Session II

좌장: **조영애** 가톨릭대 / **김용철** GIST

7월 30일 4:50-6:20

좌장 이력서

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Education

1. 1982-1986: Department of Pharmacy, Seoul National University. B.S.
2. 1986-1992: Department of Pharmacy, Seoul National University, M.S & Ph.D. (Biochemistry Major)

Experience

1. 1992-1997: **Postdoctoral Fellow**, National Institutes of Health, U.S.A
2. 1997-2000: **Instructor**, College of Medicine, The Catholic University, of Korea.
3. 2000-2005: **Assistant Professor**, College of Medicine, The Catholic University, of Korea.
4. 2005-2010: **Associate Professor**, College of Medicine, The Catholic University, of Korea.
5. 2010-present: **Professor**, College of Medicine, The Catholic University, of Korea.
6. 2009-2016: **Editor-in Chief**, Biomolecules & Therapeutics

References

1. Kim HK, Lee SG, Lee SW, Oh BJ, Kim JH, Kim JA, Lee G, Jang JD, and **Joe YA**. A subset of paracrine factors as efficient biomarkers for predicting vascular regenerative efficacy of mesenchymal stromal/stem cells. ***Stem Cells***. 37,77-88 (2019)
2. Kim HK, Ham KA, Lee SW, Choi HS, Kim HS, Kim HK, Shin HS, Seo KY, Cho YJ, Nam KT, Kim IB and **Joe YA**. Biallelic deletion of *Pxdn* in mice leads to anophthalamia and severe eye malformation ***Int. J. Mol. Sci***. 20, 6144 (2019)
3. Lee SW, Kim HK, Naidansuren P, Ham KA, Choi HS, Ahn HY, Kim M, Kang DH, Kang SW, **Joe YA**. Peroxidasin is essential for endothelial cell survival and growth signaling by sufilmine crosslink-dependent matrix assembly. ***Faseb J***. 34, 10228-10241 (2020)

좌장 이력서

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Education

1. 1983-1987: **B.S.**, School of Pharmacy, Seoul National University
2. 1987-1989: **M.S.**, School of Pharmacy, Seoul National University
3. 1989-1995: **Ph.D.**, School of Pharmacy, Seoul National University

Experience

1. 1995-2000: **Post-doc.**, National Institutes of Health (Dr. Kenneth A. Jacobson), USA
2. 2000-2001: **Research Scientist**, Univ. Alabama and ChemBridge, Inc. in USA
3. 2001-present: **Professor**, Gwangju Institute of Science & Technology (GIST)
4. 2011-2015: **Dean**, School of Life Sciences, GIST
5. 2017-2019: **Dean**, International and Public Affairs, GIST
6. 2019-present: **Director**, Center for AI-Applied High Efficiency Drug Discovery (AHEDD), GIST
7. 2019-present: **CEO**, PeLeMed, Co. Ltd. (Bio-Venture Company)
8. 2020-2020: **President**, Division of Organic & Medicinal Chemistry, PSK
9. 2020-present: **Editorial Advisory Board**, Journal of Medicinal Chemistry, ACS

References

1. “Discovery of Novel Pyrimidine-Based Capsid Assembly Modulators as Potent Anti-HBV Agents” ***J.Med.Chem.***64(9),5500-5518(2021).
2. “Discovery of Orally Active Indirubin-3’-oxime Derivatives as Potent Type 1 FLT3 Inhibitors for Acute Myeloid Leukemia” ***Eur.J.Med.Chem.***195,112205-112222(2020).
3. “Potent Suppressive Effects of 1-Piperidinylimidazole Based Novel P2X7 Receptor Antagonists on Cancer Cell Migration and Invasion” ***J.Med.Chem.***59(16),7410-7430(2016).
4. “Discovery of Novel 2,5-Dioxoimidazolidine-Based P2X7 Receptor Antagonists as Constrained Analogues of KN62” ***J. Med. Chem.*** 58(5),2114-2134(2015).
5. “Structure-activity relationships and optimization of 3,5-dichloropyridine derivatives as novel $P2X_7$receptorantagonists”***J.Med.Chem.***55(8),3687-3698(2012).
6. “5,5’-Substituted Indirubin-3’-oxime Derivatives as Potent Cyclin-Dependent Kinase Inhibitors with Anticancer Activity” ***J.Med.Chem.***53(9),3696-3706(2010).Growth.

Session II

양 영 (숙명여대 이과대)

Oncoprotein CIP2A regulates the disassembly of primary cilia and glycolytic metabolism

Oncoprotein CIP2A regulates the disassembly of primary cilia and glycolytic metabolism

Yang, Young Ph.D.

Department of Biological Systems

Research Institute of Women's Health, Sookmyung Women's University, Seoul, Republic of Korea

In most eukaryotic cells, the primary cilium is a microtubule-enriched protrusion of the plasma membrane and acts as a key coordinator of signaling pathways during development and tissue homeostasis. The primary cilium is generated from the basal body, and cancerous inhibitor of protein phosphatase 2A (CIP2A), the overexpression of which stabilizes c-MYC to support the malignant growth of tumor cells, is localized in the centrosome. Therefore, we investigated whether CIP2A plays a role in cilia assembly and metabolic regulation. CIP2A overexpression induced primary cilia disassembly through the activation of Aurora A kinase, and CIP2A depletion increased ciliated cells and cilia length in retinal pigment epithelium (RPE1) cells. CIP2A depletion also shifted metabolism toward the glycolytic pathway by altering the expression of metabolic genes related to glycolysis. However, glycolytic activation in CIP2A-depleted cells was not dependent on cilia assembly, even though enhanced cilia assembly alone activated glycolytic metabolism. Collectively, these data suggest that CIP2A is involved in the regulation of primary cilia disassembly and that CIP2A depletion induces metabolic reprogramming independent of primary cilia.

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Education

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3. 1993-1997: KAIST (Ph.D. Degree)
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Experience

1. 2005-Present: Professor. Dept of Biological Sciences, Sookmyung Women's University in Korea
2. 2012.1-2012.12 MD Anderson Cancer Center, Visiting Associate Professor.
3. 1990-2005 Korea Research Institute of Bioscience and Biotechnology
4. 1997-1999, Visiting Scientist, NINDS, MA, USA

References (Recent articles among 113 peer reviewed articles)

Jeong AL, et al., Oncoprotein CIP2A promotes the disassembly of primary cilia and inhibits glycolytic metabolism. **EMBO Rep**. (2018)

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Ji Young Park, et al., Silent mating-type information regulation 2 homolog 1 overexpression is an important strategy for the survival of adapted suspension tumor cells. **Cancer Science**. 110(9):2773-2782. (2019).

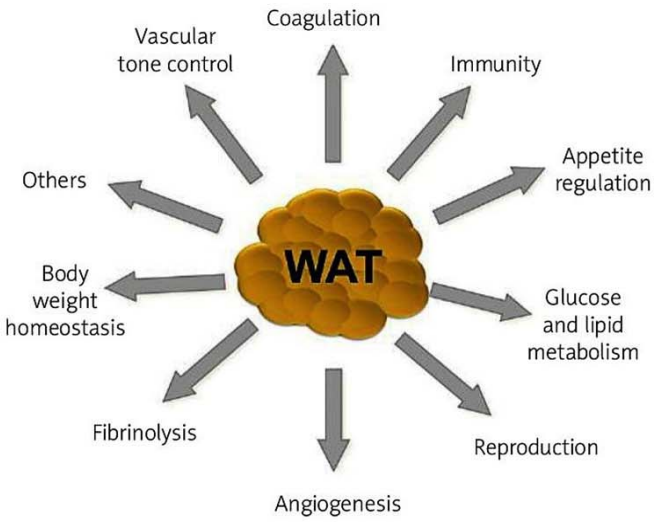
Hye In Ka, et al., Deubiquitinase USP47-stabilized splicing factor IK regulates the splicing of ATM pre-mRNA. **Cell Death Discov**. (2020)

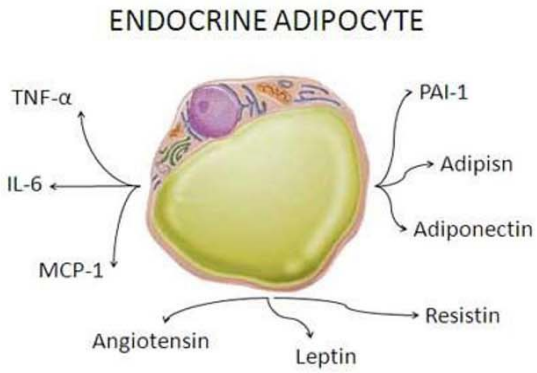
Hye In Ka, et al., Loss of splicing factor IK impairs normal skeletal muscle development. **BMC BIOLOGY.** (2021)

From immunologic role of adiponectin to metabolic role of CIP2A

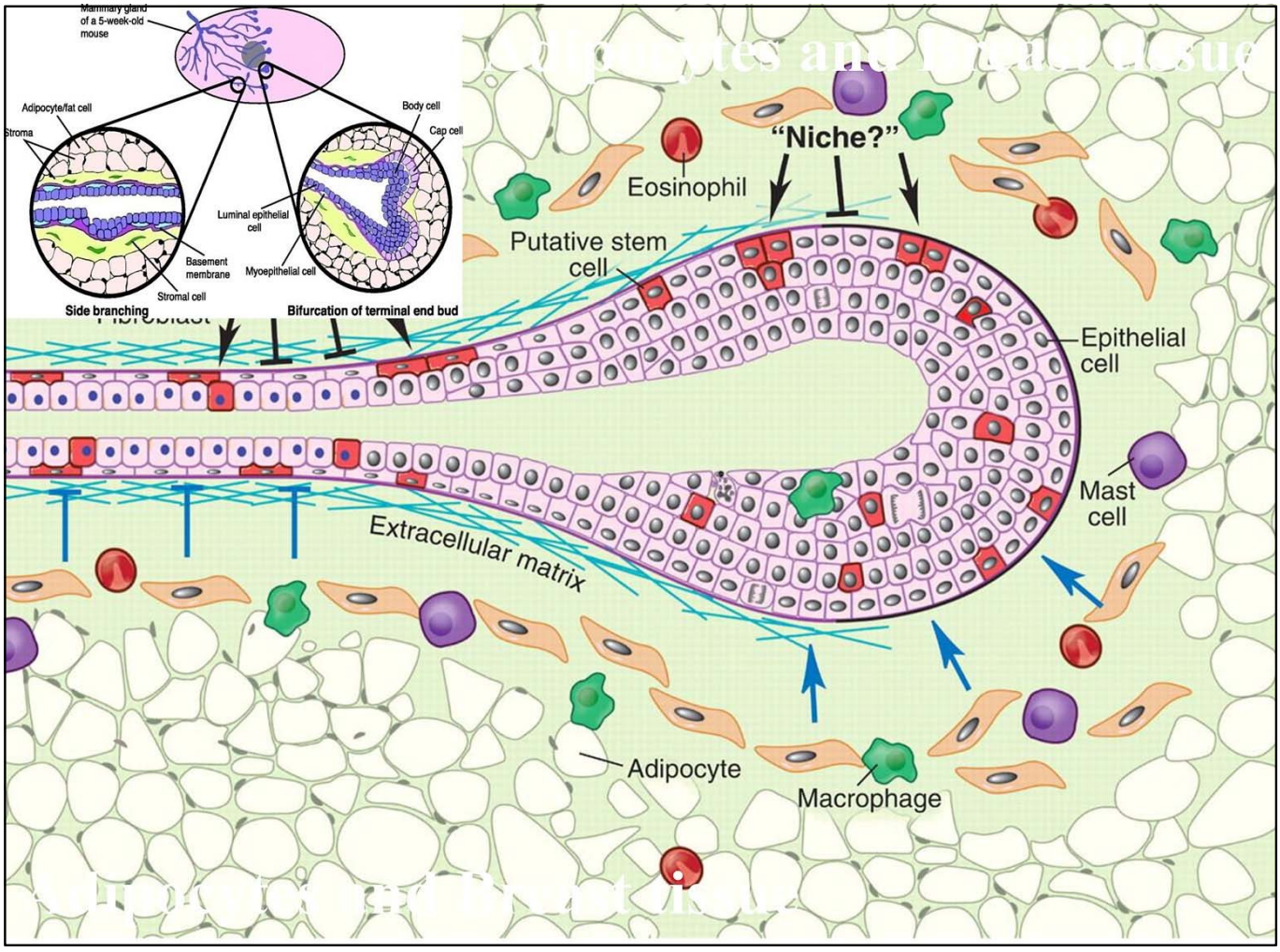
Sookmyung Women's University
Young Yang

Adipose tissues as 3rd endocrine organ



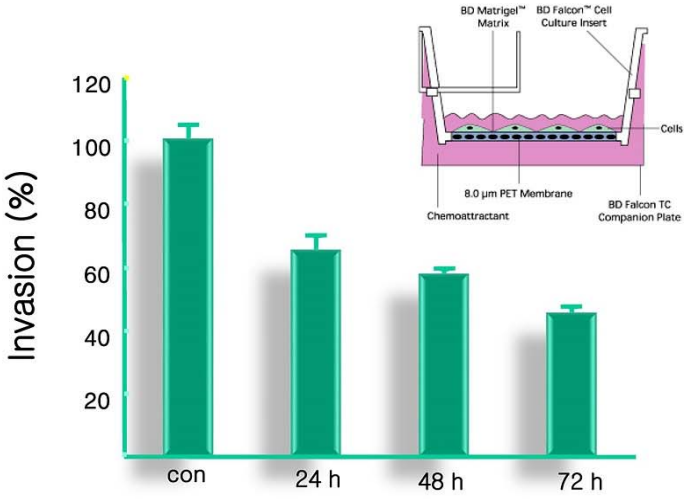


Journal of Clinical Endocrinology and Metabolism in 2006

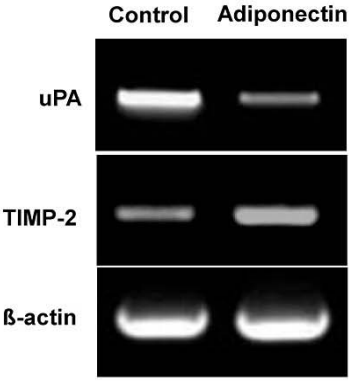


What's the role of adiponectin in cancer ?

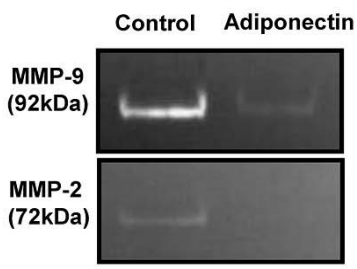
Matrigel analysis using MDA-MB-231 cells



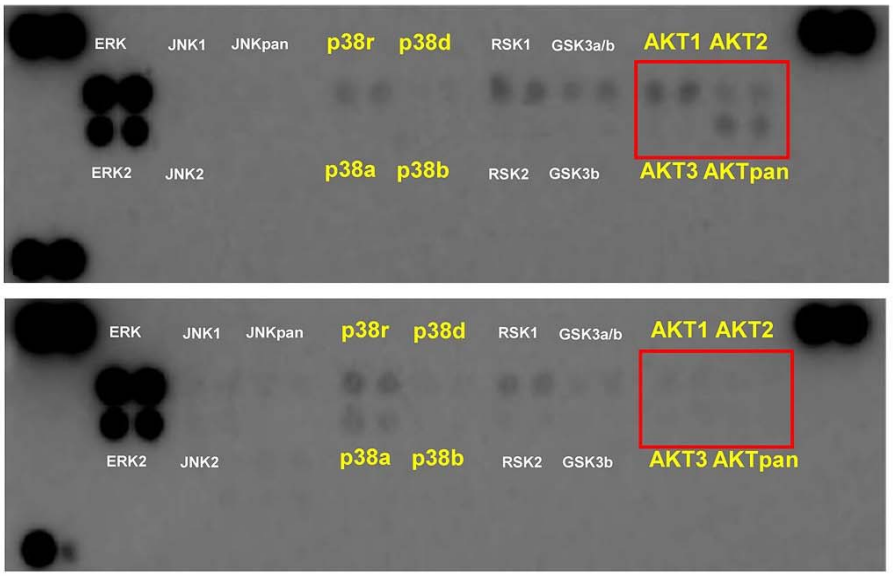
RT-PCR



Zymography

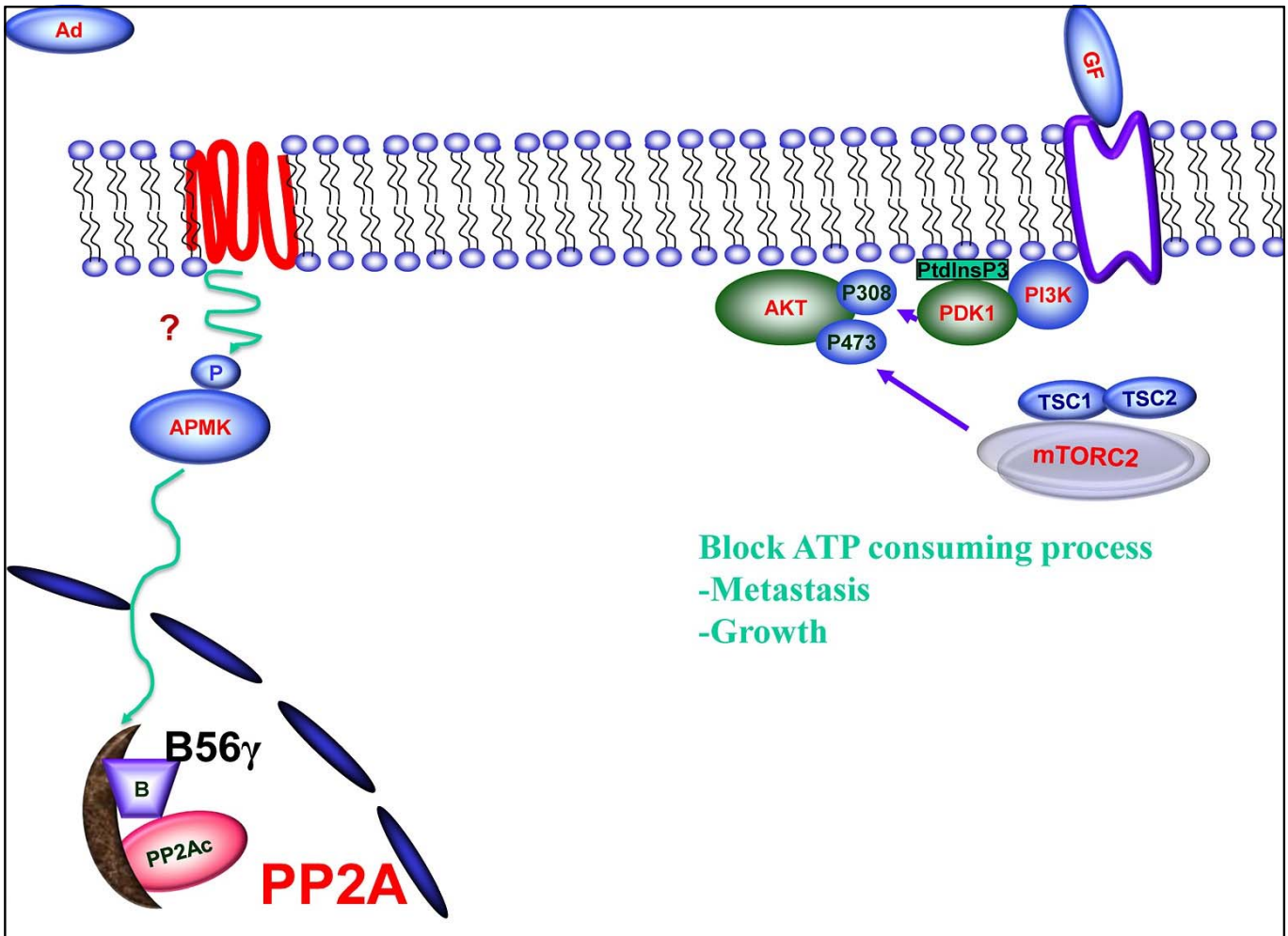


Adiponectin inactivates AKT1/2



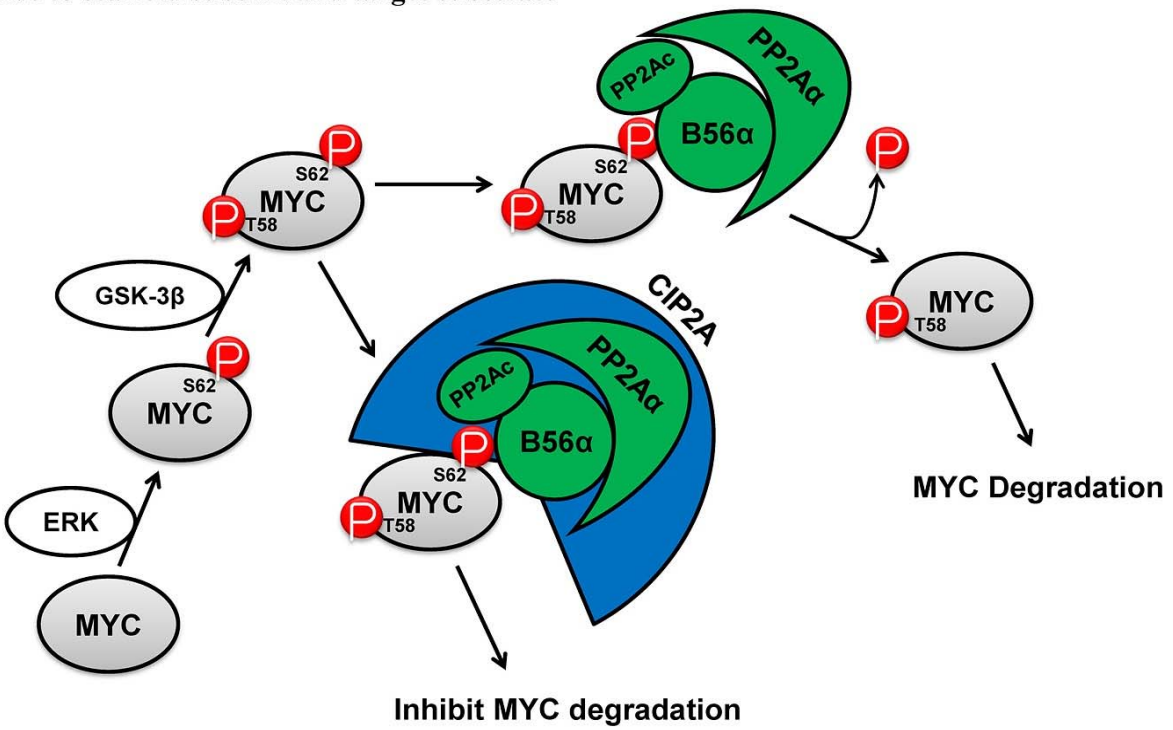
Control

Adiponectin



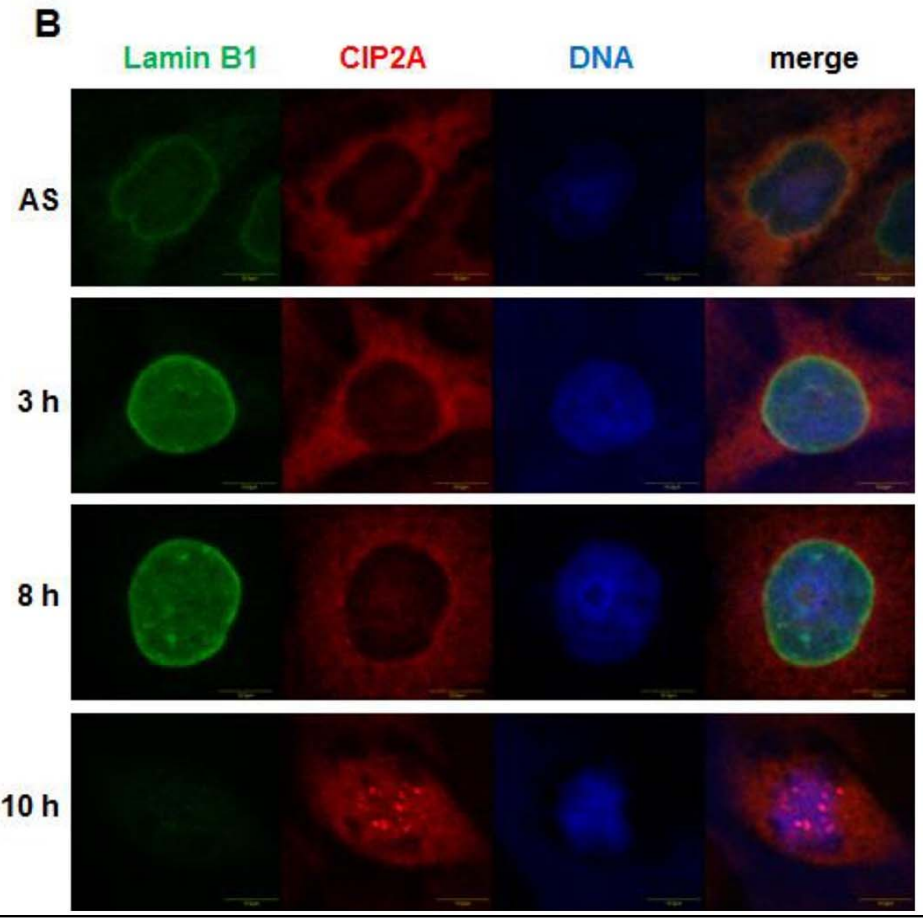
3. Cancerous inhibitor of protein phosphatase 2A (CIP2A)

binds to scaffold subunit and target substrate

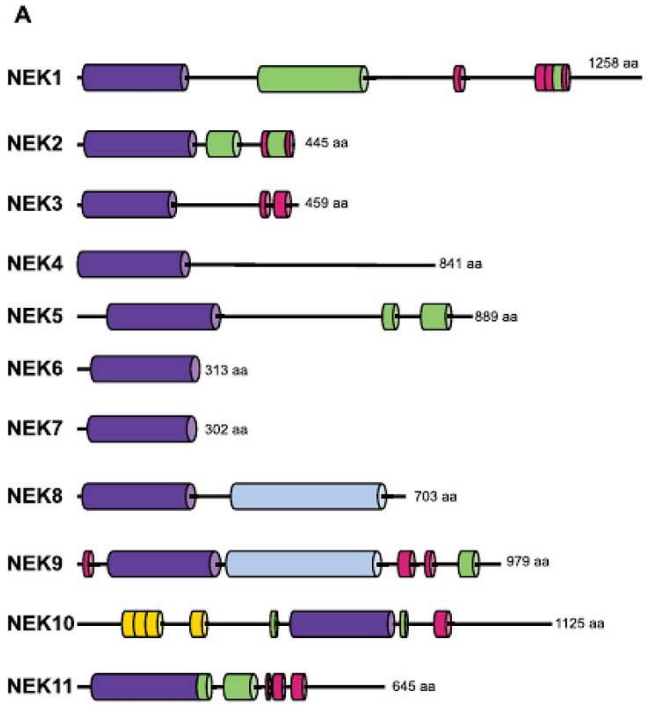


Junttila, Puustinen et al, *Cell* (2007)

CIP2A localizes at various sites during cell cycle



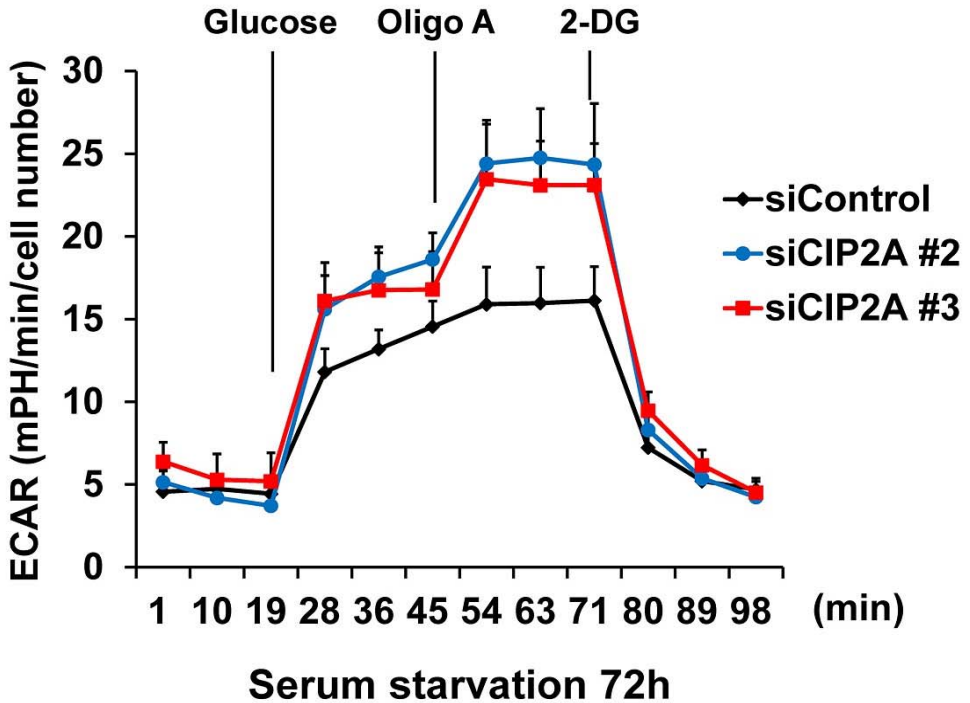
The human NIMA-related protein kinase (NEK) family.



