for genetic studies, including simultaneous paralogue knockout, functional genetic screening and precise gene correction.

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