	Activation	Localization	Function
NEK1	Genotoxic insults (IR, UV, crosslinking agents, oxidative injury)	Cytoplasm, centrosomes, cilia, sites of DNA damage	Cilia and DDR
NEK2	S, G2-M	Centrosomes	Mitosis
NEK3	Prolactin receptor stimulation	Cytoplasm	Prolactin signalling
NEK4	?	Basal bodies	Cilia
NEK5	?	?	?
NEK6	Activated by NEK9, mitosis	Mitotic spindle	Mitosis
NEK7	Activated by NEK9, mitosis	Weakly to spindle poles	Mitosis
NEK8	Serum starvation	Nucleus, centrosomes, cilia	Cilia
NEK9	Mitosis	Cytoplasm, spindle poles	Mitosis
NEK10	UV, G2-M	?	DDR
NEK11	DNA replication inhibitors and genotoxic insults, S to G2-M transition	Nucleus and/or nucleoli	DDR

Fry A M et al. J Cell Sci 2012;125:4423-4433

Knockdown of CIP2A enhances glycolysis



Session II

이 경 (동국대 약대)

Chemical biology inspired drug development for tumor remission

Chemical biology inspired drug development for tumor remission

Kyeong Lee, Ph.D.

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The goal of our MRC center, Innovative Medicine Research Center for Tumor Remission (IMRCTR) is to provide a new therapeutic basis for cancer remission by identifying novel drug candidates that target common characters of microenvironments in cancer and autoimmune diseases, which are intractable diseases. In particular, we intend to present a new therapeutic strategy to overcome cancer by remodeling microenvironmental factors such as neuro, inflammation and hypoxia (N, I, H) in integral strategy.

Several sub-programs for drug discovery are in progress and the recent results on development of small chemical using chemical biology approach will be presented. Aminoacyl-tRNA synthetase-interacting multi-functional protein 2 (AIMP2) is one of the components of multi-tRNA synthetase complex (MSC) which consists of four exons and serves as a potent tumor suppressor. AIMP2 dissociation from the MSC influences the activity of the p53, TGF-β, TNF-α and WNT signaling pathways, which inhibits tumorigenesis. AIMP2-DX2, an exon2-deleted splicing variant of AIMP2, is up-regulated in various cancers and competitively suppresses the pro-apoptotic activity of AIMP2 and promote tumorigenesis. A recent mechanism study revealed that Hsp70 is a critical determinant for cellular level of AIMP2-DX2. Specifically, a positive correlation between HSP70 and AIMP2-DX2 levels was shown in various lung cancer cell lines and patient tissues, which supports the therapeutic potential of an AIMP2-DX2 and Hsp70 inhibitors as anticancer agents. A structure-activity relationship study using a sulfonamide-based hit led to the small molecule protein-protein inhibitor, BC-DXI-495. Chemical intervention using BC-DXI-495 of the AIMP2-DX2:HSP70 interaction suppressed cancer cell growth in vitro and in vivo. We will discuss more detailed chemistry and mechanism on this series as novel AIMP2-DX2 inhibitors for development of novel cancer therapeutics.

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Education

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3. 1995-2000: University of Georgia, College of Pharmacy, USA (Ph.D. Degree)

4. 2000-2004: National Institutes of Health, USA (Postdoc)

Experience

1. 2004-2009: Senior Research Associate & Principal Investigator, Molecular Therapeutics Center, Korea Research Institute of Bioscience and Biotechnology, Daejeon, Korea

2. 2009-now: Associate Professor & Professor, College of Pharmacy, Dongguk Univeristy, Goyang, Korea

3. 2012-2018: Director, Open Translational Research Centr for Innovative Drug (NRF)

4. 2018-2027: Director, Innovative Medicine Research Center for Tumor Remission (NRF, MRC)

References (Recent articles among 172 peer reviewed articles)

1. Lu, Q.L., et al., Total Synthesis of the Neuroprotective Agent Cudraisoflavone J. J Nat Prod. 2021. **84**(4): p. 1359-1365.
2. Sivaraman, A., et al., Synthesis and Structure-Activity Relationships of Arylsulfonamides as AIMP2-DX2 Inhibitors for the Development of a Novel Anticancer Therapy. J Med Chem. 2020. **63**(10): p. 5139-5158.
3. Lim, S., et al., Targeting the interaction of AIMP2-DX2 with HSP70 suppresses cancer development. Nat Chem Biol, 2020. **16**(1): p. 31-41.
4. Kim, I.H., et al., The disubstituted adamantyl derivative LW1564 inhibits the growth of cancer cells by targeting mitochondrial respiration and reducing hypoxia-inducible factor (HIF)-1α accumulation. Exp Mol Med. 2020**. 52**(11): p.1845-1856.
5. Jalani, H.B., et al., Iodine-Promoted One-pot Synthesis of Highly Substituted 4-Aminopyrroles and Bis-4-aminopyrrole from Aryl Methyl Ketones, Arylamines, and Enamines. Advanced Synthesis and Catalysis, 2018. **360**(21): p. 4073-4079.
6. Bhattarai, D., et al., Hypoxia-inducible factor-1 (HIF-1) inhibitors from the last decade (2007 to 2016): A "structure-activity relationship" perspective. Med Res Rev, 2018. **38**(4): p. 1404-1442.
7. Naik, R., et al., Methyl 3-(3-(4-(2,4,4-Trimethylpentan-2-yl)phenoxy)-propanamido)benzoate as a Novel and Dual Malate Dehydrogenase (MDH) 1/2 Inhibitor Targeting Cancer Metabolism. Journal of Medicinal Chemistry, 2017. **60**(20): p. 8631-8646.

Chemical Biology Inspired Drug Development for Tumor Remission

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https://imrctr.dongguk.edu/

동국대학교
dongguk university

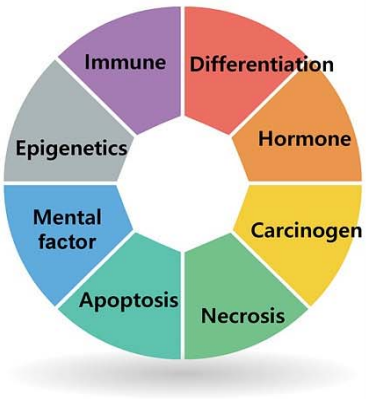
Trends in Cancer Therapeutics

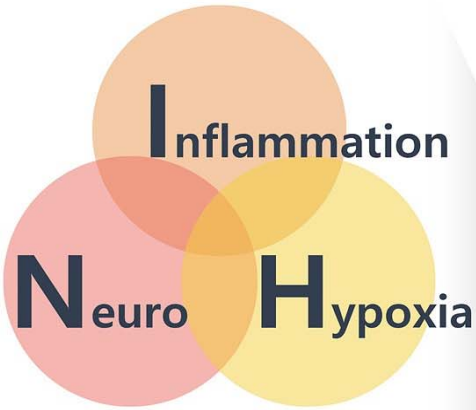
Innovative Medicine Research Center for Tumor Remission

National Research Foundation of Korea

iMRCTR Innovative Medicine Research Center for Tumor Remission

Derive new cancer-specific targets other than immunity from factors that cause cancer remission



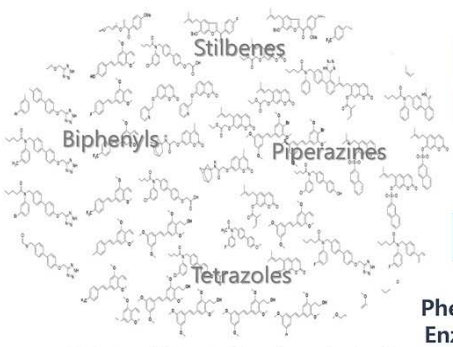


Novel Therapy for Cancer Remission

Through the single or combination action of substances that integrally regulate the NIH target, We are trying to realize the means of getting closer to the overcoming of cancer.

Open for Collaboration: Privileged Chemical Library

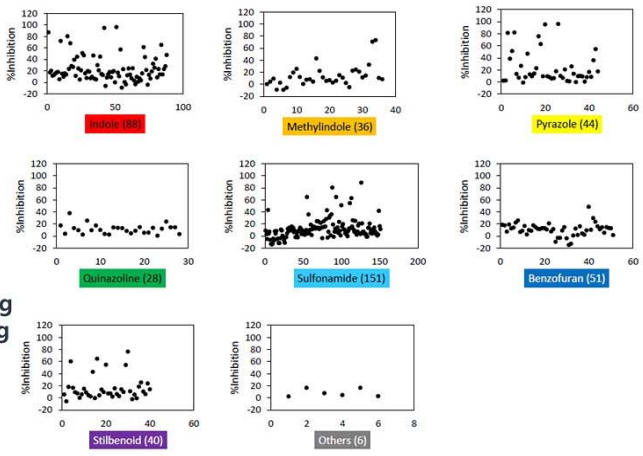
Construction of Privileged Chemical Library and
Its Application in the Development of Anticancer Agent Targeting N, I, and H



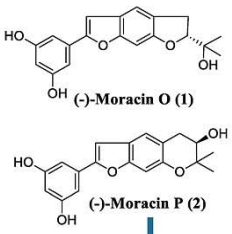
FDA- and Natural Product-derived
In House Chemical Library

구조	수
Indole	88
Methylindole	36
Pyrazole	44
Quinazoline	28
Sulfonamide	151
Benzofuran	51
Stilbenoid	40
Other	6

Phenotype Screening
Enzymatic Screening



Benzofurans



COMMUNICATION www.rsc.org/chemcomm | ChemComm

The first total synthesis of moracin O and moracin P, and establishment of the absolute configuration of moracin O†

Navneet Kaur,‡[a] Yan Xia,‡[a] Yinglan Jin,[a] Nguyen Tien Dat,[a] Kondaji Gajulapati,[b] Yongseok Choi,[b] Young-Soo Hong,[a] Jung Joon Lee[a] and Kyeong Lee*[a]

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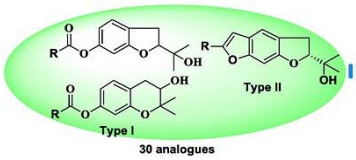
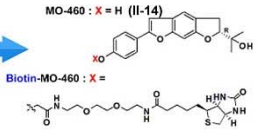
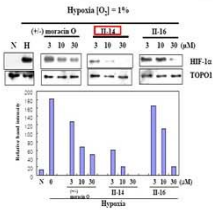
First published as an Advance Article on the web 4th March 2009
DOI: 10.1039/b823340e

HIF inhibitors

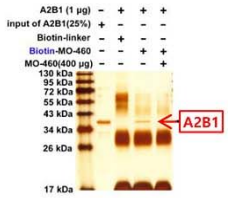




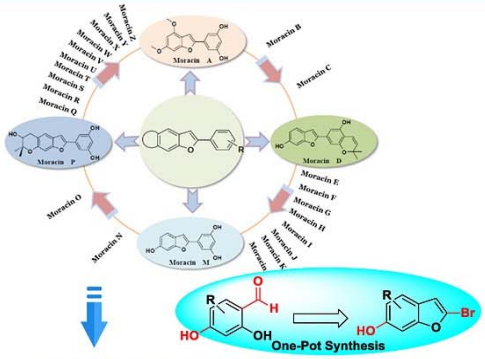
MO-460 HIF transcriptional activity



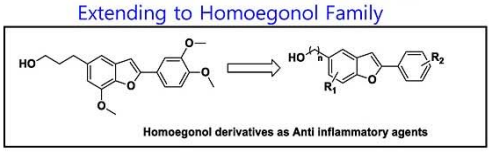
Target Identification



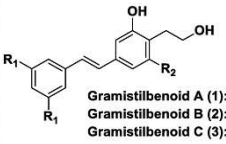
Library Expansion



Extending to Homoegonol Family



Stilbenes



JOURNAL OF NATURAL PRODUCTS

Total Synthesis of Gramistilbenoids A, B, and C

Dipesh S. Harmalkar, Qili Lu, and Kyeong Lee*

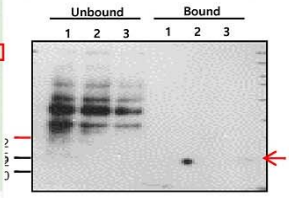
College of Pharmacy, Dongguk University-Seoul, Goyang, 10326, Republic of Korea

Anticancer

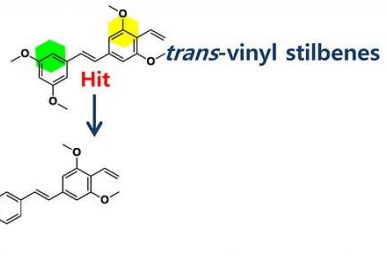
"unknown"
Target Protein

"known"
Identified as Tubulin

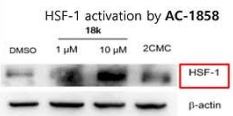
LANE	Compound
1	DMSO
2	Biotin
3	Stilbenoid AC-1743



Anti Norovirus



AC-1858 : EC_{50} = 2.43 μM; CC_{50} ≥ 100 μM; TI ≥ 41.2



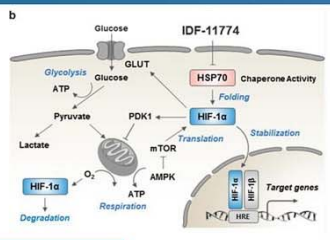
European Journal of Medicinal Chemistry

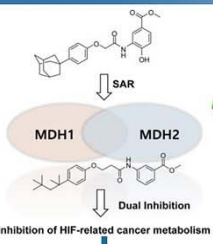
Research paper

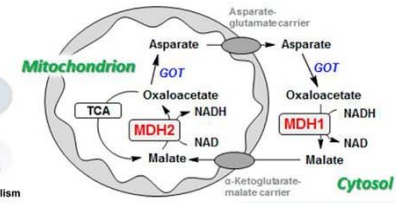
Identification of novel non-nucleoside vinyl-stilbene analogs as potent norovirus replication inhibitors with a potential host-targeting mechanism

Dipesh S. Harmalkar, Sung-Jin Lee, Qili Lu, Mi Il Kim, Jaehyung Park, Hwayoung Lee, Minkyung Park, Ahrim Lee, Choongho Lee, Kyeong Lee*

Aryloxyacetamides

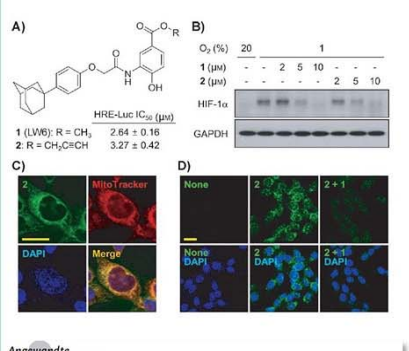






HIF-1a inhibitor

MDH1/2 dual inhibitor

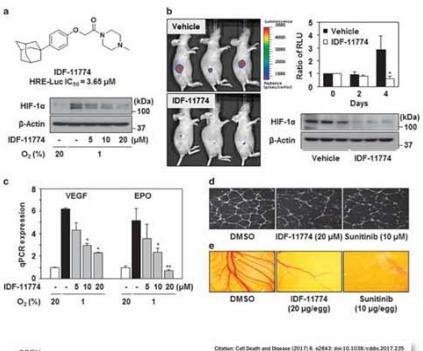


Angewandte Communications

Target Identification

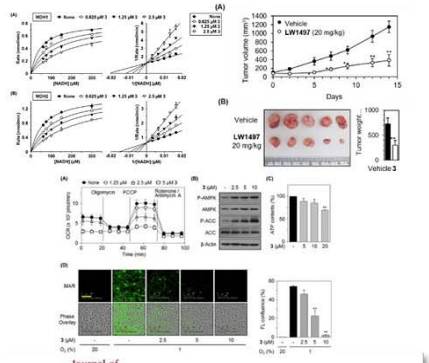
Identification of Malate Dehydrogenase 2 as a Target Protein of the HIF-1 Inhibitor LW6 using Chemical Probes

Kyeong Lee, Hyun Seung Ban, Ravi Naik, Ye Seul Hong, Seohyun Son, Bo-Kyung Kim, Yan Xia, Kyung Bin Song, Hong-Sub Lee, and Misun Won*



OPEN

The novel hypoxia-inducible factor-1α inhibitor IDF-11774 regulates cancer metabolism, thereby suppressing tumor growth



Journal of Medicinal Chemistry

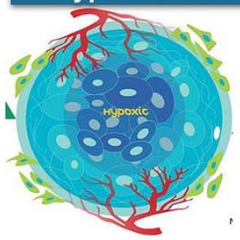
Methyl 3-(3-(4-(2,4,4-Trimethylpentan-2-yl)phenoxy)-propanamido)benzoate as a Novel and Dual Malate Dehydrogenase (MDH) 1/2 Inhibitor Targeting Cancer Metabolism

Ravi Naik, Hyun Seung Ban, Kyusic Jang, Inhyub Kim, Xuezhen Xu, Dipesh Harmalkar, Seong-Ah Shin, Minkyoung Kim, Bo-Kyung Kim, Jaehyung Park, Bonsu Ku, Sujin Oh, Misun Won, and Kyeong Lee

NIH Target: AIMP2-DX2

- AIMP2-F: Novel tumor suppressor
- AIMP2-DX2: Novel oncogene, Alternative splicing variant of AIMP2-F
- Increase of AIMP2-DX2, decrease of AIMP2: cancer progression under Hypoxia
- AIMP2-DX2 diagnosis, In vitro assay, In vivo efficacy

Hypoxia & AIMP2-DX2



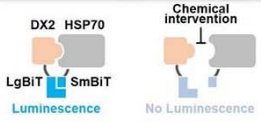
AIMP2-F ↓

AIMP2-DX2 ↑

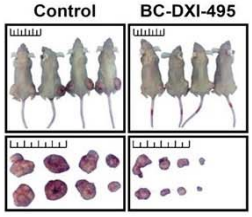
Cancer proliferation ↑

Tumor in hypoxia condition

Screening strategy

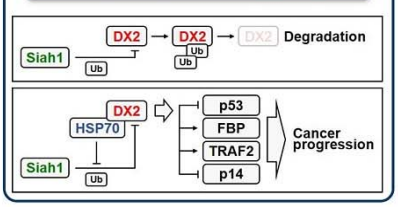


Anti-tumor efficacy

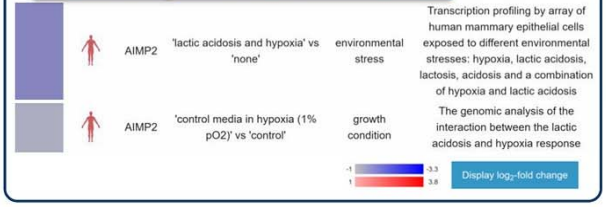


Cancers (2019)
Nature Chemical Biology (2019)
Cancer Res. (2012)
PLoS GENETICS (2008)

MOA of AIMP2-DX2



Gene expression of AIMP2-F



- AIMP2-DX2: Potent target for cancer treatment in hypoxia condition

Screening Hit

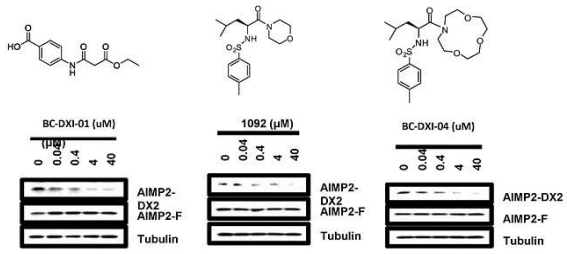


Figure: DX2 inhibition effect (WB)

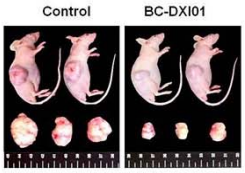


Figure: Inhibits the proliferation of lung cancer in vivo

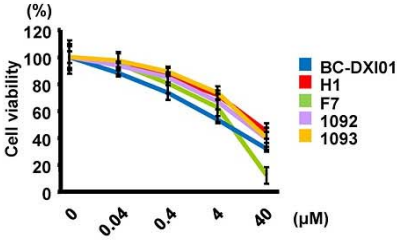
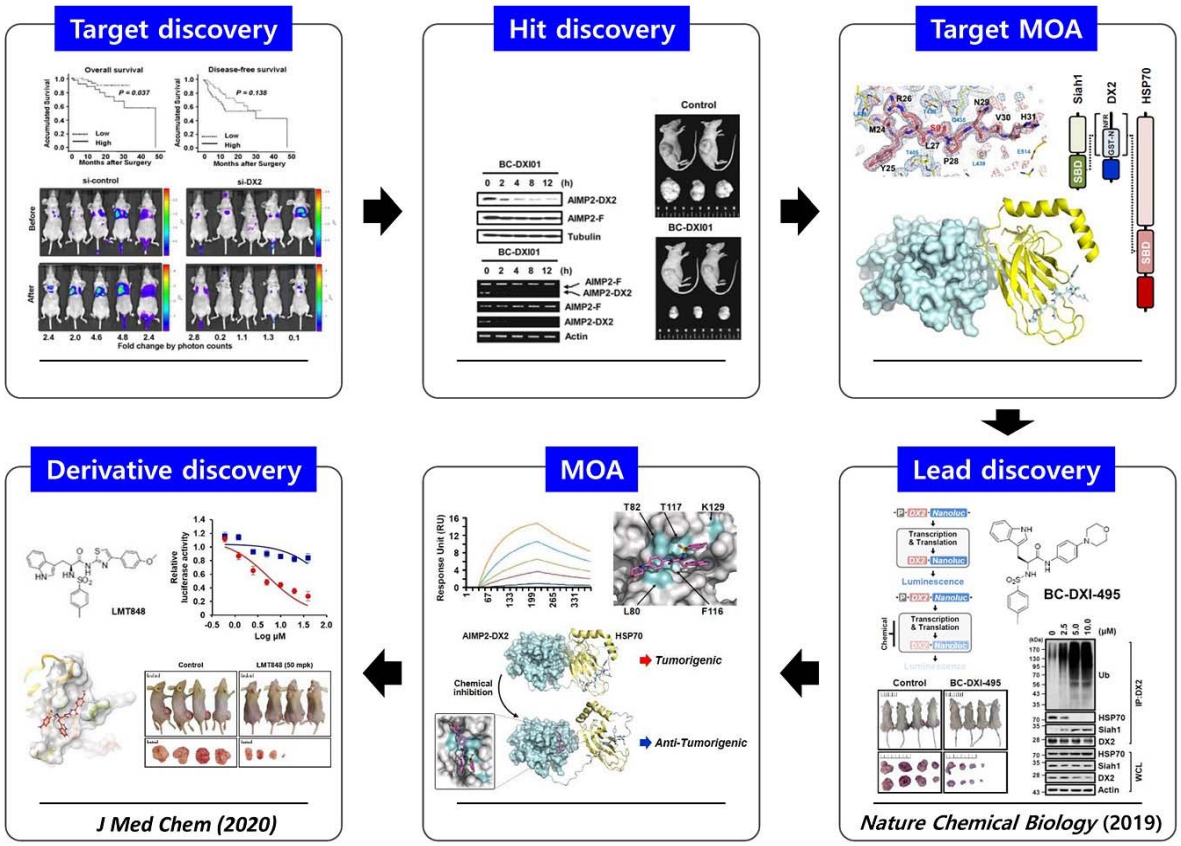


Figure: Cell death effect of novel compounds

Small Molecule PPI for DX2-Hsp70



Session II

고혁완 (연세대 생명시스템대학)

Understanding the Hedgehog signaling pathway using small - molecule probes: Closing the gap between chemistry and biology

Understanding the Hedgehog signaling pathway using small-molecule probes: Closing the gap between chemistry and biology

Hyuk Wan Ko, Ph.D.

Department of Biochemistry, College of Life Science and Biotechnology

Yonsei University, Seoul, Republic of Korea

The Hedgehog (Hh) signaling pathway regulates many aspects of the cellular process such as cell growth, survival, and fate determination. Disruption of Hh signaling in early development causes developmental disorders. Aberrant activation in the Hh pathway by somatic mutations has been linked to multiple forms of cancers in humans. Molecular logic of the Hh signaling was initially established from genetic studies in the *Drosophila* model system. They have been considered as having a conserved role in mammalian Hh signaling. Currently, many components of the Hh signaling pathway are identified from various animal model systems such as fly, zebrafish, and mouse. However, there are accumulating evidences that divergent aspects of Hh signaling between *Drosophila* and mammals exist. In a way to better understand the mammalian Hh signaling pathway, we identify the novel pathway components in the mammalian cultured cells. We screened the compound libraries to discover novel bioactive small molecules for the Hh pathway. Using chemical probes designed from identified small molecules, we found that cellular storage organelles of neutral lipid, lipid droplets play a role in regulating the Hh signaling in mammals. Downregulation of lipid droplet formation by siRNA or chemical inhibitors disrupts Hh signaling. We further revealed that molecular mechanisms of lipid droplets in regulating Hh signaling are involved in controlling the formation of primary cilia which are important cellular organelle for transducing mammalian specific Hh signaling. These studies exemplify the power of cross-field cooperation between chemistry and biology to isolate unbiased drug targets for the Hh pathway and provide a new paradigm for the Hh signaling pathway.

발표자 이력서

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Education

1. 1989-1996: Yonsei University, Seoul, Korea (B.S.)
2. 1998-2004: Rutgers University, NJ, USA (Ph.D. Degree)
3. 2005-2009: Princeton University, NJ, USA (Postdoc)

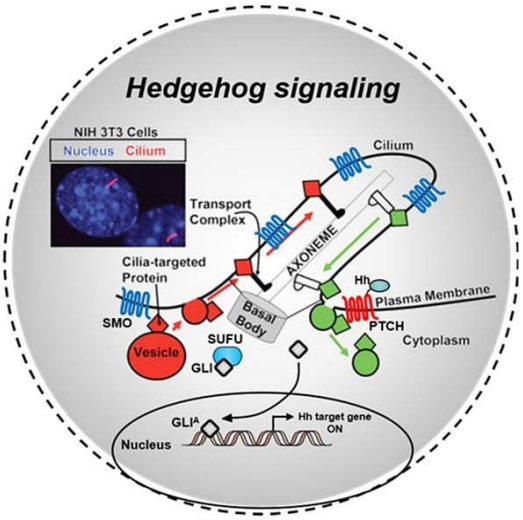
Experience

1. 2010-2012: **Assistant Professor**, Age-Related and Brain Diseases Research Center, Kyung Hee University, Seoul, Korea
2. 2012-2018: **Assistant Professor & Associate Professor**, College of Pharmacy, Dongguk University, Goyang-si, Korea
3. 2018-Present: **Associate Professor**, Department of Biochemistry, College of Life Science and Biotechnology, Yonsei University, Seoul, Korea

References (Recent articles among 56 peer reviewed articles)

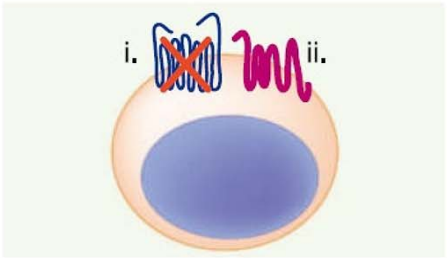
1. Moon, K. H. et al. Dysregulation of sonic hedgehog signaling causes hearing loss in ciliopathy mouse models. ***Elife***, 9:e56551, doi:10.7554/eLife.56551 (2020).
2. Lee, E. J. *et al.* Autophagy induction promotes renal cyst growth in polycystic kidney disease. ***EBioMedicine,*** 16, 102986, doi:10.1016/j.ebiom.2020.102986 (2020).
3. Lee, H and Ko H. W. Cell cycle-related kinase is a crucial regulator for ciliogenesis and Hedgehog signaling in embryonic mouse lung development. ***BMB Rep,*** 53, 367-372, doi:10.5483/BMBRep.2020.53.7.295 (2020).
4. Shin, J. O. *et al.* Activation of sonic hedgehog signaling by a Smoothened agonist restores congenital defects in mouse models of endocrine-cerebro-osteodysplasia syndrome. ***EBioMedicine,*** 49, 305-317, doi:10.1016/j.ebiom.2019.10.016 (2019).
5. Bosakova, M. K. *et al.* Fibroblast growth factor receptor influences primary cilium length through an interaction with intestinal cell kinase. ***Proc Natl Acad Sci*** 116, 4316-4325, doi:10.1073/pnas.1800338116 (2019).

Understanding the Hedgehog signaling pathway using small-molecule probes: Closing the gap between chemistry and biology

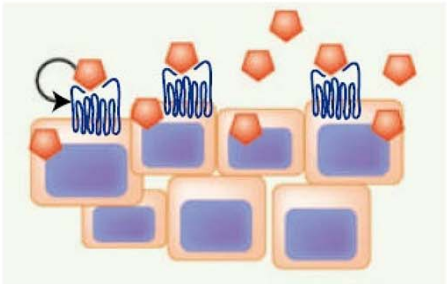


Hyuk Wan Ko, Ph.D.
Yonsei University

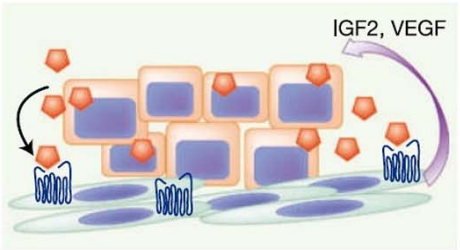
Hedgehog signaling activation in cancers



Type I. Mutational activation
- Basal cell carcinoma
- Medulloblastoma
- Pediatric brain tumor
- Rhabdomyosarcoma

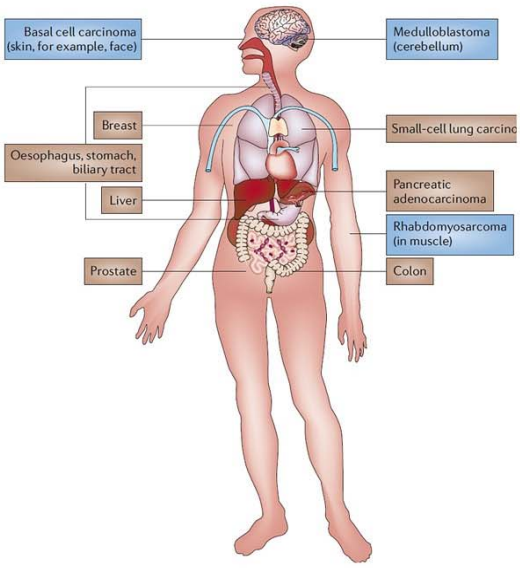


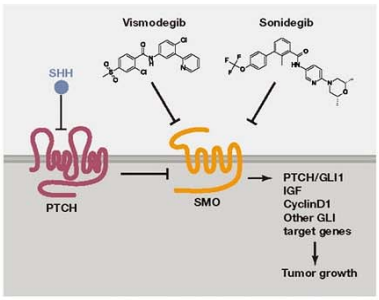
Type II. Autocrine
- Colorectal
- Prostate
- Liver
- Breast
- Ovarian
- Brain
- Melanoma



Type III. Paracrine
- Pancreatic
- Leukemia

Targeting Hedgehog signaling for drug discovery





The hedgehog (Hh) signaling pathway is aberrantly activated in a majority of basal cell carcinomas (BCC). Vismodegib and sonidegib are targeted inhibitors of Smoothened (SMO). Both drugs are approved for use in locally advanced BCC (laBCC), with vismodegib also approved for metastatic BCC (mBCC).

NAME
Vismodegib (Erivedge) and sonidegib (Odomzo)

APPROVED FOR
Locally advanced BCC (vismodegib and sonidegib) and metastatic BCC (vismodegib)

TYPE
Small molecules

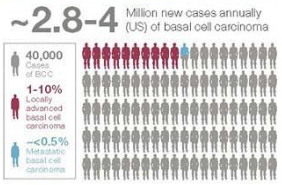
MOLECULAR TARGETS
Vismodegib and sonidegib bind to and inhibit Smoothened (SMO), a transmembrane protein involved in Hh pathway signal transduction.

CELLULAR TARGETS
Extracellular Hh ligands bind to the receptor patched (PTCH), alleviating PTCH-mediated inhibition of SMO. Uninhibited SMO signals through several proteins, including SUFU, leading to activation of Gli-mediated gene transcription (e.g., PTCH/GLI, IGF, cyclin D) and cellular proliferation.

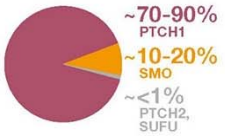
EFFECTS ON TARGETS
Inhibition of SMO results in decreased Gli levels, reduction of Gli-controlled transcription, and reduced cellular proliferation.

DEVELOPED BY
Vismodegib | Curis > Genentech/Roche
Sonidegib | Novartis

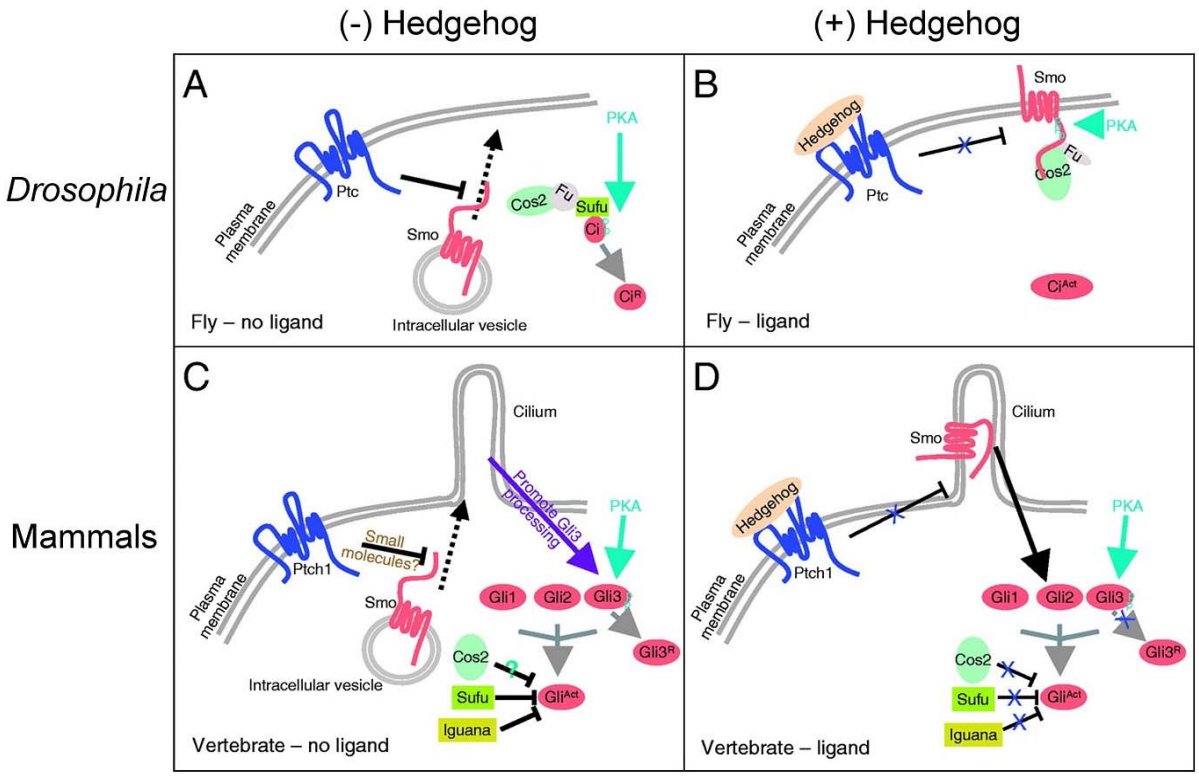
Basal cell carcinoma incidence



Sporadic mutations in BCC

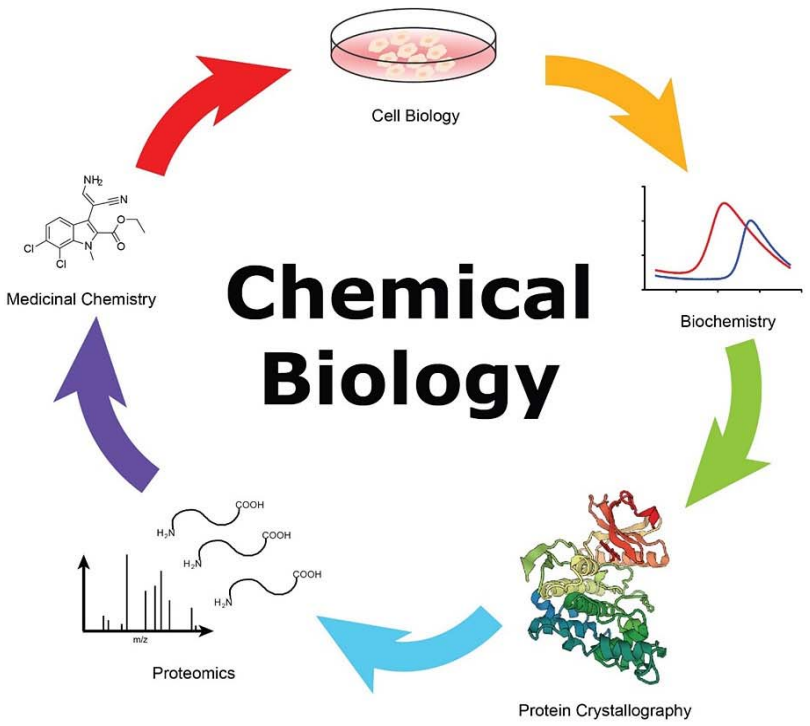


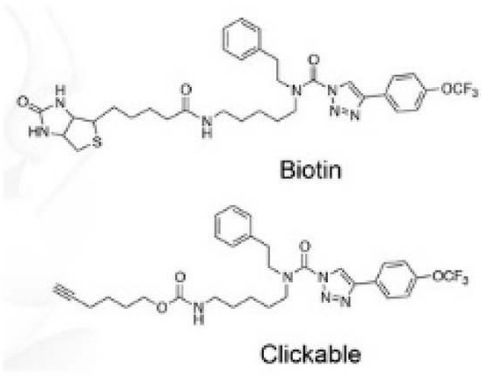
Divergence of Hedgehog signal transduction mechanisms



Huangfu D et al. (2006) Development

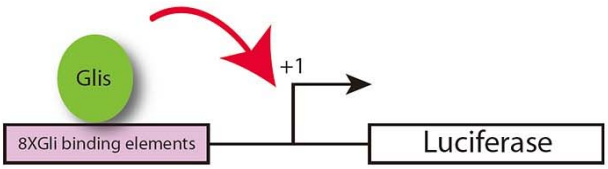
Chemical biology approache to identify the Hh components

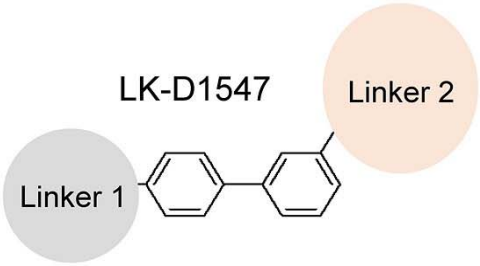


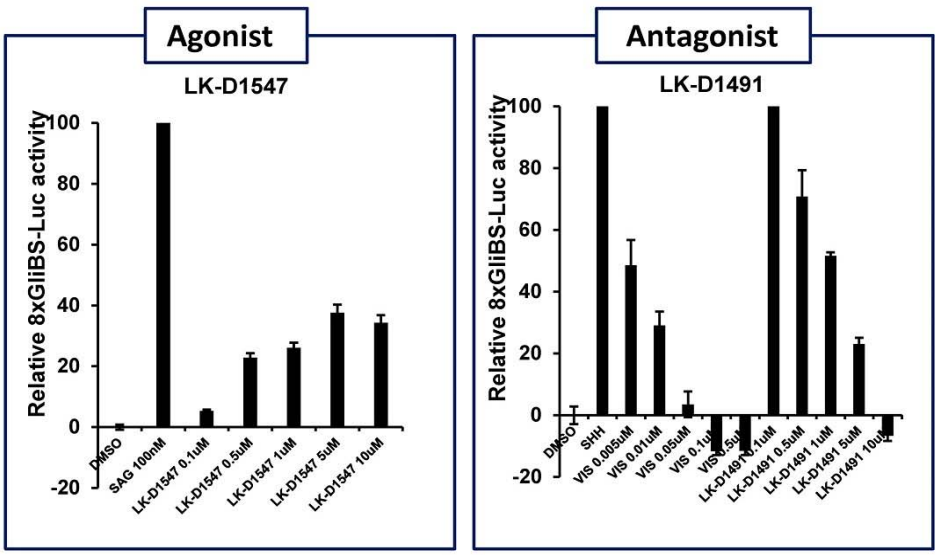


Activity-Based Probe

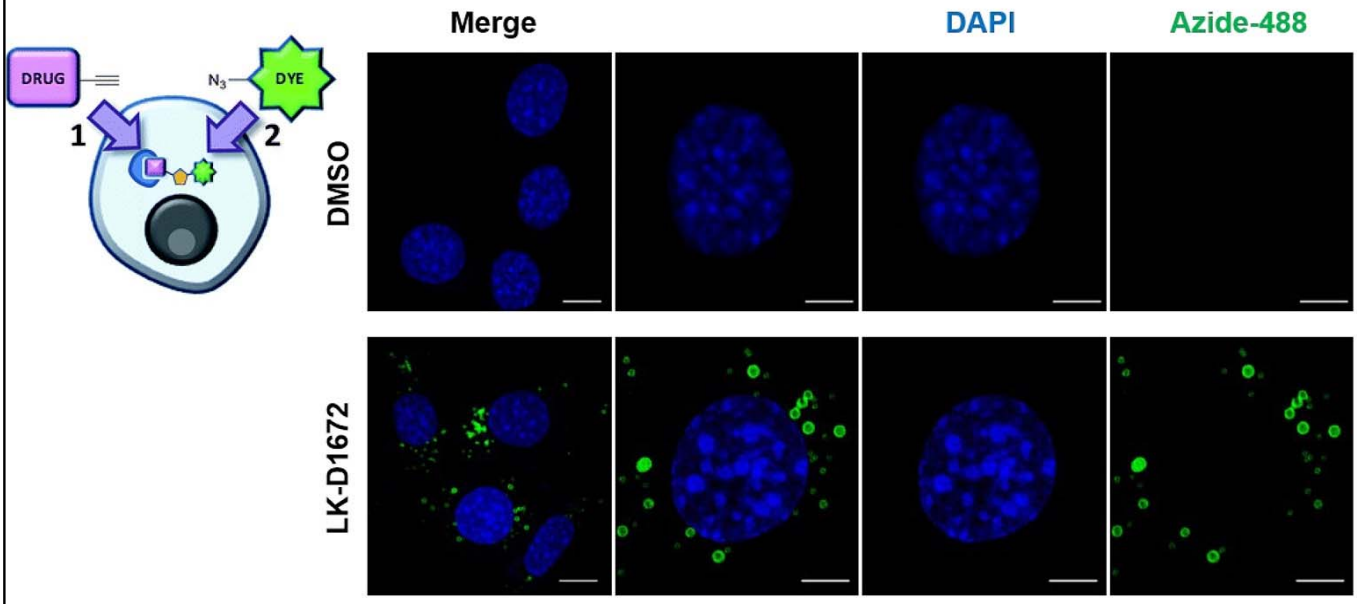
Hh pathway activity screening for Pyrazole derivatives



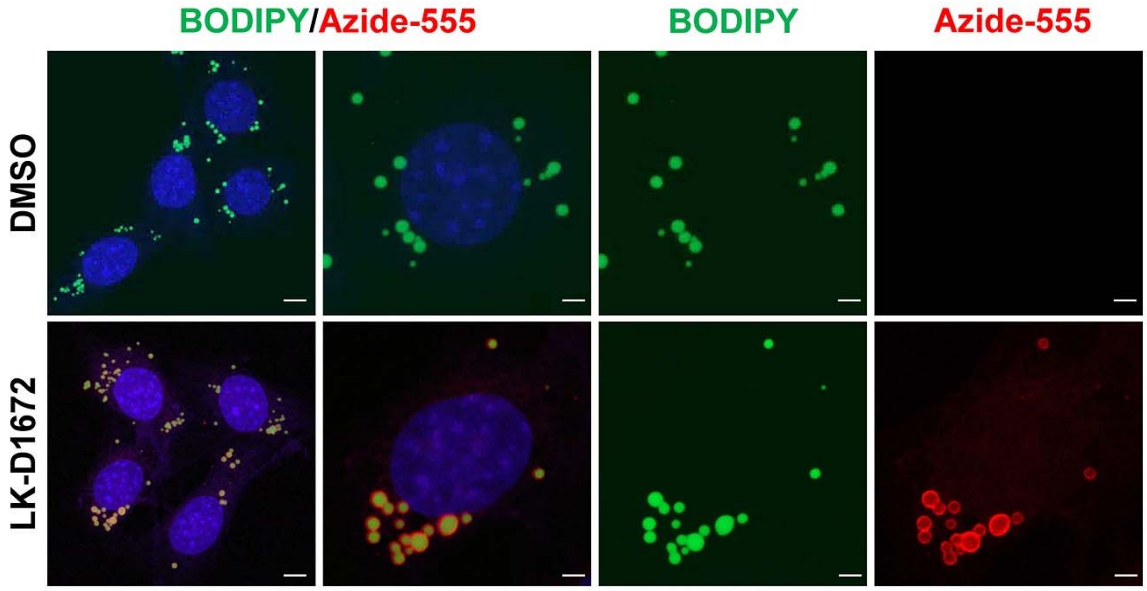




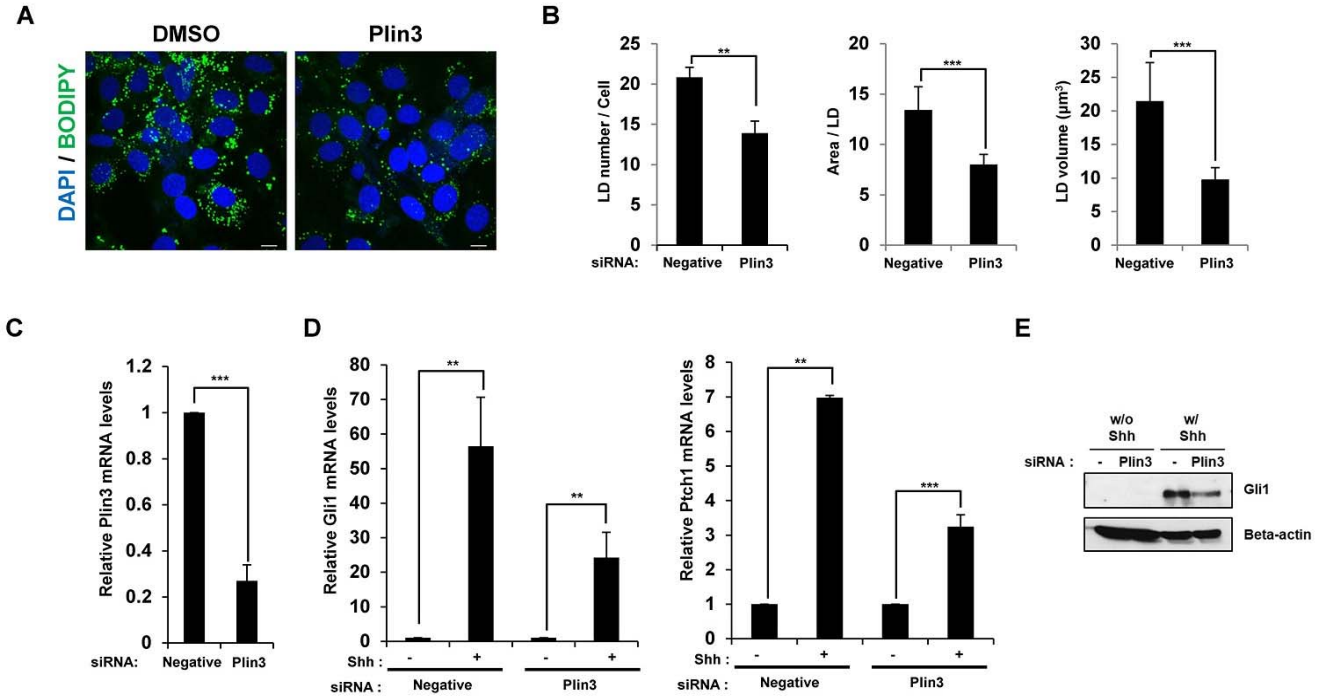
Cellular localization of bioactive chemical for Hh pathway



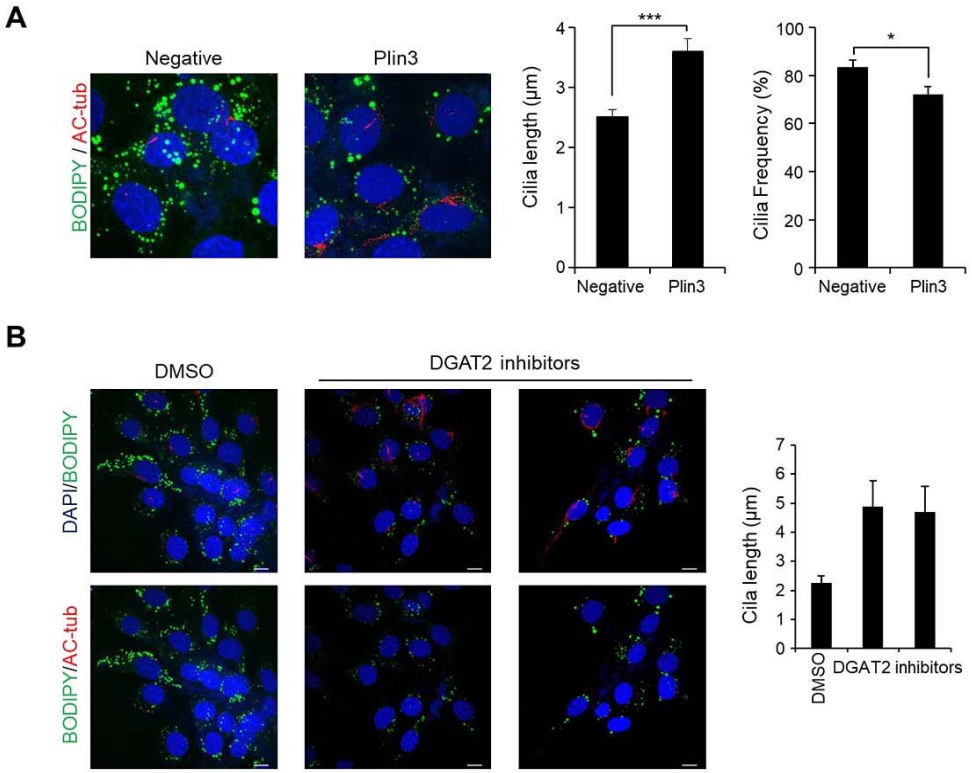
Pyrazole compound modulating Hh pathway activity localizes in lipid droplets



Lipid droplets are necessary for Hh signal transduction



Lipid droplets regulate ciliogenesis



Session III

좌장: **박종훈** 숙명여대 / **육종인** 연세대

7월 30일 7:30-9:00

좌장 이력서

Jong Hoon Park, Ph.D.

Professor

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E-mail: parkjh@sookmyung.ac.kr

Education

1. 1980-1987: **B.S.**, Department of Biochemistry, Yonsei University, Seoul
2. 1987-1989: **M.S.**, Department of Biochemistry, Yonsei University, Seoul
3. 1990-1996: **Ph.D.**, Department of Biochemistry, Yonsei University, Seoul

Experience

1. 2001- : **Professor,** Department of Biological Science, Sookmyung Women's University
2. 2007-2008: **Chief**, Industry-Academic cooperation Foundation in Sookmyung Women's University
3. 2011- : **Director**, Korean Society for Biochemistry and Molecular Biology
4. 2016-2019: **Committee Member**, National Science Museum
5. 2017-2018: **Chairman**, Presidential Advisory council on Science & Technology, Basic Science & Infra Committee
6. 2018-2020: **Chairman**, Ministry of Science and ICT, Science Technology · ICT internationalization Project Promotion Committee
7. 2020- : **Vice President**, Korean Society for Biochemistry and Molecular Biology

References

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2. Impact of miR-192 and miR-194 on cyst enlargement through EMT in autosomal dominant polycystic kidney disease. **Faseb Journal** (2019 Feb) 33(2):2870-2884
3. The autophagy regulator p62 controls PTEN-dependent ciliogenesis. **Frontiers in cell and developmental biology** (2020 June) 8(465)
4. Autophagy induction promotes renal cyst growth in polycystic kidney disease. **EBioMedicine** (2020 Oct)
5. TAZ/Wnt-β-catenin/c-MYC axis regulates cystogenesis in polycystic kidney disease. **PNAS (Proceedings of the National Academy of Sciences of the United States of America)** (2020 Nov) 117(46):29001-29012

Session III

육종인 (연세대학교 치과대학)

Cell-based assay system of 3C-like protease for Covid-19 therapeutics

좌장 이력서

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Professor
Department of Oral Pathology
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CEO
MET Life Sciences, Seoul, Korea
E-mail: jiyook@yuhs.ac

Education

1. 1981-1987: College of Dentistry, Yonsei University. D.D.S.
2. 1991-1995: Department of Oral Pathology, College of Dentistry, Yonsei University (Ph.D)

Experience

1. 1996-1997: **Lecturer**, College of Dentistry, Yonsei University
2. 1998-2003: **Assistant Professor**, College of Dentistry, Yonsei University
3. 2001-2003: **Visiting Scholar**, University of Michigan, U.S.A.
4. 2003-2008: **Associated Professor**, College of Dentistry, Yonsei University
5. 2009-present: **Professor**, College of Dentistry, Yonsei University
6. Founder: **President**, MET Life Sciences

Academic Society

1. 1996-present: **Board member**, Korean Society of Oral & Maxillofacial Pathology
2. 2006-present: **Member**, Kor. Soc. of Biochem. & Mol. Biol. (KSBMB)

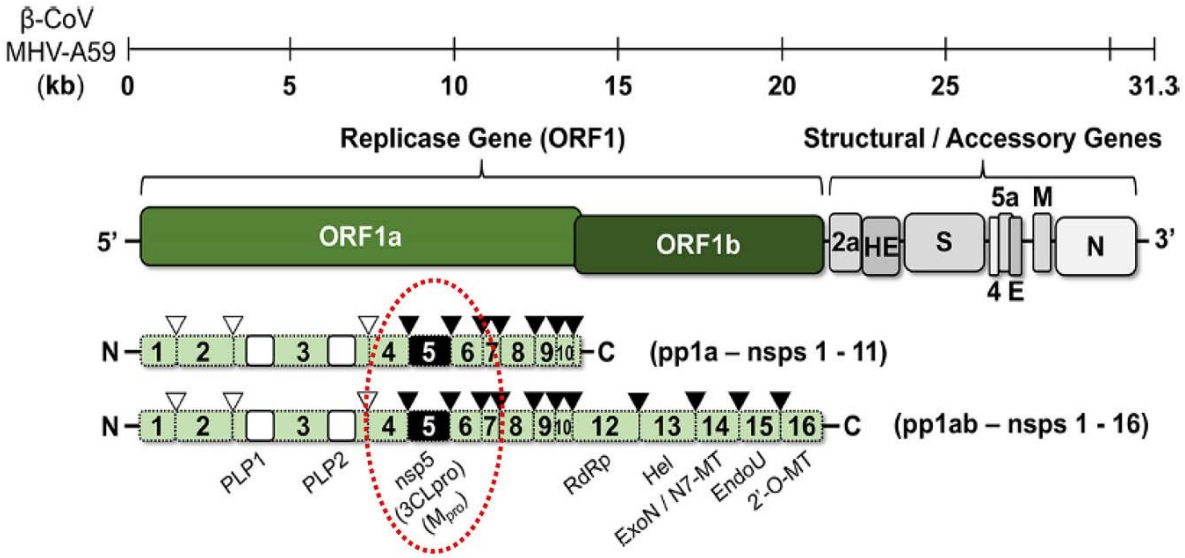
Cell-based Assay Systems of 3C-like protease ($3CL^{pro}$) for SARS-CoV-2 Therapeutics

Jong In Yook

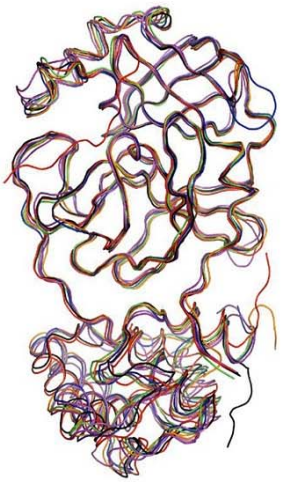
MET Life Sciences

Yonsei University College of Dentistry

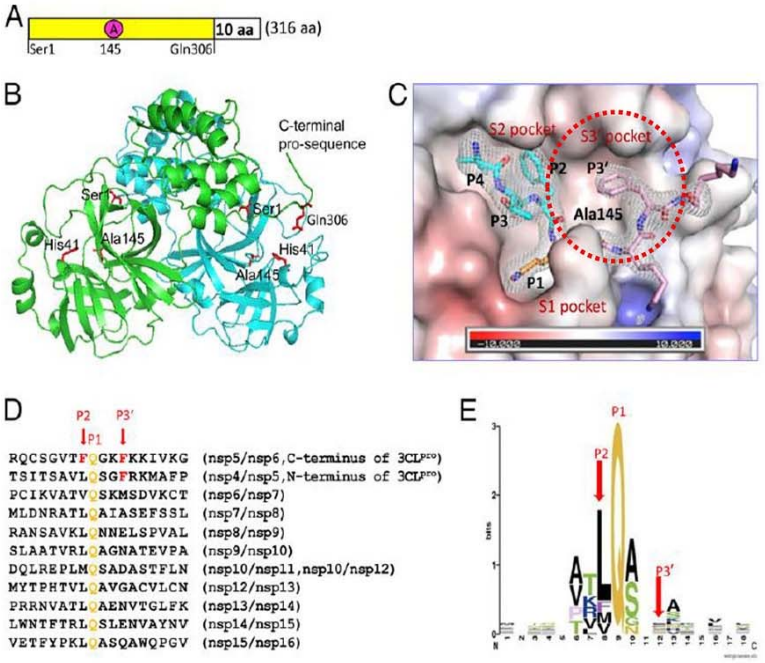
SARS-CoV-2 genome organization and polyprotein processing



3CL^{pro} is highly conserved and Cys145 is key residue for its catalytic activity



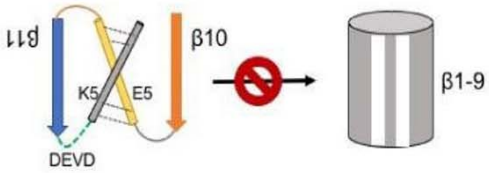
SARS-CoV-2
SARS-CoV
MERS-CoV
HCoV-229E
HCoV-OC43
HCoV-HKU1
HCoV-NL63



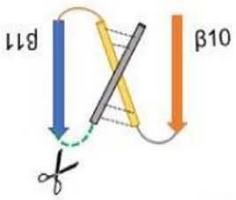
PNAS 2016, 113, 12997

Assay systems for 3CL^{pro} inhibitors

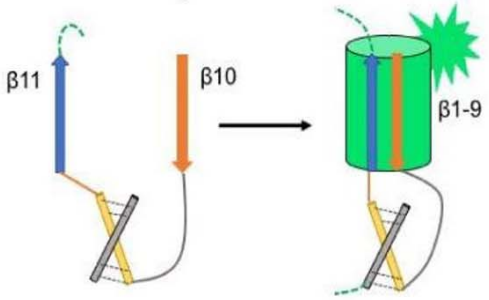
Inactive FilpGFP



Cleavage by 3CL^{pro}

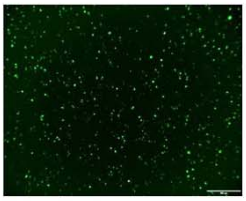


Active GFP



Dox (-)

Dox (+)



Session III

강상원 (이화여대 자연과학대/바스테라 대표)

An adaptive signaling for survival against oxidative stress in cancer

An adaptive signaling for survival against oxidative stress in cancer cells

Sang Won Kang

Department of Life Science

Ehwa Womans University, Korea

Aerobic organisms are under a constant challenge from oxidative stress (OS), which is one of key factors that determine the cell fate {Finkel, 2000 #406}. Mitochondria are the major subcellular organelles susceptibly responding to OS {Dyall, 2004 #167;Newmeyer, 2003 #38}. Upon severe OS condition, the retrograde signaling by mitochondria executes programmed cell death by releasing pro-apoptotic factors, such as cytochrome c, apoptosis-inducing factor (AIF), and Smac/DIABLO. In this presentation, I show that HSP60 is the first mitochondrial factor that transmits a survival signal to nucleus in response to OS. In the mild OS-challenged cancer cells, mitochondria liberated HSP60 to cytosol. The HSP60 release occurs through the assembly of a mitochondrial membrane pore by the p38-dependent phosphorylation of mitochondrial fission factor 1 (MFF1). Consequently, the released HSP60 induces activation of the IKK complex and induction of the NF-kB-dependent gene expression.

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Education

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2. 1986-1988: M.S., Biochemistry, Yonsei Univ., Seoul, Korea
3. 1991-1994: Ph.D., Biochemistry, Yonsei Univ., Seoul, Korea

Experience

1. 1994-1995: Postdoc fellow, KRIBB, Korea
2. 1995-1999: Postdoc fellow, NHLBI/NIH, USA
3. 1999-2002: Staff Scientist, NHLBI/NIH, USA
4. 2002-present: Professor, Ehwa Womans University, Korea
5. 2018-present: CEO, VasThera Co. Ltd.

References (Recent articles among 56 peer reviewed articles)

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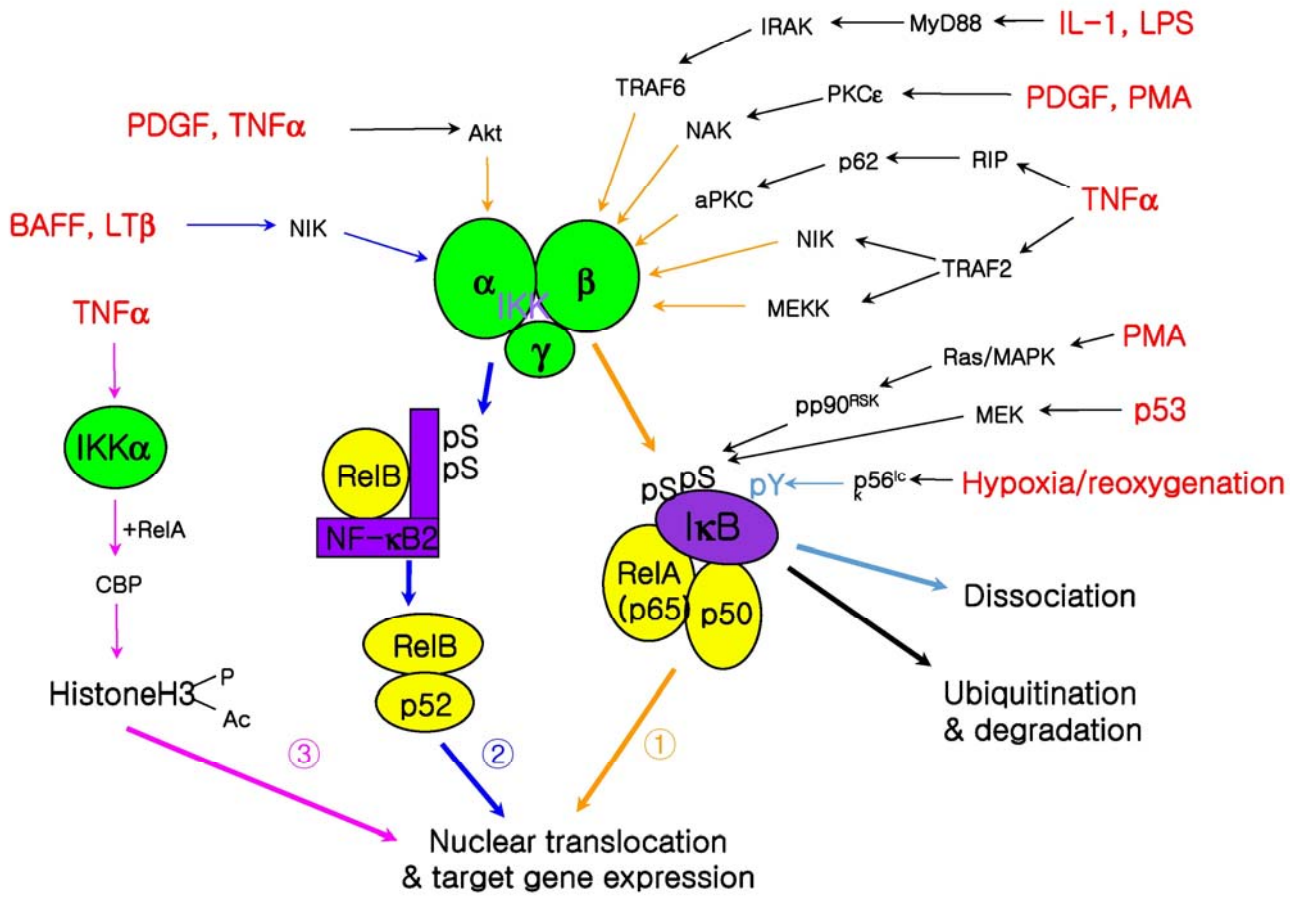
An Adaptive Signaling for survival against oxidative stress in cancer cells

Ewha Womans University/Life Science
Kang, Sang Won

Convergent NF-κB activation pathway



Multiple layers of IKK regulation

Ubiquitination

-NEMO is ubiquinated
-NEMO binds to RIP1(Lys63polyUbs)
-NEMO is sumolyated and ubiquitinated by DNA damage

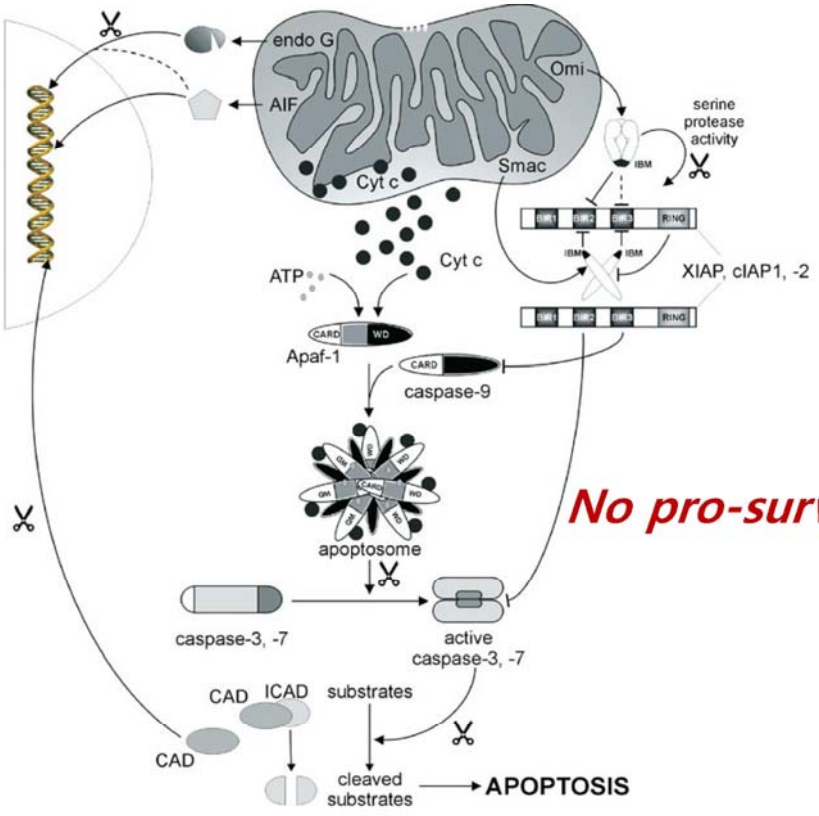
Phosphorylation

- NIK
- MEKK1
- MEKK2/3
- HPK1
- MLK3
- TAK1

IKK interactome

- Hsp90/Cdc37
- Hsp27
- Hsp70
- ELKS
- PP2C
- ???

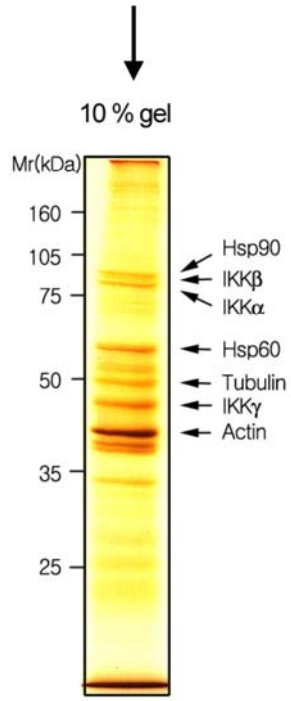
Mitochondrial pro-apoptotic proteins

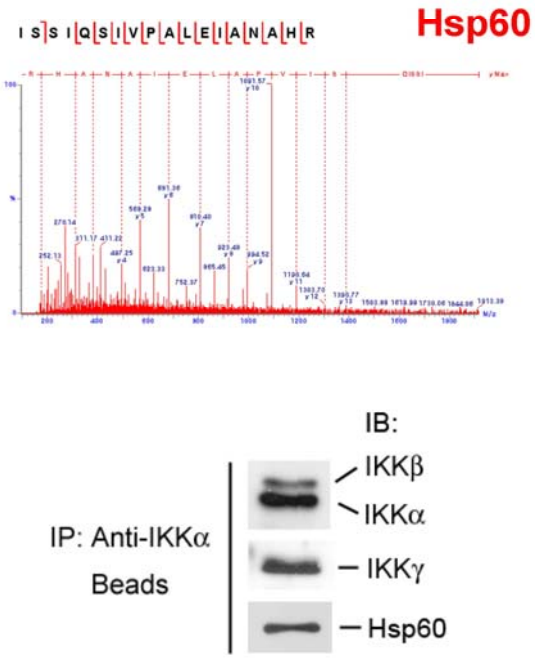


No pro-survival protein ever!!

Discovery of Hsp60 as IKK-binding protein

Immuno-affinity purification of IKK complex using anti-IKKα antibody-conjugated beads

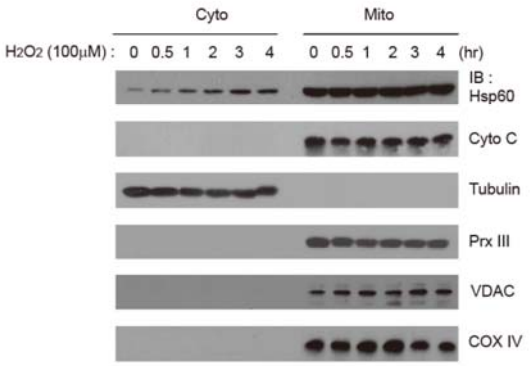


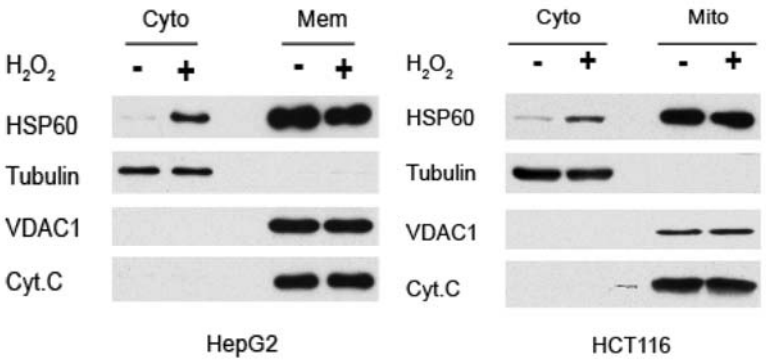


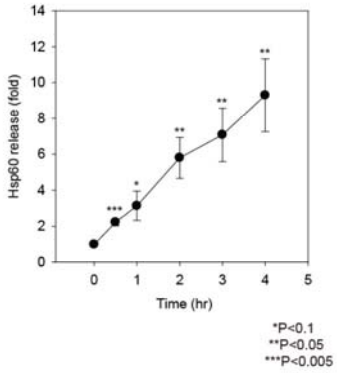
Origin of cytosolic Hsp60?

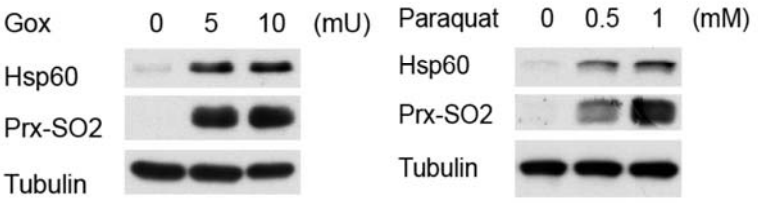
"Molecular survival messenger from mitochondria"

Mitochondria release Hsp60 upon oxidative stress

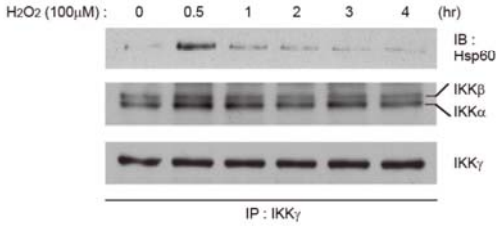


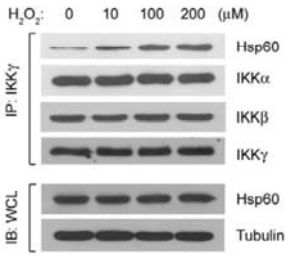


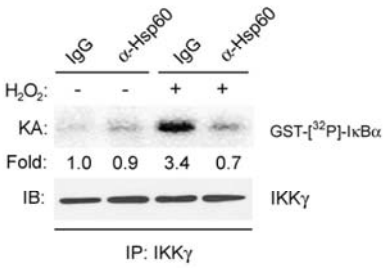


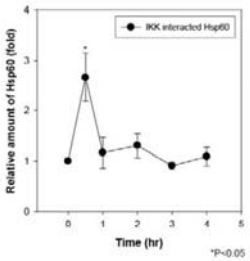


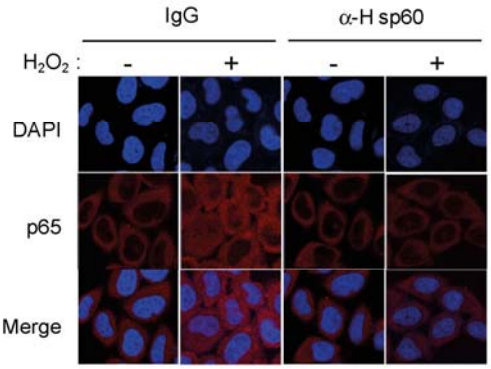
Released Hsp60 interacts with and activate IKK

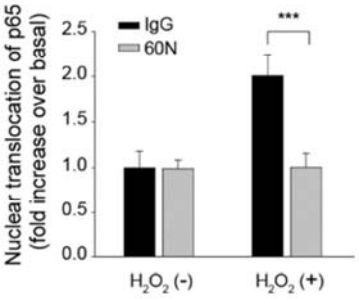












Session III

민경훈 (중앙대 약대)

Facile strategies for the discovery of novel kinase inhibitors

Facile strategies for the discovery of novel kinase inhibitors

Kyung Hoon Min, Ph.D.

College of Pharmacy, Chung-Ang University, Seoul, Republic of Korea

The therapeutic potential of kinase inhibitors has been rapidly expanding since the great success of Gleevec. Intensive investigation over the past 30 years has resulted in the FDA approval of about 40 kinase inhibitors. Phosphorylation is a essential process for every signal transduction cascades, indicating that kinases can be therapeutic targets for many diseases by dysregulation of signaling pathways. It has been reported that kinase inhibitors can act as key regulators for the treatment of immunological, inflammatory, degenerative, metabolic diseases as well as cancers. Novel pathological roles of kinases are being revealed, indicating that the field of kinase drug discovery is still immature.

Recently, a great deal of attention has been paid to discover of mutant selective EGFR kinase inhibitors, especially, 4th generation EGFR inhibitors, which selectively inhibit EGFR bearing C797S mutation. In addition, CSF1R, MER/AXL and LRRK2 are also interesting as potential targets for cancer immunotherapy, Crohn's disease and Parkinson's disease.

Regarding discovering novel inhibitors for the kinases, academia and startup companies have to approach with a different strategy unlike big pharma equipped with automatic HTS system and huge chemical libraries. Herein, we would demonstrate that facile strategies including the replacement for the hinge-binding moiety, shifting of substituents, and micro-variation of substituents could provide promising candidates in academia.

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4. 2002-2006 **The Scripps Research Institute**, San Diego, USA (PostDoc, Advisor: Prof. Peter Schultz)

Experience

1. 2007-2008: **Senior Scientist**, Division of Drug Discovery, Korea Research Institute of Chemical Technology, Deajon. Korea
2. 2008-current: **Professor**, College of Pharmacy, Chung-Ang University Seoul, Korea

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1. Lee, J. K.; Park, J.; Kim, J.; Kim J.; Choi, C.; Min, K. H. Discovery of potent colony-stimulating factor 1 receptor inhibitors by replacement of hinge-binder moieties. *Eur J Med Chem* **2021,** 216, 113298
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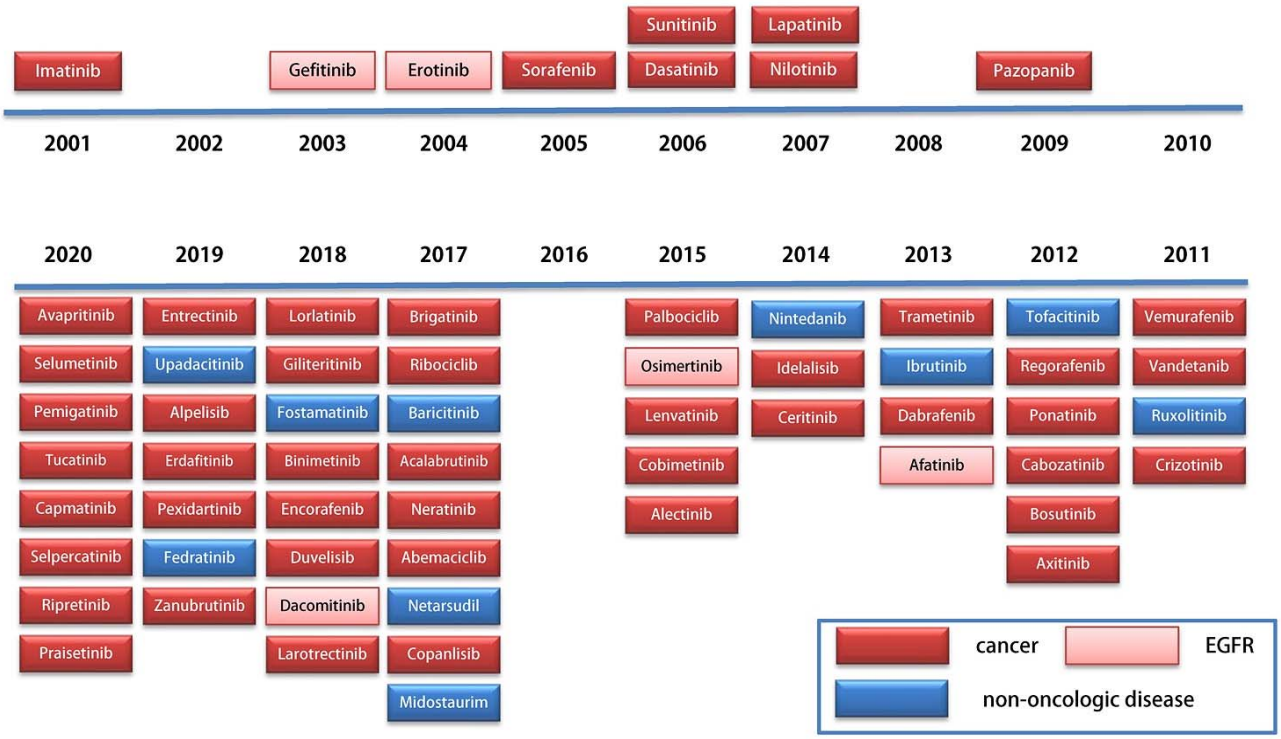
4. Kang, S. J.; Lee, J. W.; Chung, S. H.; Jang, S. Y.; Choi, J.; Suh, K. H.; Kim, Y. H.; Ham, Y. J.; **Min, K. H.***, Synthesis and anti-tumor activity of imidazopyrazines as TAK1 inhibitors. *Eur J Med Chem* **2019**, 163, 660-670.
5. Song, J.; Yoo, J.; Kwon, A.; Kim, D.; Nguyen, H. K.; Lee, B. Y.; Suh, W.; **Min, K. H.***, Structure-Activity Relationship of Indole-Tethered Pyrimidine Derivatives that Concurrently Inhibit Epidermal Growth Factor Receptor and Other Angiokinases. *PLoS One* **2015**, 10 (9), e0138823.

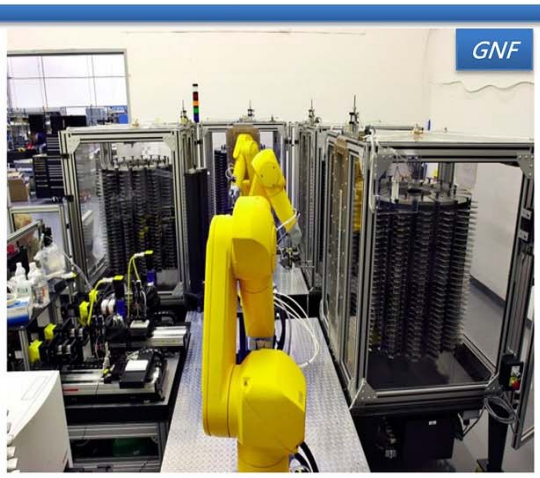
FACILE DISCOVERY OF KINASE INHIBITORS

민 경 훈
중앙대학교 약학대학

FDA Approved Kinase Inhibitors



Screening Automation



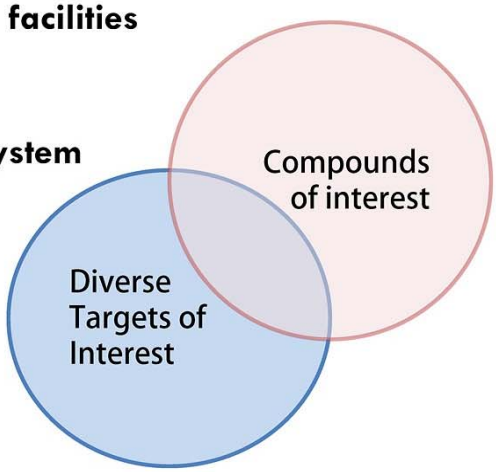
High Throughput Screening (HTS) -

- 3 million compounds/day enables large number of screens (180 screens of 175 million compounds), while maintaining low cost (~5% of standard)
- Low volume 1536-well screening leads to low Screening costs (1/20th conventional)
- Low volume affords low compound usage and costs (1 mg enables up to 40,000 screens)
- Diverse screening formats (fluorescence, FRET, luminescence, SPA, high content imaging)
- Informatics-support for cross-screen metadata analysis, and activity profile generation for key compounds enhances early lead decisions

Hit identification In Individual Researchers

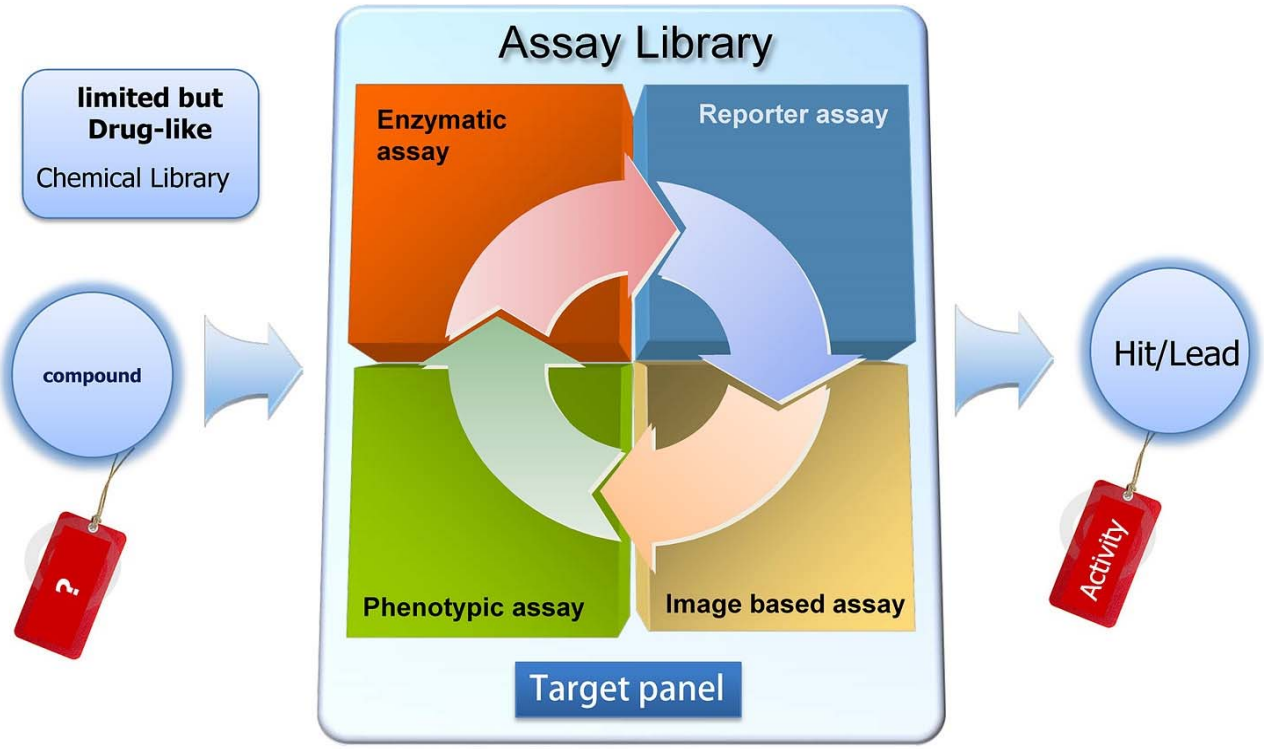
Hurdles

- **Small chemical library**
- **Lack of man-power and facilities**
- **A few targets**
- **Low throughput assay system**



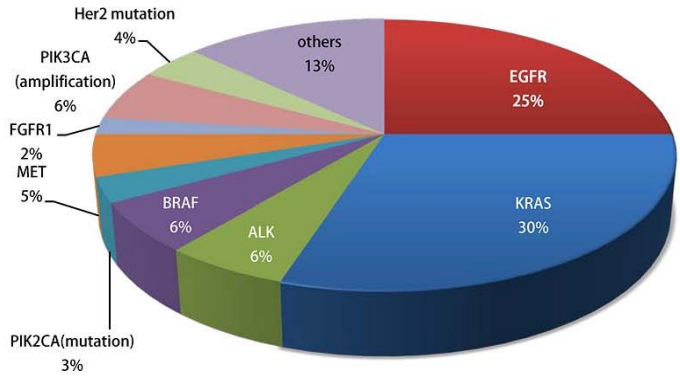
4

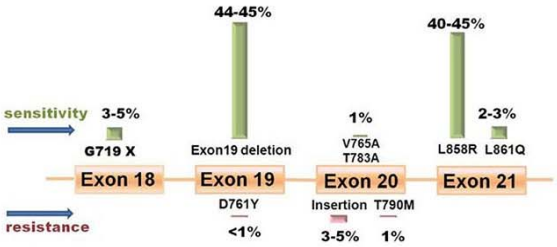
Assay Library



EGFR C797S

Molecular Characterization in Adenocarcinoma





The frequency of EGFR mutations

EGFR Tyrosine Kinase Mutation

- About 10% of Western patients and **50% of Asian patients**, with the global average being 25%
- Major mutation: Exon 19 deletion (44%), L858R (41%)

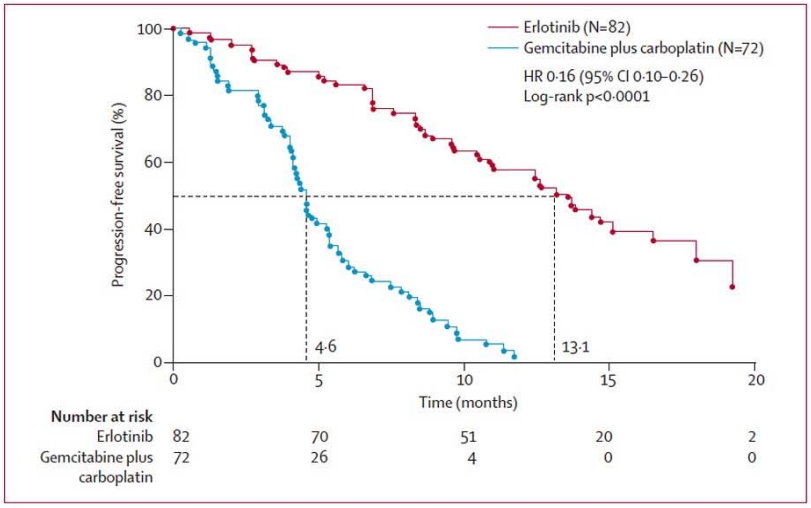
➢ Therapy :

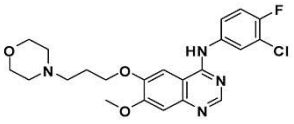
- ✓ 1st generation EGFR TKIs : erlotinib (Tarceva®), gefitinib (Iressa®)
- ✓ 2nd generation EGFR TKI : afatinib (Gilotrif®)

EGFR C797S

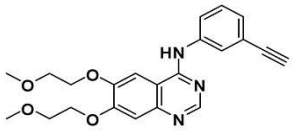
Erlotinib versus chemotherapy

Progression-free survival in both treatment groups





Gefitinib (Iressa, 2003)



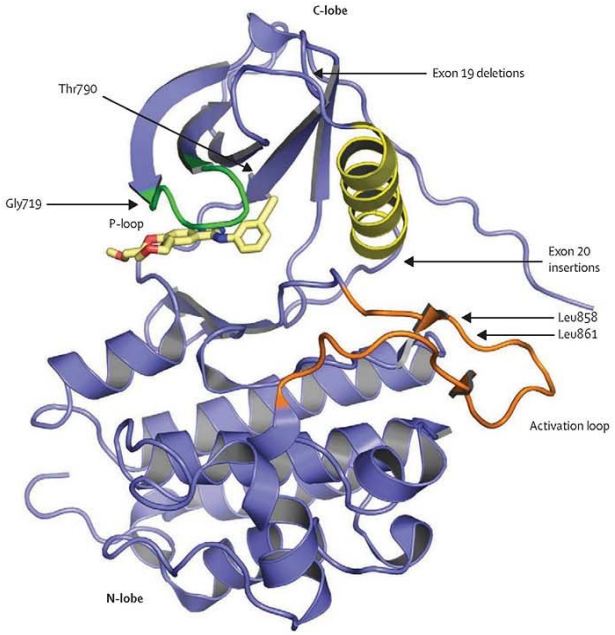
Erlotinib (Tarceva, 2004)

- 165 patients with advanced *EGFR* mutation(activating mutation of *EGFR* (exon 19 deletion or exon 21 L858R point mutation)-positive NSCLC
  - ✓ 82 in the erlotinib group
  - ✓ 72 in the chemotherapy group

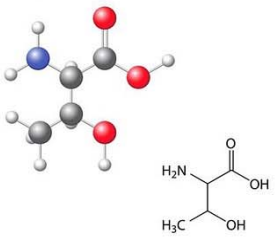
Lancet Oncol 2011; 12: 735 – 42

EGFR C797S

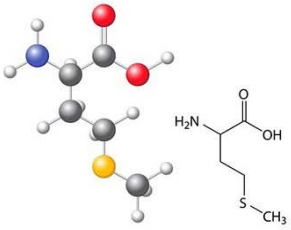
Gatekeeper mutation T790M



Threonine

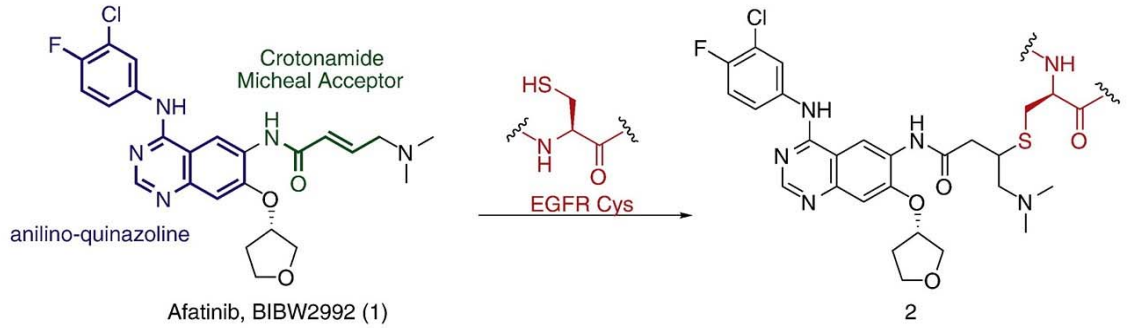


Methionine



EGFR C797S

Afatinib (Gilotrif®) Binding Mode

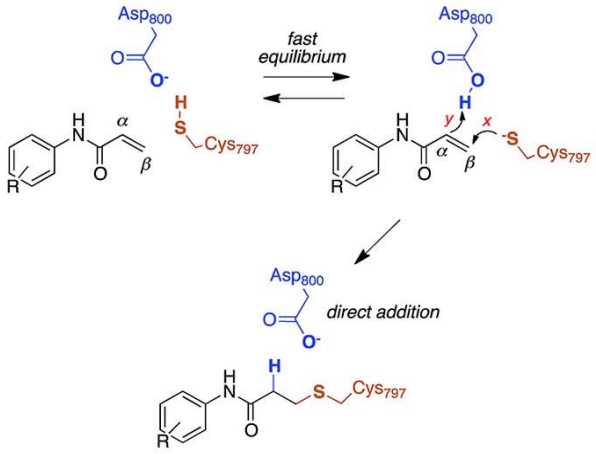


EGFR: Cys 797
HER2: Cys 805
HER4: Cys 803

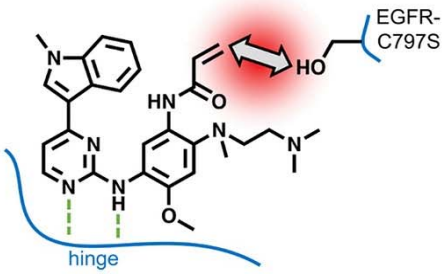
EGFR C797S

Resistance Mechanism

Mode of Action



Resistance



Session III

강석구 (연세대 의대)

Molecular signature of cancer origin cells and cancer origin area

Molecular signature of cancer origin cells and cancer origin site

Seok-Gu Kang, M.D, Ph.D.

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Neural stem cells (NSCs) of the subventricular zone (SVZ) accumulate mutations during the normal aging process. These alterations have been recently regarded as the beginning point of glioblastoma (GBM). Unlike accessible tumors, identification of molecular changes in the provoked precancerous lineage cells has been difficult in GBM. Here we report characteristics of GBM origin site cells (GBMOcs) and translates them to the human GBM. Genome-edited somatic mutation electroporation (EP) model creates GBM in the rodent model arising from the tdTomato-positive cells (GBMOcs) of SVZ (Cas9-Cre plasmid with sgRNAs for *Pten* and *Trp53*; FVB+B6 mice with floxed-*tdTomato*). Using the model, we isolated tdTomato-positive cells from the SVZ (10-weeks after EP). These cells were assessed with neurosphere formation assay, fluorescent microscopy, 3D-invasion assay, orthotopic allograft model, single-cell RNA-sequencing, and whole-genome-sequencing. We compared the results with control origin-site cell types, tumor-derived cells, as well as the Severance bulk RNA-sequencing data (GBM, tumor-free SVZ, and tumor-free cortex). The SVZ-derived tdTomato-positive cells (GBMOcs) created neurospheres in the neurosphere culture media. However, the GBMOcs were non-tumorigenic and not changed the survival by 150-days after orthotopic allograft. Whole-genome-sequencing found no copy number variation in the mutated GBMOcs (*Trp53* and *Pten*). Single-cell velocity revealed GBMOcs are showing a stream of differentiation from B cell marker-expressing cells to oligodendrocyte progenitor cell (OPC) marker-expressing cells, and these cells are highly migratory than the control cells. We found *NNAT* may transform OPC to GBM in both human and mouse models, and functional details will be demonstrated. We found the mutated GBMOcs are not distinguishable from the normal cells by the CNV. The GBMOcs were migratory and expressed OPC markers. The firework pattern may arise from the elevated expression of *NNAT* in the SVZ.

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Education

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Experience

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4. 2012–2018: Clinical Associate Professor and Clinical Professor, Dept. of Neurosurgery, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

5. 2018–present: Professor, Dept. of Neurosurgery, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

6. 2020–present: Professor, Dept. of Medical Science, Yonsei University Graduate School, Seoul, Korea

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2. Yoon, et al. Glioblastoma cellular origin and the firework pattern of cancer genesis from the subventricular zone. ***J Korean Neurosurg Soc***. 2020 Jan;63(1):26-33.

3. Lim, et al. Crosstalk between GBM cells and mesenchymal stem-like cells promotes the invasiveness of GBM through the C5a/p38/ZEB1 axis. ***Neuro Oncol***. 2020 Mar; 22(10):1452-1462.

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5. Park, et al. Regulation of bioenergetics through dual inhibition of aldehyde dehydrogenase and mitochondrial complex I suppresses glioblastoma tumorspheres.

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6. Kim, et al. Inhibition of glioblastoma tumorspheres by combined treatment with 2-deoxyglucose and metformin. ***Neuro Oncol***. 2017 Feb; 19 (2): 197-207.

7. Yoo, et al. Proinvasive extracellular matrix remodeling in tumor microenvironment in response to radiation. ***Oncogene***. 2018 Jun; 37 (24): 3317-3328.

8. Park, et al. Effect of combined anti-PD-1 and temozolomide therapy in glioblastoma. ***Oncoimmunology***. 2019 Jan; 8 (1): e1525243.

9. Park, et al. Transcriptome profiling-based identification of prognostic subtypes and multi-omics signatures of glioblastoma. ***Sci Rep***. 2019 Jul 22;9(1):10555

10. Yoon, et al, Co-expression of cancer driver genes: IDH-wildtype glioblastoma-derived tumorspheres. ***J Transl Med***. 2020 Dec;18(1):482.

Session IV

좌장: **박성혁** 서울대 / **박현우** 연세대

7월 31일 8:30-10:30

좌장 이력서

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Professor

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Education

1. 1988-1992: College of Pharmacy, Seoul National University, Seoul, Korea, B.S.
2. 1992-1996: College of Pharmacy, Seoul National University, Seoul, Korea, M.S.
3. 1996-2001: University of Illinois at Chicago, Chicago, IL, Ph.D.

Experience

1. 1996-1996: **Lecturer**, Seoul Municipal University
2. 2001-2005: **Postdoctoral Fellow**, Harvard Medical School, Boston, MA
3. 2008-2008: **Visiting Assistant Professor**, Harvard Medical School, Boston, MA
4. 2005-2009: **Assistant Professor**, Inha University, College of Medicine
5. 2009-2011: **Associate Professor**, Inha University, College of Medicine
6. 2011-2015: **Associate Professor**, Seoul National University, College of Pharmacy
7. 2017-2018: **Visiting Professor**, Harvard Medical School, Boston, MA
8. 2015-present: **Professor**, Seoul National University, College of Pharmacy

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2. Cha *et al.* ***ChemSci,***(2021).
3. Ngyen *et al.* ***Anal Chem***,(2020).
4. Cha *et al.* ***Anal Chem***, (2020).
5. Bajzikova *et al.* ***Cell Metabol***, (2018).
6. Wen *et al.* ***BBA Mol Cell Biol Lipid,*** (2018).
7. Bezawork-Geleta *et al.* ***Nat Comm.,*** 9(1),2221(2018).
8. Xu *et al.* ***Proc Natl Acad Sci U.S.A.***115,4152(2018).
9. Lee *et al.* ***Anal Chem.*** 89,1078(2017).
10. Jin *et al.* ***Angew. Chem. Int Ed. Engl,*** 55, 7939 (2016)

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Translational Cancer Research Laboratory
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Education

1. 2000-2006: **B.S.**, Department of Biology, Yonsei University, Seoul
2. 2006-2010: **Ph.D.**, Department of Pharmacology
   Yonsei University College of Medicine, Seoul (PI: Min Goo Lee)
3. 2010-2011: **Postdoctoral Fellow**, Department of Pharmacology
4. 2012-2016: **Postdoctoral Fellow**, Department of Pharmacology & Moores Cancer Center
   University of California San Diego (PI: Kun-Liang Guan)

Experience

1. 2016.9- : **Assistant Professor**, Department of Biochemistry, Yonsei University, Seoul
2. 2019.1- : **SUHF Fellow**, Suh Kyungbae Foundation
3. 2020.7- : **Director**, AST Metastasis Research Center

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1. Park JH, Pyun WY, Park HW, Cancer Metabolism: Phenotype, Signaling and Therapeutic Targets. **Cells**. 2020 Oct 16;9(10):E2308
2. Hepburn MS, Wijesinghe P, Astell C, Park HW, Hwang Y, Choi YS, Kennedy BF, Three-dimensional imaging of cell and extracellular matrix elasticity using quantitative micro-elastography. **Biomed Opt Express**. 2020 Jan 14;11(2):867-884
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6. Kim LC, Moroishi T, Meng Z, Jeong HS, Plouffe SW, Sekido Y, Han J, Park HW, Guan KL, Regulation of Hippo pathway transcription factor TEAD by p38 MAPK-induced cytoplasmic translocation. **Nature Cell Biology** (2017) Jul 28;19(8):996-1002 (* co-correspondence)
7. Strnadel J, Choi S,…. Park HW, Bui J, Kelber J, Bouvet M, Guan KL, Klemke RL, eIF5A-PEAK1 Signaling Regulates YAP1/TAZ Protein Expression and Pancreatic Cancer Cell Growth. **Cancer Res**. (2017) Apr 15;77(8):1997-2007

Session IV

박한수 (GIST 의생명공학/지놈엔컴퍼니 대표)

Microbiome research and development

Microbiome research and development

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Department of Biomedical Science and Engineering,

Gwangju Institute of Science and Technology, Gwangju, Korea

The gut microbiome of patients with disease is believed to influence the development of disease, as well as the efficacy of the drugs. Human Microbiome research was conducted to understand how microbial communities impact on human health. However, the genomic characteristics and detailed functions of effective bacterial strains have not been fully clarified. In this study, we utilized an integrated approach, involving metagenome, bacterial whole genome/transcriptome, mouse intestinal transcriptome, and mouse serum metabolome analysis, to decipher whether bacterial strain-specific differences influence the disease susceptibilities and efficacy of therapeutics in various diseases.

발표자 이력서

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Education

1. 1998: Seoul National University College, Seoul, Korea (M.D.)
2. 2001: Seoul National University Graduate school of Medicine, Seoul, Korea (M.S.)
3. 2007: Seoul National University Graduate school of Medicine, Seoul, Korea (Ph.D.)

Experience

1. 1998-1999: Clinical doctor, Seoul National University Hospital, Korea
2. 2009-2013: Research Associate in Pathology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA
3. 2013-2016: Senior Researcher, The Jackson Laboratory for Genomic Medicine, Farmington, CT, USA
4. 2016-Present: Assistant Professor, Gwangju Institute of Science and Technology, Korea
   CEO, Genome and Company, Korea

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1. Lactobacillus fermentum promotes adipose tissue oxidative phophorylation to protect against diet-induced obesity. ***Experimental & Molecular Medicine*** 2020 Sep : 52,pages1574-1586 (2020).
2. Sodium butyrate inhibits high cholesterol-induced neuronal anyloidogenesis by modulating NRF2 stabilization-mediated ROS levels:involvement of NOX2 and SOD1. ***Cell Death & Disease*** 2020 June, DOI: 10.1038/s41419-020-2663-1 (2020)
3. Amplification of transglutaminase 2 enhances tumou-promoting inflammation in gastric cancers. ***Experimental & Molecular Medicine*** 2020:volume 52, pages854-864 (2020)
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5. Alterations in the Rho pathway contribute to Epstein-Barr virus-induced lymphomagenesis in immunosuppressed environments. ***Blood.*** 2018:blood-2017-07-797209 (2018)

Microbiome Research and Development

Hansoo Park, M.D., Ph.D.

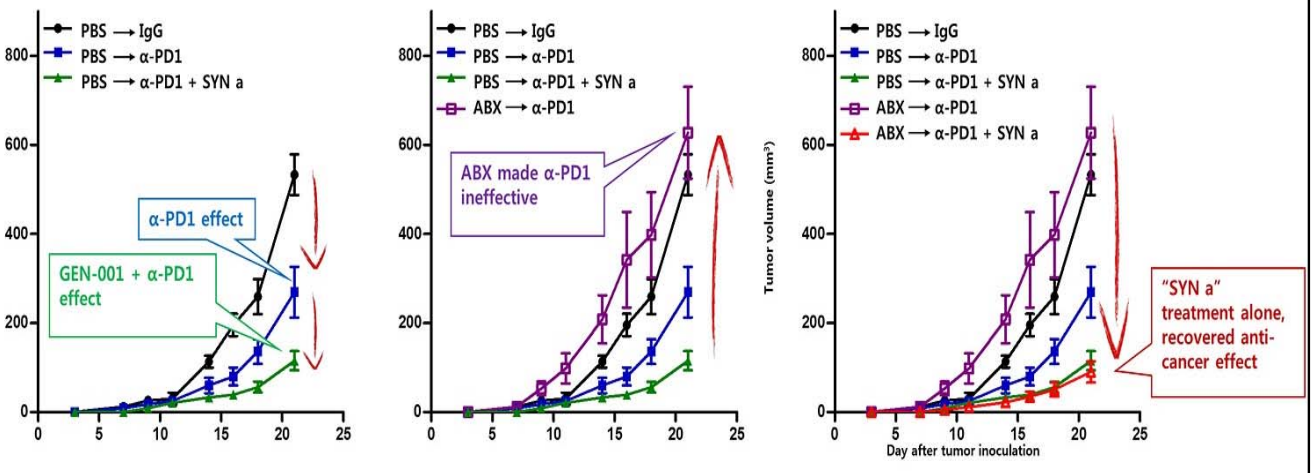
GIST

GENOME&CO

Immuno-Oncology microbiome: Mechanism of Action (4)

Microbiome | Sole efficacy

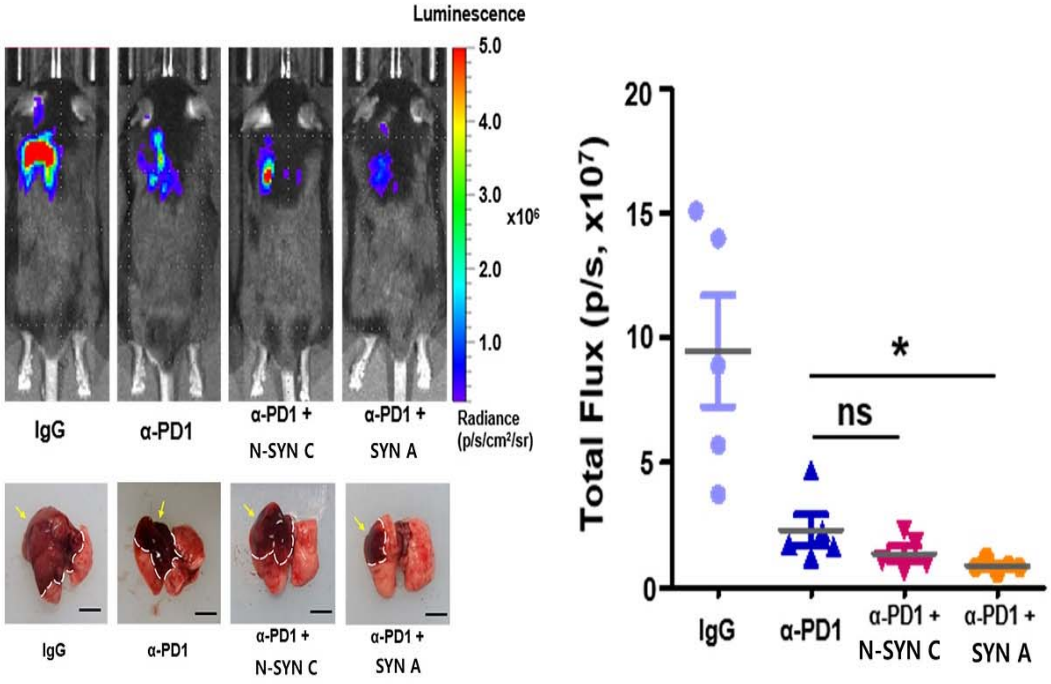
Effect of SYN a strain in germ-free mouse



SYN a alone, except for the effects of commensal microbiota, is sufficient for enhancing anti-PD-1 efficacy

2

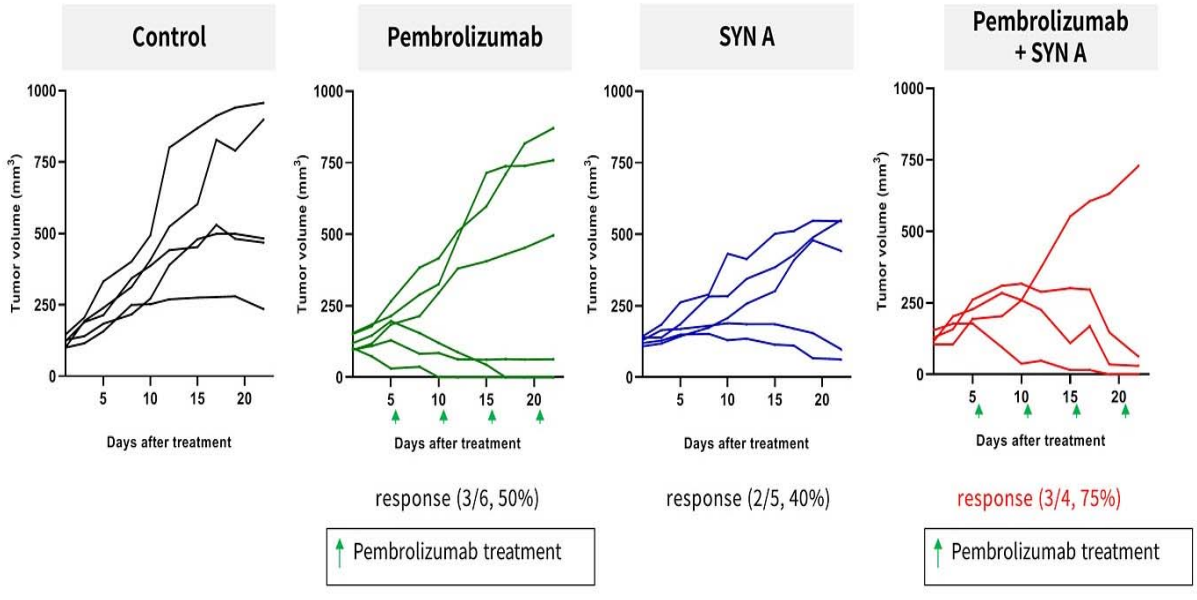
Immuno-Oncology microbiome: Mechanism of Action (5)



Orthotopic Syngeneic Model study: Anti-cancer effects on Lung cancer mouse model

Immuno-Oncology microbiome: Mechanism of Action (6)

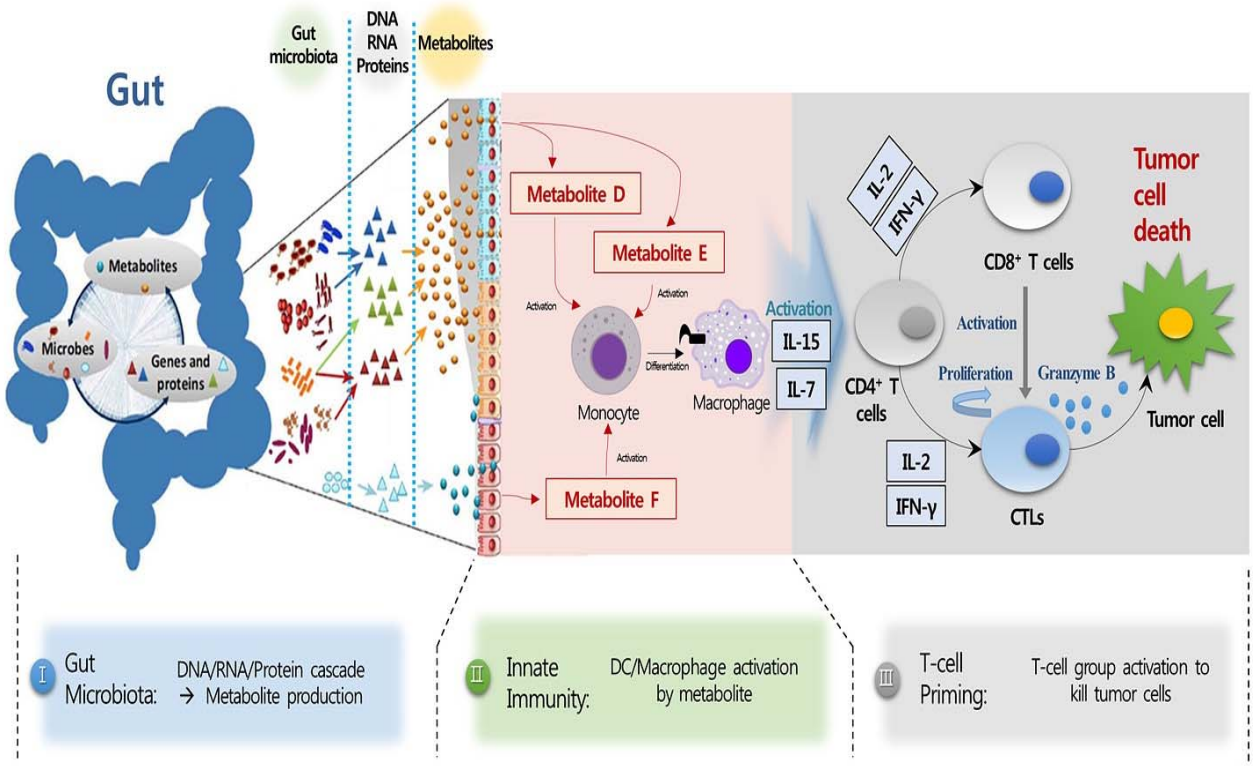
Microbiome | Humanized PDX



Humanized PDX study: Anti-cancer effects on Hu-PDX100 model

Immuno-Oncology microbiome: Mechanism of Action

Microbiome | Mechanism



5

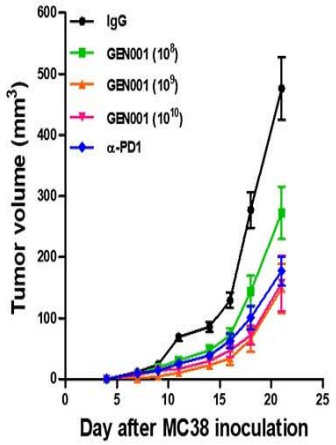
In-vitro Pharmacology: Identification, Function, and Safety

Purpose		Details	
Identification	16S RNA sequencing	Enzyme activity	• The experiments listed in the Identification are basic ones on microorganisms, and the purpose of experiment is that the strain is a **properly identified**.
	Gram staining	Catalase test	
	Carbohydrate fermentation	Gas production	
Functional Properties	Acid tolerance	• Experiments to check whether **bacteria survive in acidic digestive juice or bile acid**. (Probiotics is most important to live and settle down to the gut)	TEER (Transepithelial/trans-endothelial electrical resistance) • Experiments are conducted to confirm that **probiotics is well adhered to the gut** by increasing gut cell resistance (TEER), **leading to strengthening the gut.**
	Bile tolerance	• Artificial GIT is used to confirm viable cell activity against artificial gastric juice.	Intestinal cell adhesion ability
	Artificial GIT (Gastrointestinal Tract)		Antimicrobial activity • The probiotics that are well established in the gut regulate the environment of the gut microorganisms, and prevent the gut colonization and disease incidence when entering harmful bacteria. Experiments to confirm **Bacteriocin production and antimicrobial activity which inhibit pathogen activity.**
			Bacteriocin production
Safety	Antibiotics sensitivity test	• Antibiotic resistance means that a mutant strain is produced, which means that it can eventually be transformed into a pathogen.	Gelatinase test • Confirm that the gelatin(constituent of the human body) is discomposed (**to check whether probiotics is toxic**)
	Hemolysis test	• In the case of pathogens, the infection of the body destroys red blood cells and causes disease. Non-hemolytic reaction by probiotics means that probiotics is not toxic.	Proteolytic test • Confirm that the protein(constituent of the human body) is discomposed (**to check whether probiotics is toxic**)
	Biogenic amine test	• Experiment to confirm the ability of probiotics to form and degrade amines that can cause allergies using amino acid precursors	Lecithinase test • Confirm that phospholipid(constituent of the human body) is discomposed (**to check whether probiotics is toxic**)

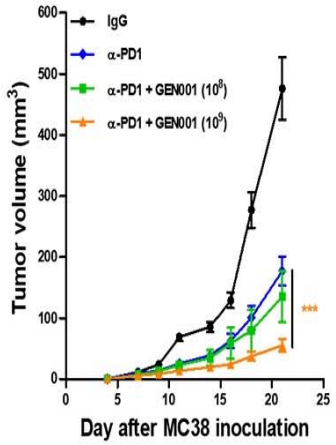
6

In-vivo Pharmacology : The anti-tumor effects of GEN-001 (Dose-dependency)

GEN001 single treatment



Anti-PD1 + GEN001 treatment



Dose-dependent efficacy was demonstrated in single and combination treatment

Target Product Profile

Product Description	• **Natural form, a single strain bacteria** isolated from healthy human
Mechanism of Action (MoA)	• Enhancement of bacteroidales-specific **memory T-cell** responses • Enhancement of **dendritic cell/macrophage** maturation
Indication	• **Advanced solid tumors** • **Gastrointestinal** cancers: gastric cancer, MSS-CRC, ESCC and HCC
Regimen	• **Add-on/maintenance therapy to anti-PD-(L)1** treated patients
Dosage and Administration	• Oral Enteric Capsule **$1x10^{11}$ CFU/day, QD**
Development Stage	• **IND approved to US FDA and** Phase 1b/2a started **(April, 2020)**
Intellectual Property	• **Patent Application filed**: **PCT** (US, Europe) **Korea, China, Taiwan** • Japan (Preparing a patent-application)
Target Market	• **US, Europe**, Japan, China, Korea

Clinical Development Plan of GEN-001

GEN-001 Clinical trial roadmap

1

Study 101(US)

Phase I/II (n=~100)
(Advanced solid tumors)

- **Part A(n=~20)**: **Safety** of GEN-001 + Anti-PD-(L)1 ('Combination')
- **Part B(n=~20)**: **Immunologic efficacy** of Combination
- **Part C(n ≥ 60)**: **Clinical efficacy** of Combination

2

Study 102(Korea)

Phase I/II (n ≥ 50)
(GI cancers)

- **Gastric, Gastroesophageal and Colon cancers**
- **Anti-PD-(L)1 Naïve patients**

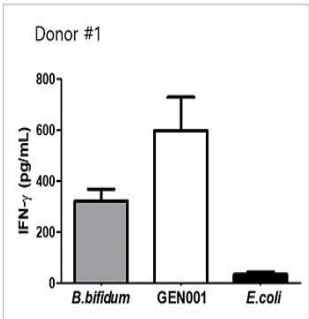
Next development will be determined based on the overall benefit/risk assessment of results from studies

9

[Immuno-oncology Microbiome] Competitiveness (GEN-001)

Pharmacology

Efficacy



GEN-001 shows superior efficacy compared to the other microbiome strains

Safety

GRAS
GENERALLY RECOGNIZED AS SAFE BY THE FDA

GEN-001 species is listed in GRAS

Development & Commercialization

Global Strategic Partnership

MERCK Pfizer

LG Chem

Clinical trials collaboration and supply agreement with Merck/Pfizer

License agreement (East Asia) with LG Chem

Clinical Development

Human clinical trials will include various populations and cancer type (US and Korea)

Session IV

지헌영 (연세대 의대)

mTOR inhibitors alleviate hearing loss resulting from OSBPL2 mutation

mTOR inhibitors alleviate hearing loss resulting from OSBPL2 mutations

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Department of Pharmacology

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Hearing loss is the most common cause of sensory disorders. Adult-onset hearing loss constitutes a substantial burden on the adult population worldwide and is associated with higher rates of hospitalization, falls and frailty, depression, and dementia. Moreover, hearing loss is becoming an increasingly prevalent disability, due to the global aging population. However, there are no effective therapeutic strategies for hearing loss so far.

Intracellular accumulation of mutant proteins causes proteinopathies, which lack targeted therapies. Autosomal dominant hearing loss (DFNA67) is caused by frameshift mutations in OSBPL2. Here, we show that DFNA67 is a toxic proteinopathy. Mutant OSBPL2 accumulated intracellularly and bound to autophagy proteins. Consequently, its accumulation led to defective endolysosomal homeostasis and impaired autophagy. Transgenic mice expressing mutant OSBPL2 exhibited hearing loss, but Osbpl2 knockout mice or transgenic mice expressing wild-type OSBPL2 did not. Rapamycin decreased the accumulation of mutant OSBPL2 and partially rescued hearing loss in mice. Rapamycin also partially improved hearing loss and tinnitus in individuals with DFNA67. Our findings indicate that dysfunctional autophagy is caused by mutant proteins in DFNA67; hence, we recommend rapamycin for DFNA67 treatment.

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Education

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2. 2002-2006: Yonsei University College of Medicine, Seoul, Korea (M.D.)
3. 2006-2011: Yonsei University College of Medicine, Seoul, Korea (Ph.D.)

Experience

1. 2011-2013: Postdoctoral Research Fellow, University of Michigan, Ann Arbor, USA
2. 2013-2015: Instructor, Boston Children's Hospital / Harvard Medical School, Boston, USA
3. 2015-now: Assistant & Associate Professor, Department of Pharmacology, Yonsei University College of Medicine, Seoul, Korea

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1. Kim, K. W. et al. Genome-wide association study identifies TNFSF15associated with childhood asthma. ***Allergy***. 2021 May 22. doi: 10.1111/all.14952. Online ahead of print.
2. Kim, J. M. et al. Microbiome analysis reveals that Ralstonia is responsible for decreased renal function in patients with ulcerative colitis. ***Clin Transl Med***. 2021;11(3):e322. doi: 10.1002/ctm2.322.
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4. Jung, J. et al. Rare KCNQ4 variants found in public databases underlie impaired channel activity that may contribute to hearing impairment. ***Exp Mol Med.*** 2019;51(8):1-12. doi: 10.1038/s12276-019-0300-9.
5. Choi, Y. J. et al. Mutations of ADAMTS9 Cause Nephronophthisis-Related Ciliopathy. ***Am J Hum Genet.*** 2019;104(1):45-54. doi: 10.1016/j.ajhg.2018.11.003.
6. Shin, D. H. et al. A recurrent mutation in KCNQ4 in Korean families with nonsyndromic hearing loss and rescue of the channel activity by KCNQ activators. ***Hum Mutat.*** 2019;40(3):335-346. doi: 10.1002/humu.23698.
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YONSEI UNIVERSITY

mTOR inhibitors alleviate hearing loss resulting from *OSBPL2* mutations

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Department of Pharmacology,
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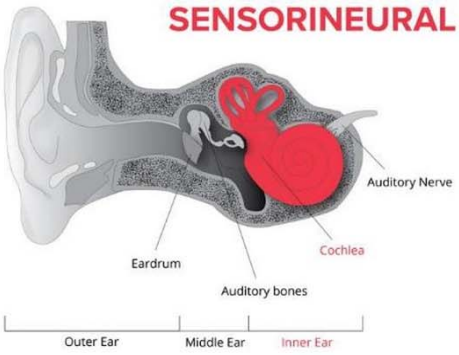
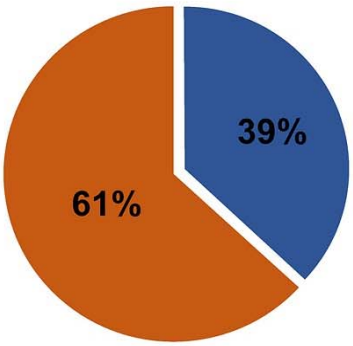
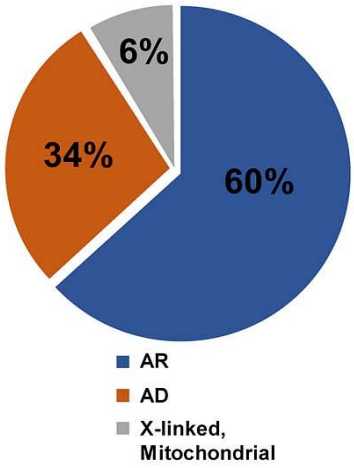
Severance

Hearing loss

Introduction 01



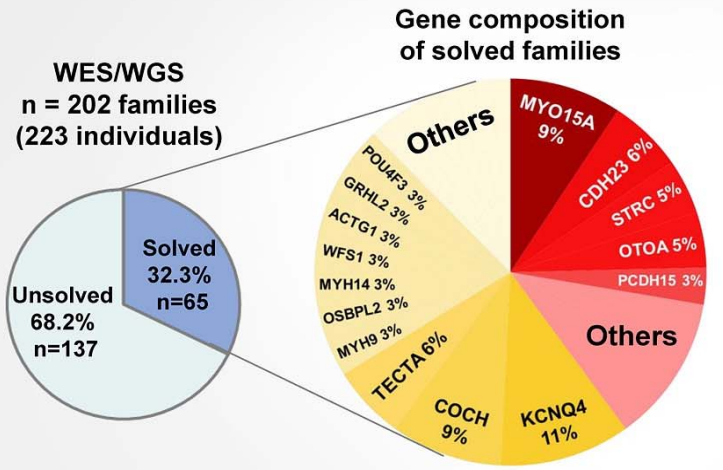


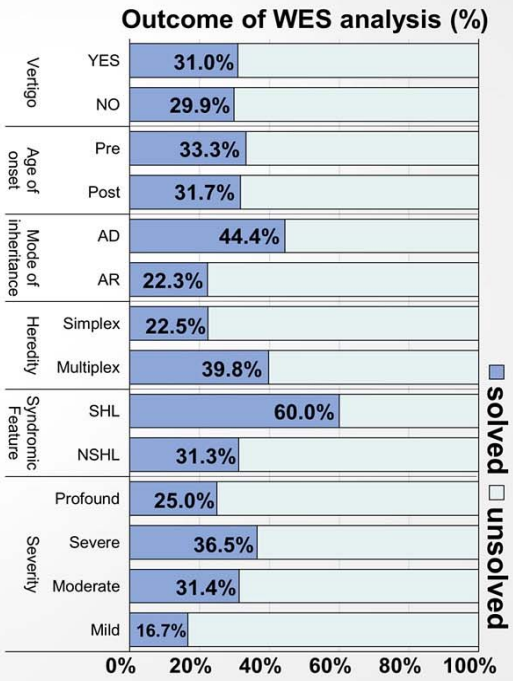


- Hearing loss is a common sensorial disorder, with an incidence of 1 in 500–1000 among children.
- Of the more than 123 genes associated with nonsyndromic hearing loss (NSHL), approximately 60~70% contribute to AR-NSHL.

DiStefano, M.(2020). Expert interpretation of genes and variants in hereditary hearing loss. *Medizinische Genetik*, *32*(2), 109-115.

Genetic study of hearing loss



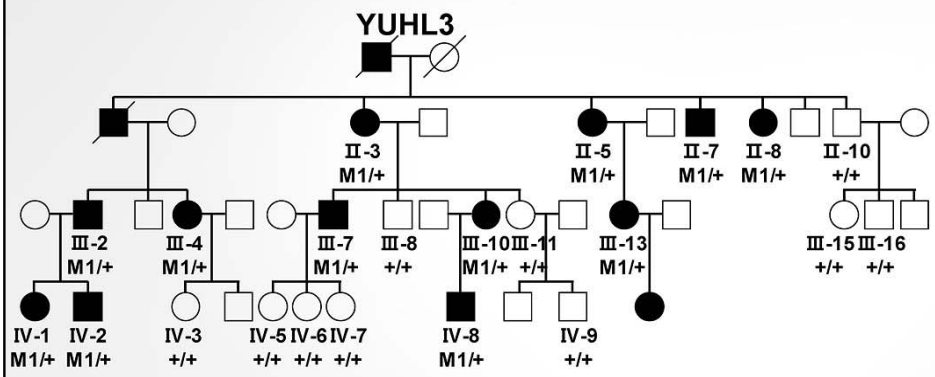


Goal

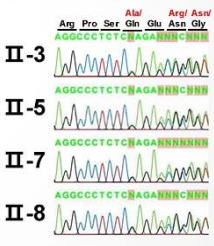
- Elucidate **novel genetics** and **pathobiology** of hearing loss!

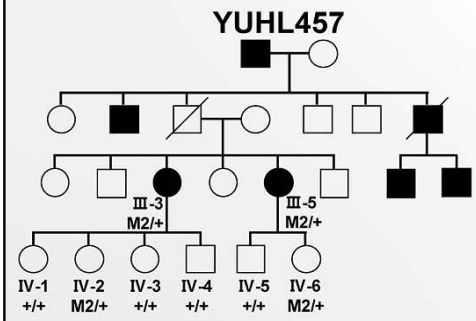
Delineate the novel pathogenic mechanism and suggest therapeutic approaches

Identification of *OSBPL2* mutations in large autosomal-dominant pedigrees with hearing loss

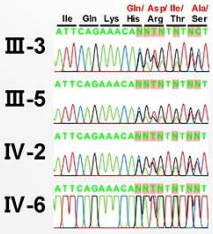


YUHL3
OSBPL2
c.158_159AAdel
p.Gln53Argfs*100

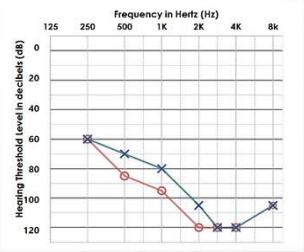




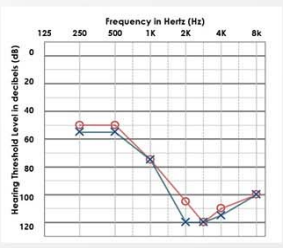
YUHL457
OSBPL2
c.177_178delAC
p.His60Gln*93



YUHL3: III-13



YUHL457: III-3



OSBPL2 mutations cause late-onset progressive hearing loss in human, but….

Genetics inMedicine | ORIGINAL RESEARCH ARTICLE

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Identification of *OSBPL2* as a novel candidate gene for progressive nonsyndromic hearing loss by whole-exome sequencing

Guangqian Xing, MD[1], Jun Yao, PhD[2], Bin Wu, MSc[3], Tingting Liu, MD[1], Qinjun Wei, MD[2], Cheng Liu, MD[1], Yajie Lu, MSc[2], Zhibin Chen, MD[1], Heng Zheng, PhD[4], Xiaonan Yang, MSc[3] and Xin Cao, PhD[2]

c.153_154delCT
p.Gln53Argfs*100

[Genet Med. 2015;17(3):210-8]

RESEARCH — Open Access

OSBPL2 encodes a protein of inner and outer hair cell stereocilia and is mutated in autosomal dominant hearing loss (*DFNA67*)

Michaela Thoenes[1], Ulrike Zimmermann[2], Inga Ebermann[1], Martin Ptok[3], Morag A Lewis[4], Holger Thiele[5], Susanne Morlot[6], Markus M Hess[7], Andreas Gal[8], Tobias Eisenberger[9], Carsten Bergmann[9,10], Gudrun Nürnberg[5], Peter Nürnberg[5,11], Karen P Steel[4], Marlies Knipper[2] and Hanno Jörn Bolz[1,9*]

c.141_142delTG
p.Arg50Alafs*103

[Orphanet J Rare Dis. 2015;10:15]

RESEARCH ARTICLE — Open Access

A novel pathogenic variant in OSBPL2 linked to hereditary late-onset deafness in a Mongolian family

Ningjin Wu[1,2†], Husile Husile[1,3†], Liqing Yang[1,3†], Yaning Cao[4], Xing Li[5], Wenyan Huo[1,3], Haihua Bai[3,5], Yangjian Liu[6*] and Qizhu Wu[1,3*]

c.158_159delAA
p.Gln53Argfs*100

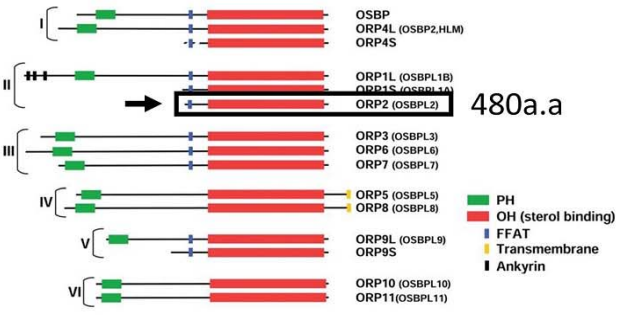
[BMC Med Genet. 2019;20(1):43]

OSBPL2

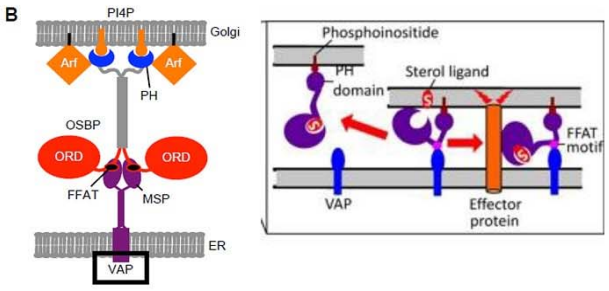
Introduction

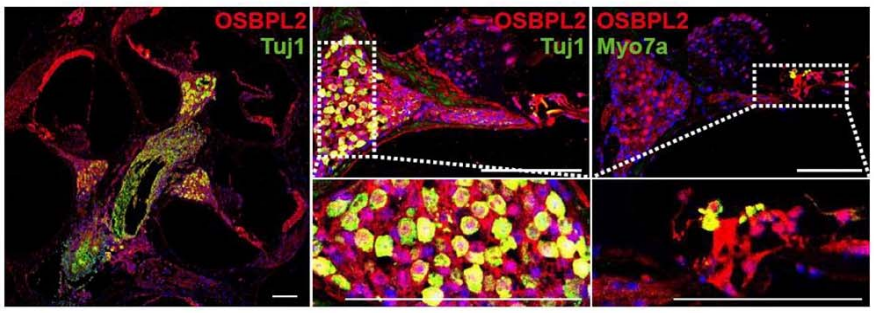
04

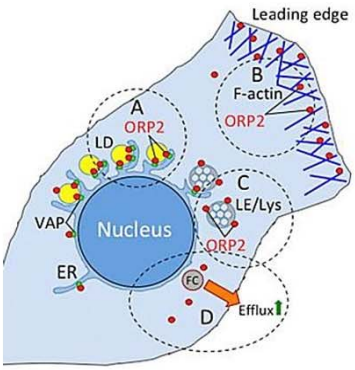
Biochem. J. (2010) 429, 13–24



M. Weber-Boyvat et al. / Biochemical Pharmacology 86 (2013) 89–95



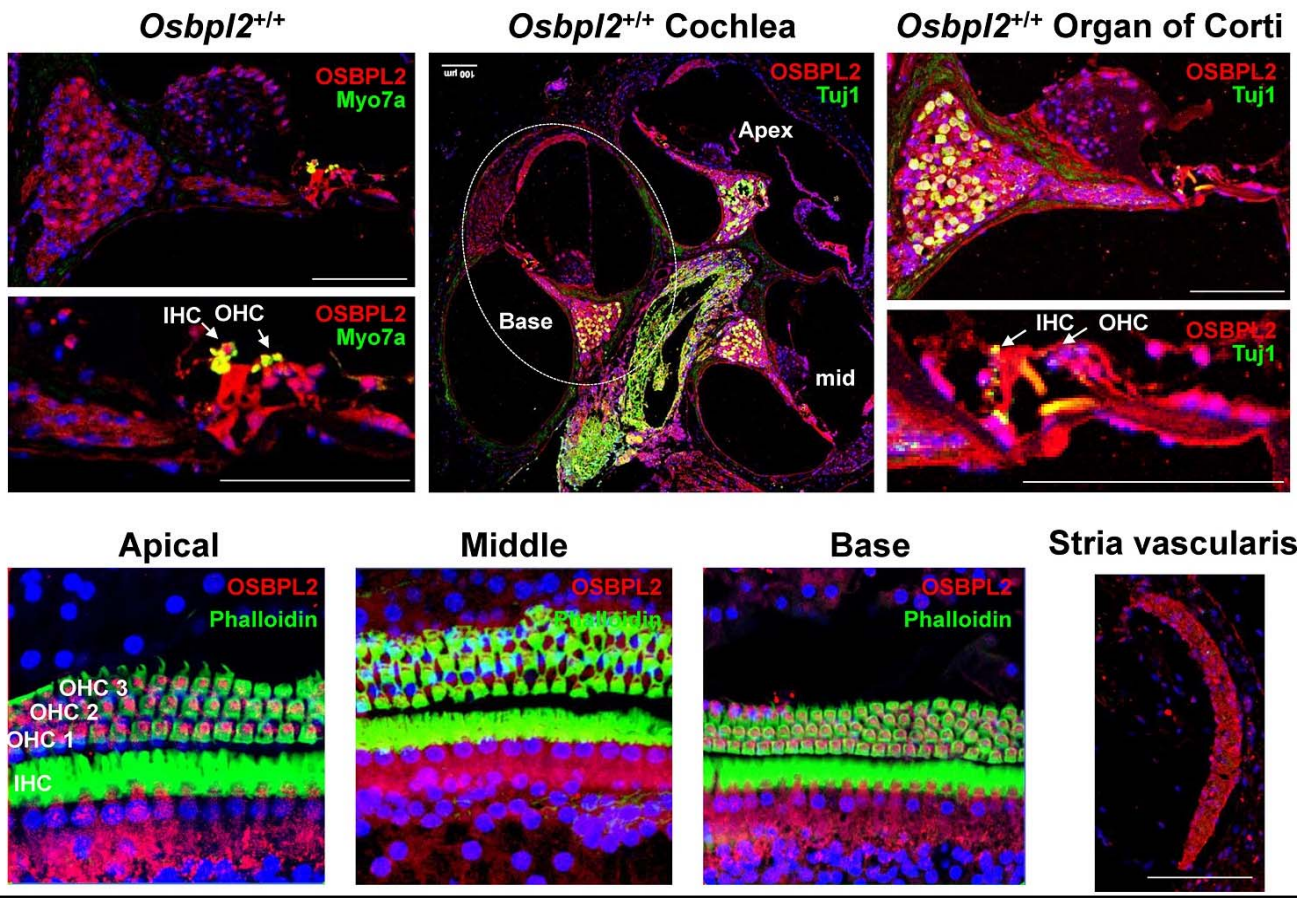




- The **oxysterol-binding protein (OSBP)-related proteins** (ORPs) are a family of lipid transfer proteins (LTPs).
- constitute a family of **sterol and phosphoinositide binding** and **transfer proteins** in eukaryotes that are conserved from yeast to humans.
- They are lipid-binding proteins implicated in many cellular processes related with oxysterol, including signaling, vesicular trafficking, lipid metabolism, and nonvesicular sterol transport.

A. Koponen et al. / Biochimie 158 (2019) 90e10191

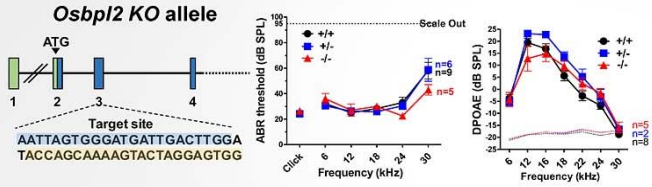
Expression of *Osbpl2* in murine cochlea



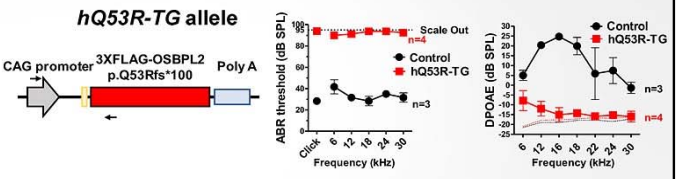
Transgenic mice overexpressing mutant OSBPL2 (hQ53R-TG) recapitulate hearing loss

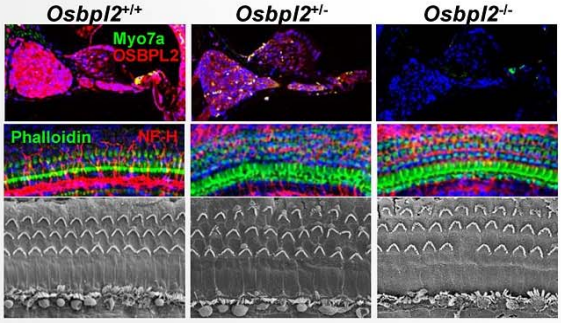
Generation of two different mouse models to examine two hypotheses

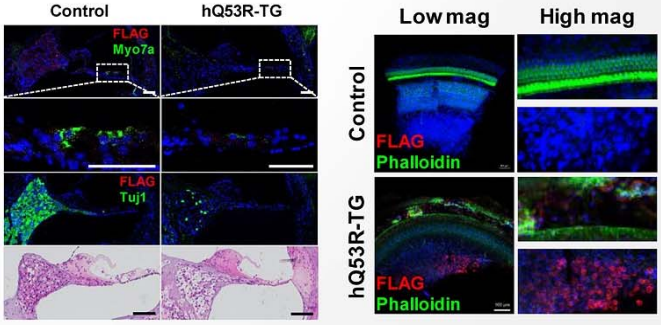
Osbpl2$^{-/-}$ or *Osbpl2*$^{+/-}$ mice



Human *OSBPL2* p.Q53Rfs*100 transgenic mice (hQ53R-TG)







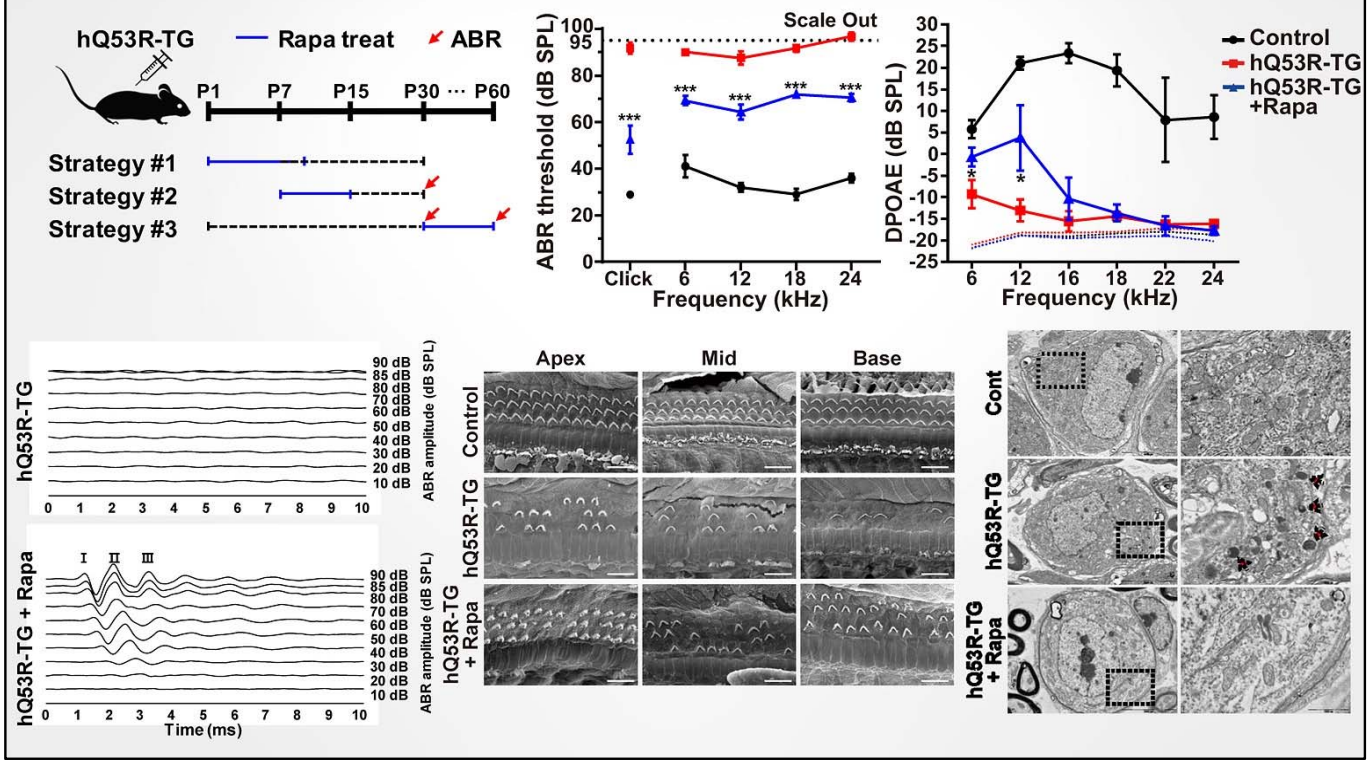
Summary

- No hearing loss phenotype
- Exclude loss-of-function or dominant-negative effect of mutant allele
- Exclude haploinsufficiency

Summary

- Early-onset hearing loss phenotype
- Suggest **gain-of-function** effect of mutant allele!!

Rapamycin partially rescues hearing loss phenotypes of hQ53R-TG mice



Conclusions

- We elucidated the molecular mechanism underlying DFNA67, a **proteinopathy** caused by mutant *OSBPL2* protein which is associated with **lysosomal defects** and **impaired autophagy**.
- We established a **mouse model for DFNA67** – transgenic mice expressing human mutant OSPBL2.
- We suggested **rapamycin** as a **therapeutic candidate for DFNA67**, for which currently no medical intervention is available. Given that DFNA67 is an adult-onset NSHL, genetic testing and early detection of OSBPL2 mutations is highly crucial for the prevention and treatment of hearing loss.

Session IV

권호근 교수 (연세대 의대)

Immuno-modulator potency of gut microbiota and
their therapeutic implication in inflammatory disorders

Immuno-modulator potency of gut microbiota and their therapeutic implication in inflammatory disorder

Gi-Cheon Kim, Ph.D and Ho-Keun Kwon, Ph.D.

Department of Biological Systems

Department of Microbiology and Immunology, Yonsei University College of Medicine, Seoul, Republic of Korea

The prevalence of inflammatory disorders has dramatically increased over the past decade, particularly in developed countries. The “hygiene hypothesis,” first proposed in 1989, has become a widely accepted answers for this stiff increment. In this circumstance, a line of recent studies has broken new ground that shows the co-evolvement of a human being with trillions of microbes (microbiota), considered as “hidden organ” due to their immense impact on human health and disease. For example, recent advances in microbiome research have enlightened indispensable roles of microbiota on induction, training, and function of host immune system and inflammatory diseases. However, the lack of precise molecular and cellular mechanisms of microbiota-based therapies has restrained their application for the treatment of inflammatory disorders. Here, we have identified FoxP3^{+} regulatory T cells (Tregs) inducing bacteria and elucidated the action mechanisms for their therapeutic potentials in inflammatory disorders.

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3. -2017: **Post-doc,** Dept. of Microbiology and Immunobiology, Harvard Medical School, Boston, MA
   - Mentor: Prof. Christophe Benoist (MD.Ph.D.)& Diane Mathis (Ph.D.)
4. -2011: **Doctoral degree,** Dept. of Life Sciences, GIST, Gwang-ju, South Korea
   - Mentor: Sin-Hyeog Im (Ph.D)

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2. Gi-Cheon Kim, Choong-Gu Lee, Ravi Verma, Dipayan Rudra, Taemook Kim, Keunsoo Kang, JongHee Nam, Young Kim, Sin-Hyeog Im, Ho-Keun Kwon, ETS1 suppresses tumorigenesis of human breast cancer via trans-activation of canonical tumor suppressor genes. **FRONT ONCOL**, 2020, 10(642).

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4. Ho-Keun Kwon, Hui-Min Chen, Diane Mathis & Christophe Benoist. FoxP3 scanning mutagenesis reveals functional variegation and mild mutations with atypical autoimmune phenotypes. **Proc Natl Acad Sci USA.** 2018 Jan 9;115(2):E253-E262.

5. Ho-Keun Kwon, Hui-Min Chen, Diane Mathis & Christophe Benoist. Different molecular complexes that mediate transcriptional induction and repression by FoxP3. **Nat Immunol.** 2017 Nov;18(11):1238-1248

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"Inspire The World"

Immuno-modulator potency of gut microbiota and their therapeutic implication in inflammatory disorders

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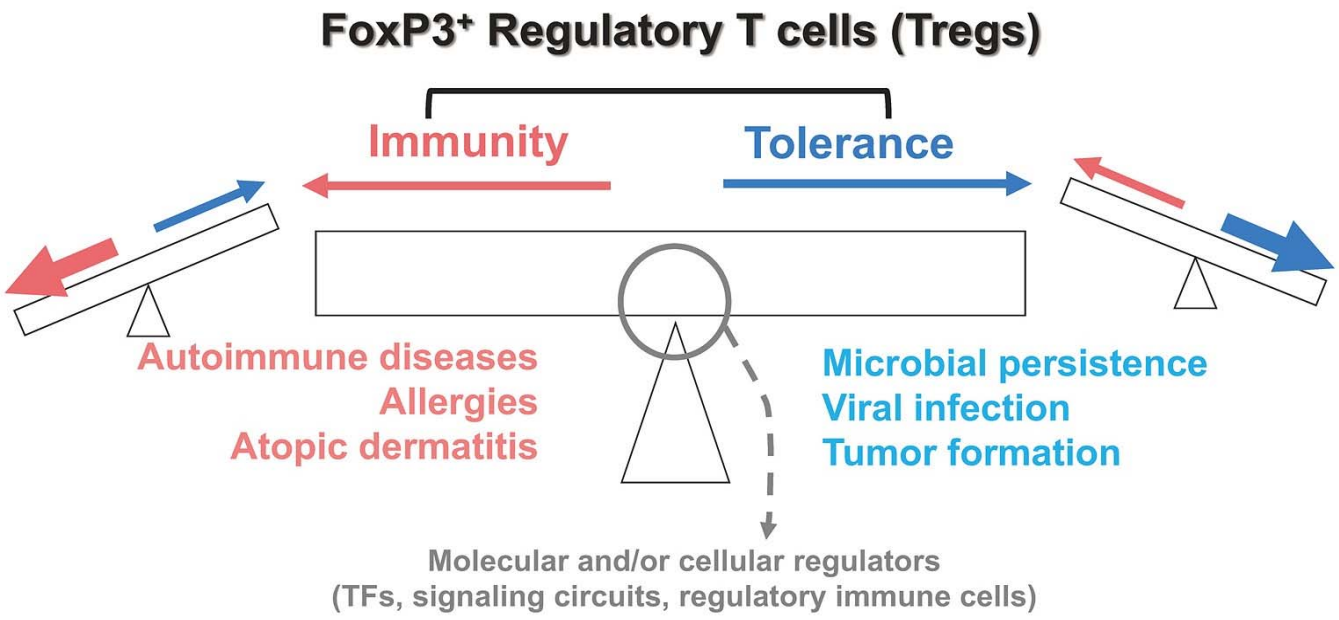
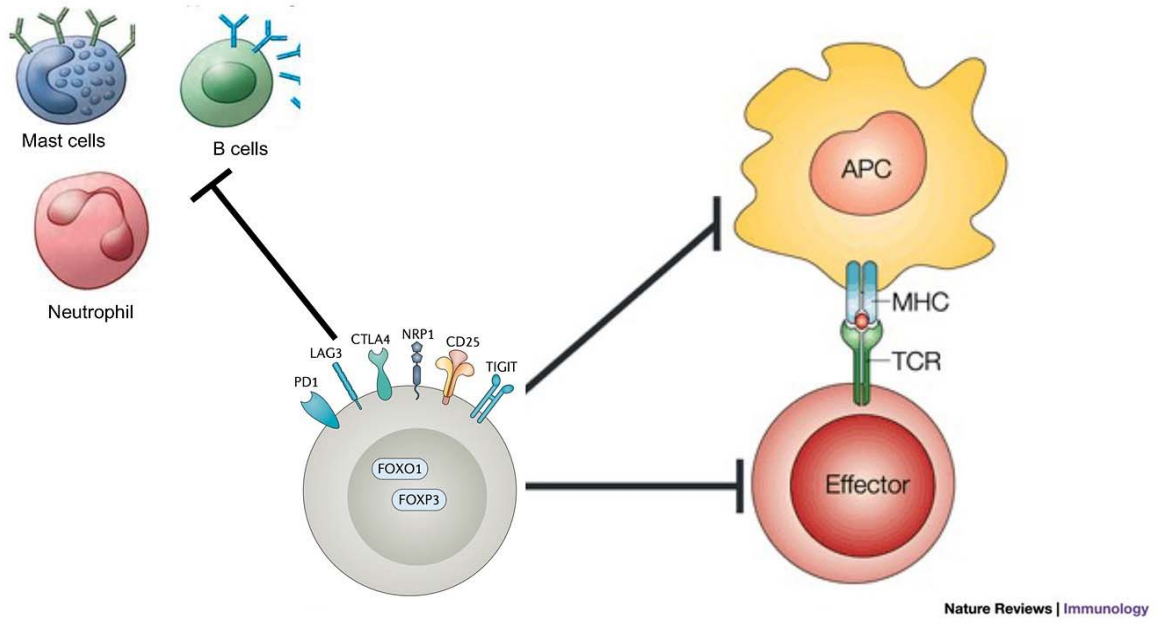
Immunological Homeostasis



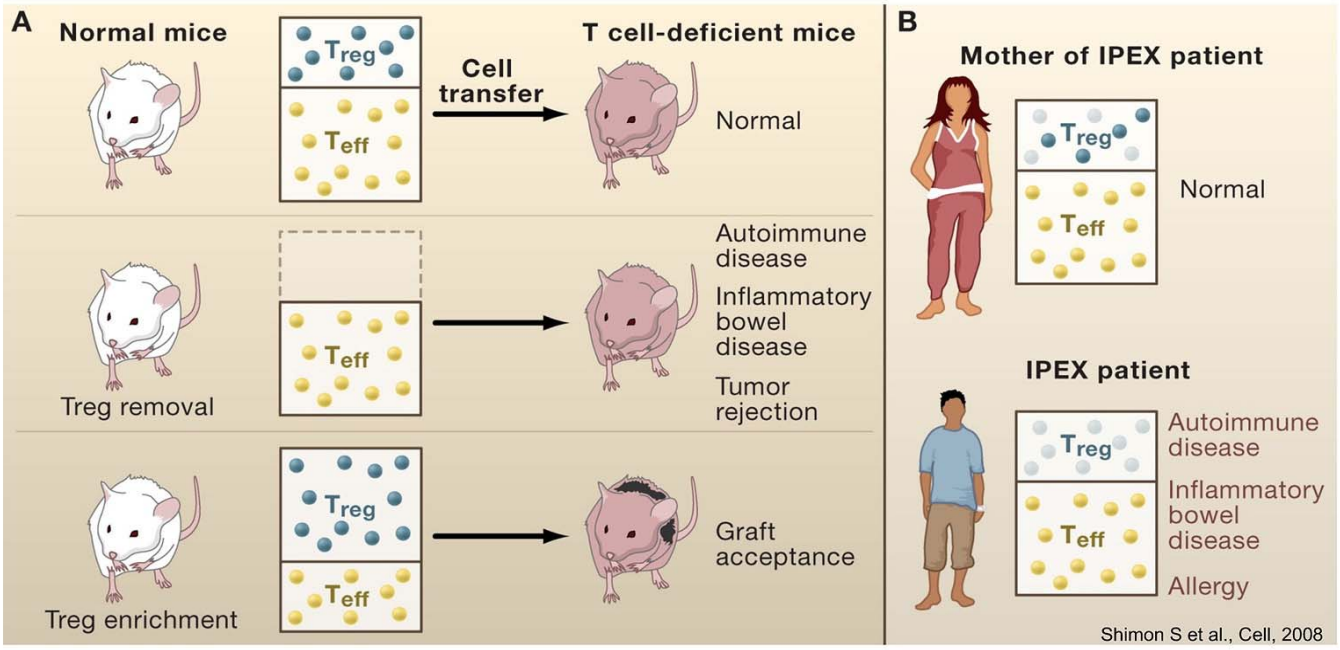
Jeffrey A. Bluestone et.al. *Nature*, 2012
Gerd Bouma et.al., *Nat Immunol*, 2003
Shokrollah Elahi, *Front. Immunol*,2014

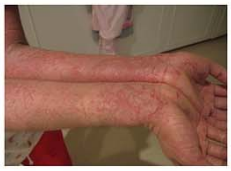
What are FOXP3⁺ Regulatory T cells (Tregs)?



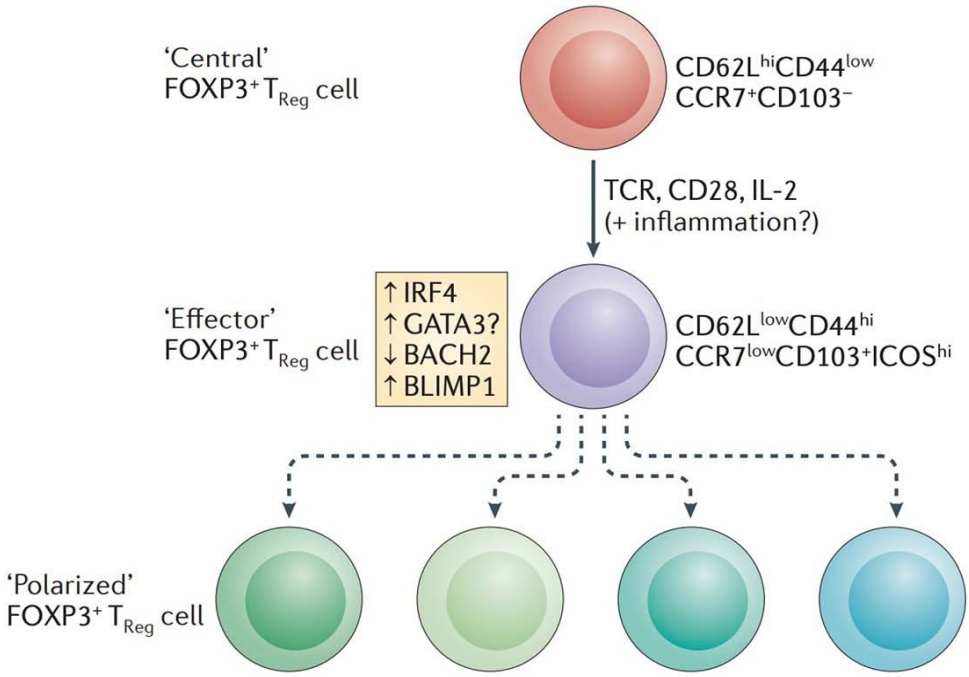
- Rare immune population: 0.01% in total immune cells
- Suppress almost all types of inflammation in body.
- High expression of PD1, CTLA4, CD25 and unique expression of FOXP3
- Loss of Foxp3 = Loss of Tregs

Are Tregs important in immunological homeostasis?





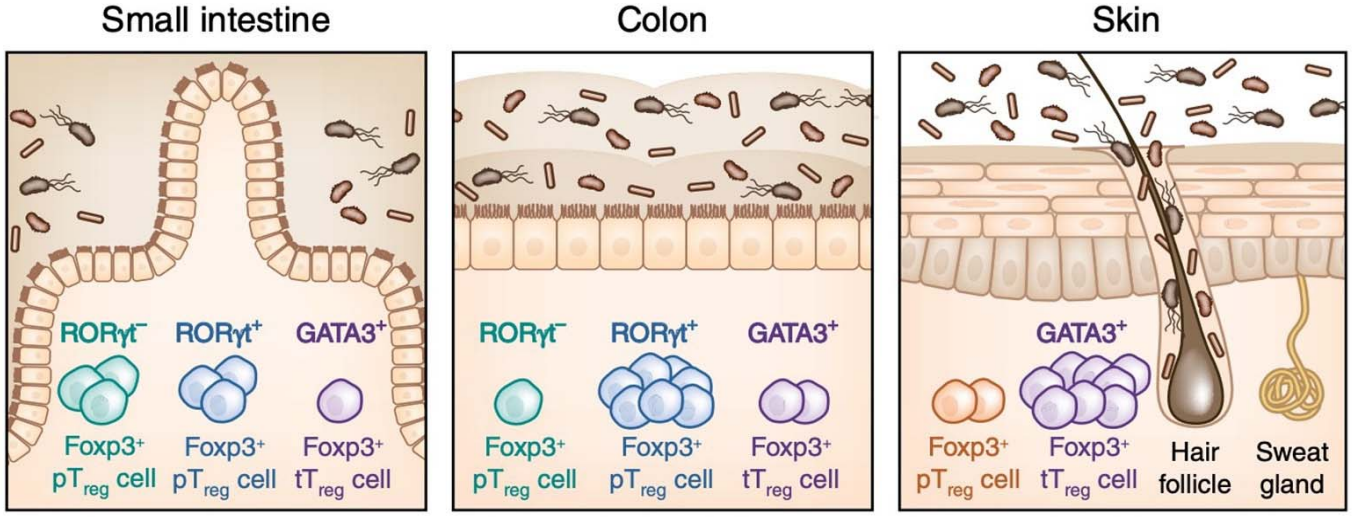
Tregs differentiation and diversity



Regulates	Skin and lung inflammation	Gut homeostasis	Germinal centres	Adipose metabolism
Transcription factors	FOXP3 T-bet	FOXP3 STAT3	FOXP3 BCL-6	FOXP3 PPARγ

Liston, A., & Gray, D. H. D. *Nat. Rev. Immunol., 2014*

Subsets of Tregs in skin and colon



- Food digestion
- Nutrient absorption

- Water and mineral absorption
- Fiber fermentation
- Excretion of waste

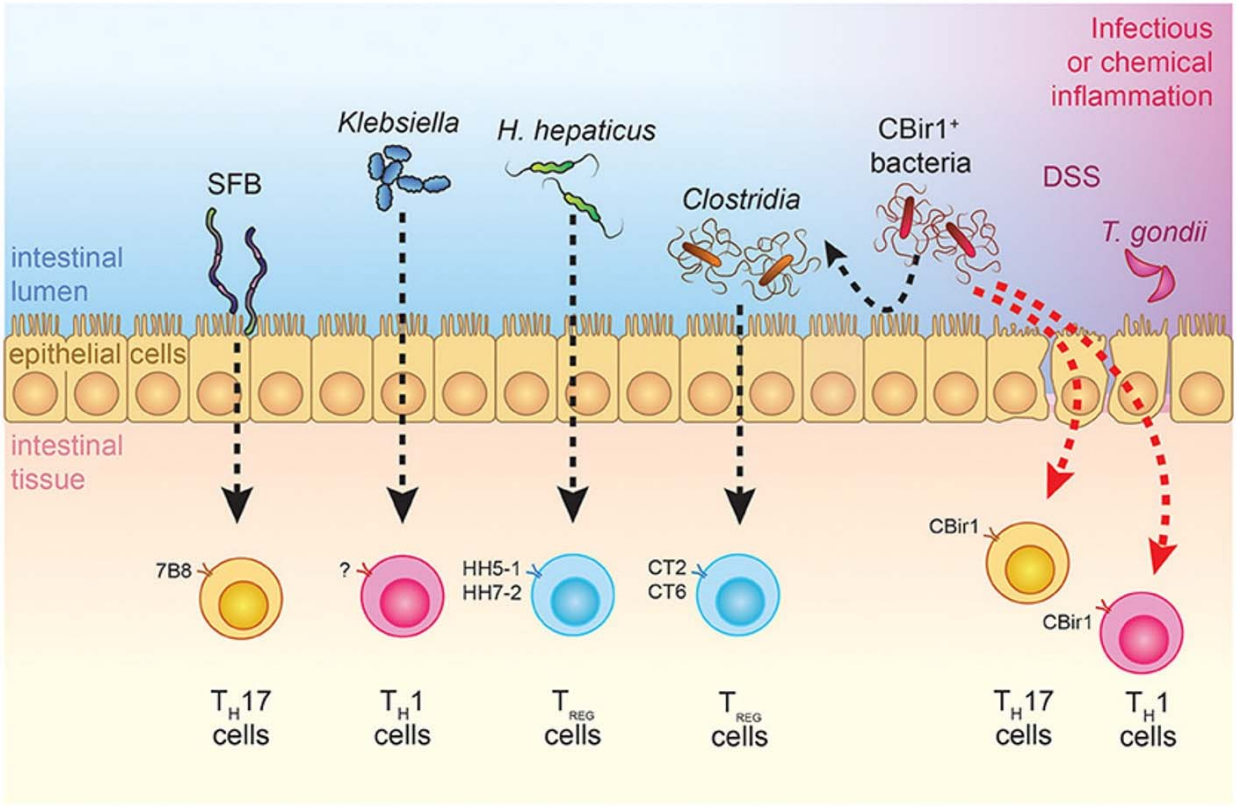
- Protection from injury
- Thermoregulation
- Sensation

- RORgt+ Tregs: Tolerance to microbiota
- RORgt- Tregs: Tolerance to food antigen
- GATA3+ Tregs: Tissue repair

- Hair morphogenesis
- Tissue homeostasis

Natasha W et al., Nat. Immunol., 2019

Diverse effects of gut bacteria on host immune



Chiara S et al., Front. Immunol., 2018

Session IV

조 준 교수 (GIST 생명공학)

Compromised translation of host mRNAs upon COVID-19 infection

SARS-CoV-2 infection impinges on protein synthesis in the respiratory tissue.

Jun Cho, Ph.D.

Department of Biomedical Science & Engineering

Gwangju Institute of Science & Technology, Gwangju, Republic of Korea

COVID-19 (Coronavirus disease 19)은 2019년 중국 우한에서 첫 감염 사례가 보고된 이래, 빠른 속도로 전파되어 세계적 대유행 (pandemic)을 일으켰다. 현재까지 1억 7000만명 이상의 감염 사례가 보고되고, 4백만명에 가까운 사망자를 낳은 COVID-19 대유행은 여전히 진행 중이며, 예방, 방역, 치료를 위한 막대한 의료 비용의 지출과 '사회적 거리두기'라는 전례없는 일상 생활의 변화마저 불러일으키고 있다.

COVID-19 대유행을 해결하고, 추후 유사한 사태의 재발을 방지하기 위한 효과적 치료, 예방책의 마련을 위해서 필수적으로 선행되야 하는 것은 이 감염성 질환의 병리 기전의 이해일 것이다. COVID-19은 이전에 발생한 SARS (servere acute respiratory syndrome, 2002-2004), MERS (Middle East Respiratory Syndrome, 2012-2014)의 원인이었던 Corona 바이러스 계통의 새로운 변형체 SARS-CoV-2 바이러스의 감염에서 기인한다. 이전 두 사례들과 비교하여 SARS-CoV-2 바이러스는 상대적으로 낮은 치사율과 압도적으로 높은 전파성의 차이를 보이는데, 이는 RNA 바이러스의 잦은 변이로 인한 새로운 형질 획득과 그로 인한 숙주의 반응 차이에서 초래되는 것으로 예상된다.

대유행 사태의 심각성으로 인해, SARS-CoV-2 감염으로 인한 병리를 이해하기 위한 생물학계, 의학계의 연구는 다양한 접근법들을 토대로 수행되었고 현재도 활발히 진행 중이다. 그 중 하나로 대용량 염기서열 분석 기법 (high-throughput sequencing technology)은 RNA가 유전정보물질인 Corona 바이러스, SARS-CoV-2의 바이러스 유전자 발현 기전과 숙주 세포 및 조직의 유전자 발현 기전의 변화를 해석하는데 유용한 툴로써 이용되어 왔다. 그 사례들로, 대용량 염기서열 분석기법의 한 플랫폼인 나노포어를 이용하여 2020년 완전한 형태의 SARS-CoV-2 유전체 (genome) 지도가 처음으로 특정되었으며, 가장 보편화된 플랫폼인 Illumina의 RNA-seq을 이용한 COVID-19 환자의 조직 단위의 유전자 발현, 더 나아가 single cell RNA-seq을 이용한 조직 내 구성 세포 단위의 SARS-CoV-2 감염 발병 유전자 발현의 변화를 밝혀냄으로써, SARS-CoV-2 감염 단계에서 바이러스와 숙주 조직의 유전자 조절과 병리와의 연결 고리가 일부 제시된 바 있다.

그러나 상기의 RNA-seq 기반의 실험적 접근법은 유전자 발현의 마지막 단계인 RNA에서 단백질로의 번역 과정의 변화를 살필 수 없다는 한계점을 지닌다. 면역 세포들을 포함한 조직의 다양한 세포들은 바이러스와 같은 외부 병원균의 침입에 반응하여 DNA에서 RNA를 생성하는 전사 단계 뿐 아니라 이 후의 번역 단계에서도 다양한 조절 경로를 지닌다. SARS-CoV-2의 감염 시의 바이러스와 숙주의 유전자 조절에 있어서도 다양한 단백질 번역의 변화가 있을 것으로 예상되나, 현재로써는 전장유전체 수준 (genome-wide level)에서의

변화는 제한된 환경인 in vitro 배양 세포를 숙주로 한 연구 사례만이 존재할 뿐이다. 우리는 인간화된 유전자 조작 생쥐 (humanized transgenic mouse)의 폐 조직에서 SARS-CoV-2 감염 시 단백질 번역 양상을 ribosome profiling이라는 단백질 번역에 특화된 대용량 염기서열 분석 기법을 이용하여 전장유전체 수준에서 해석하였다. 분석 결과는, SARS-CoV-2의 감염이 폐 조직에서 광범위한 단백질 합성의 균형을 망가뜨리고, 이러한 현상이 유전자 집단 단위 또는 유전자 구조 단위의 규칙성을 따르고 있음을 보여주고 있다. 본 연구의 결과는 기존에 알려지지 않았던 Corona 바이러스의 병리 기전의 새로운 이해와 관련 감염 질환의 잠재적 치료법 개발의 방향을 제시하는데 기여할 것으로 예상된다.

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SARS-CoV-2 infection impinges on protein synthesis in the respiratory tissue.

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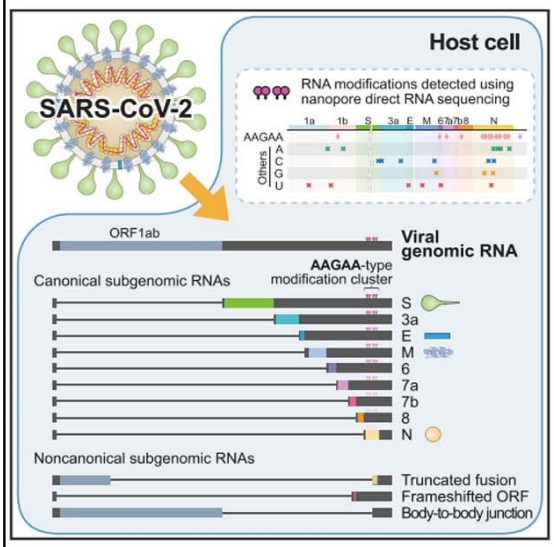
Gwangju Institute of Science and Technology

Genome-wide studies on SARS-CoV-2 infection



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Resource

The Architecture of SARS-CoV-2 Transcriptome

Dongwan Kim,[1,2] Joo-Yeon Lee,[3] Jeong-Sun Yang,[3] Jun Won Kim,[3] V. Narry Kim,[1,2,4,*] and Hyeshik Chang[1,2,*]

CellPress Cell

Article

Imbalanced Host Response to SARS-CoV-2 Drives Development of COVID-19

Daniel Blanco-Melo,[1,2,9] Benjamin E. Nilsson-Payant,[1,2,9] Wen-Chun Liu,[1,3,9] Skyler Uhl,[1,2] Daisy Hoagland,[1,2] Rasmus Møller,[1,2] Tristan X. Jordan,[1,2] Kohei Oishi,[1,2] Maryline Panis,[1,2] David Sachs,[4] Taia T. Wang,[5,6,7] Robert E. Schwartz,[8,*] Jean K. Lim,[1,*] Randy A. Albrecht,[1,3,*] and Benjamin R. tenOever[1,2,3,10,*]

nature immunology RESOURCE
https://doi.org/10.1038/s41590-020-0762-x
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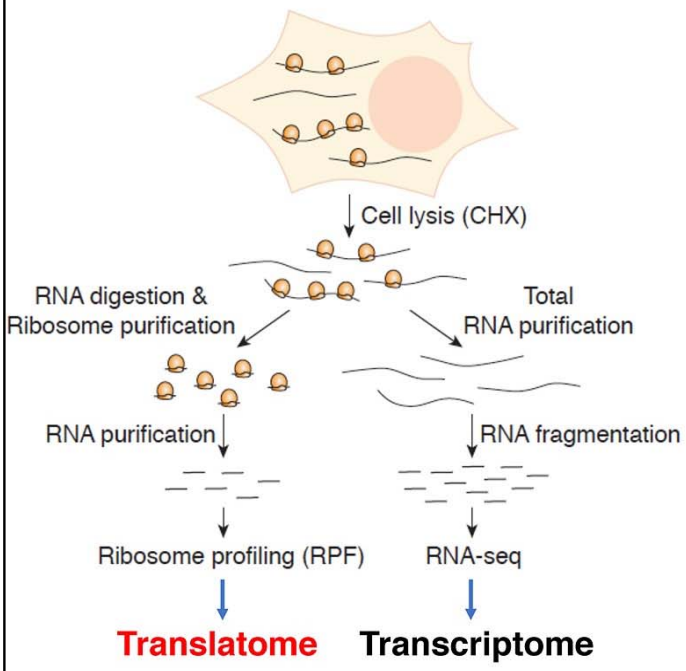
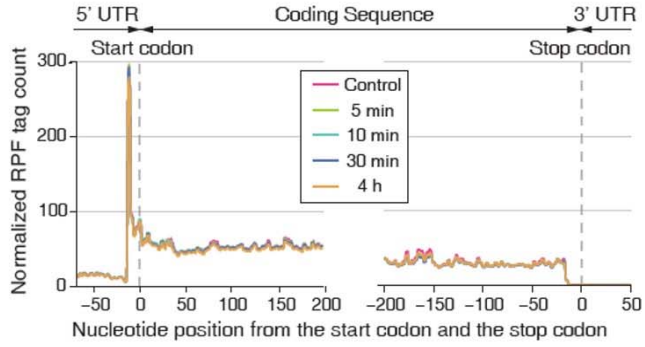
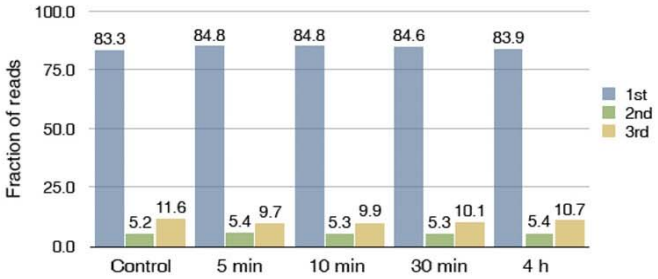
Single-cell landscape of immunological responses in patients with COVID-19

Ji-Yuan Zhang[1,9], Xiang-Ming Wang[2,9], Xudong Xing[3,9], Zhe Xu[1,9], Chao Zhang[1], Jin-Wen Song[1], Xing Fan[1], Peng Xia[1], Jun-Liang Fu[1], Si-Yu Wang[1], Ruo-Nan Xu[1], Xiao-Peng Dai[1], Lei Shi[1], Lei Huang[1], Tian-Jun Jiang[1], Ming Shi[1], Yuxia Zhang[4], Alimuddin Zumla[5,6], Markus Maeurer[7,8], Fan Bai[2]✉ and Fu-Sheng Wang[1]✉

Ribosome profiling







Ribosome profiling detects *in vivo* movement of ribosomes (translational activity).

Genome-wide studies on SARS-CoV-2

Article

The coding capacity of SARS-CoV-2

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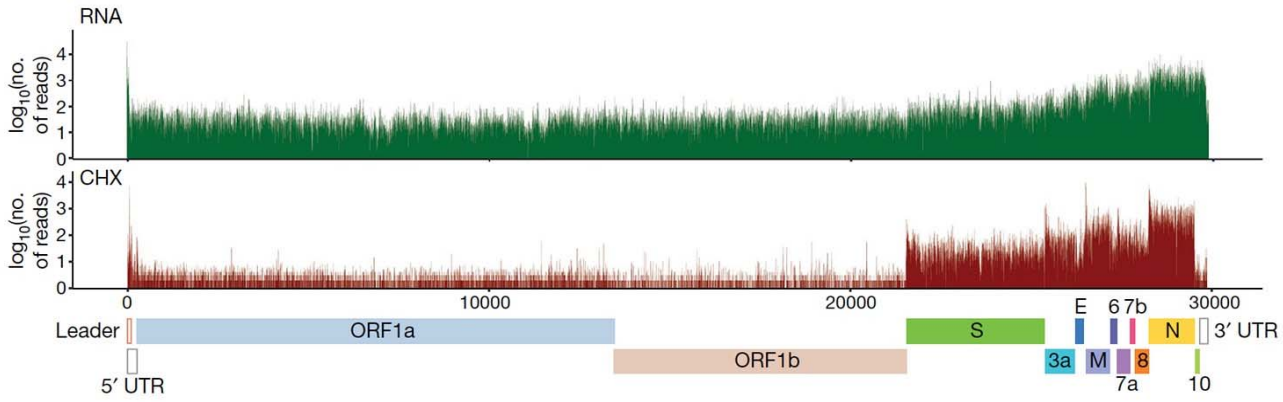
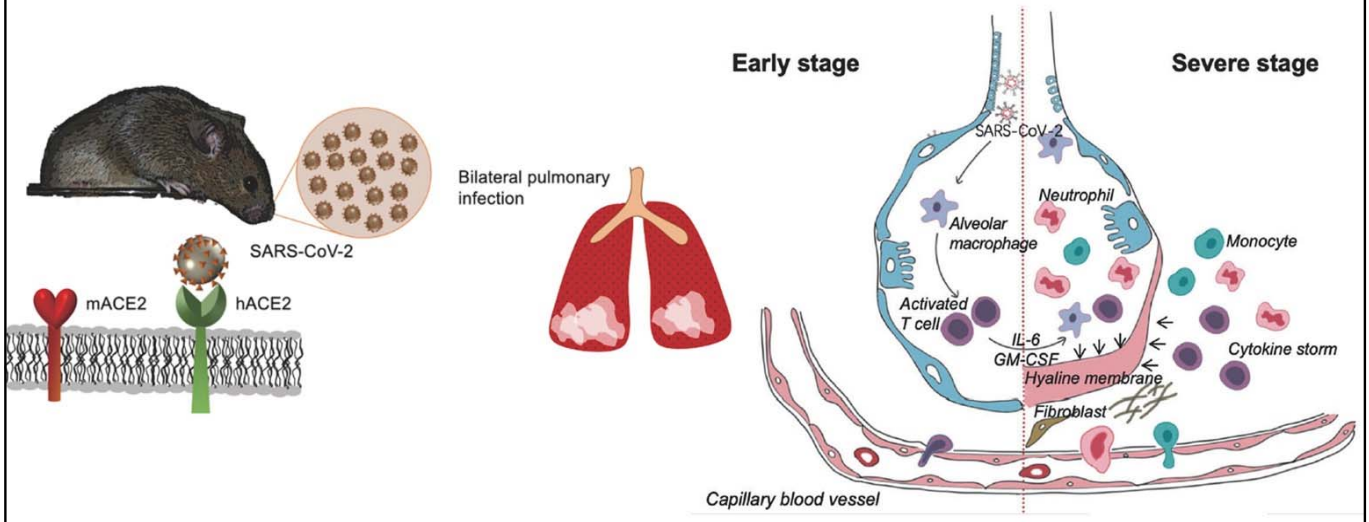


Mouse models for COVID19 infection study



The early phase (set 1)

SARS-CoV-2 infection → Day 2
Day 1
Control (uninfected)

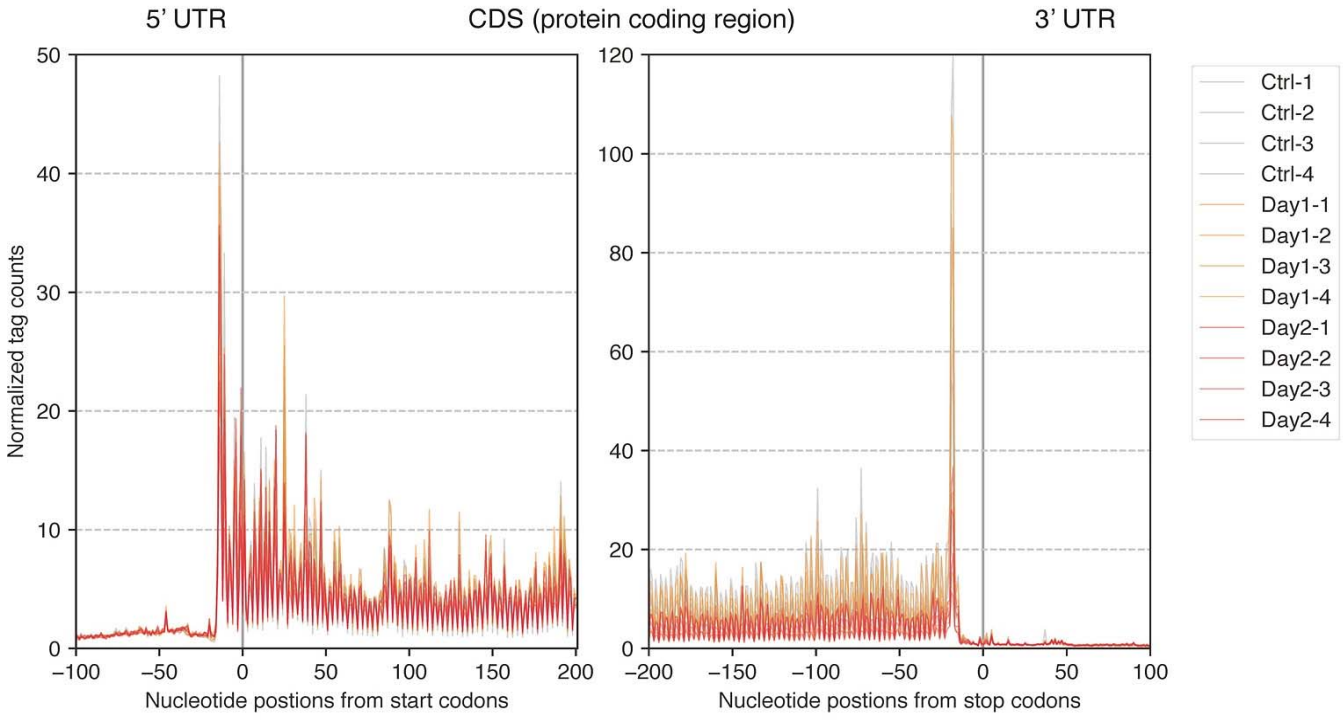
The late phase (set 2)

SARS-CoV-2 infection → Day 7
Day 5
Control (uninfected)

4 mice for each

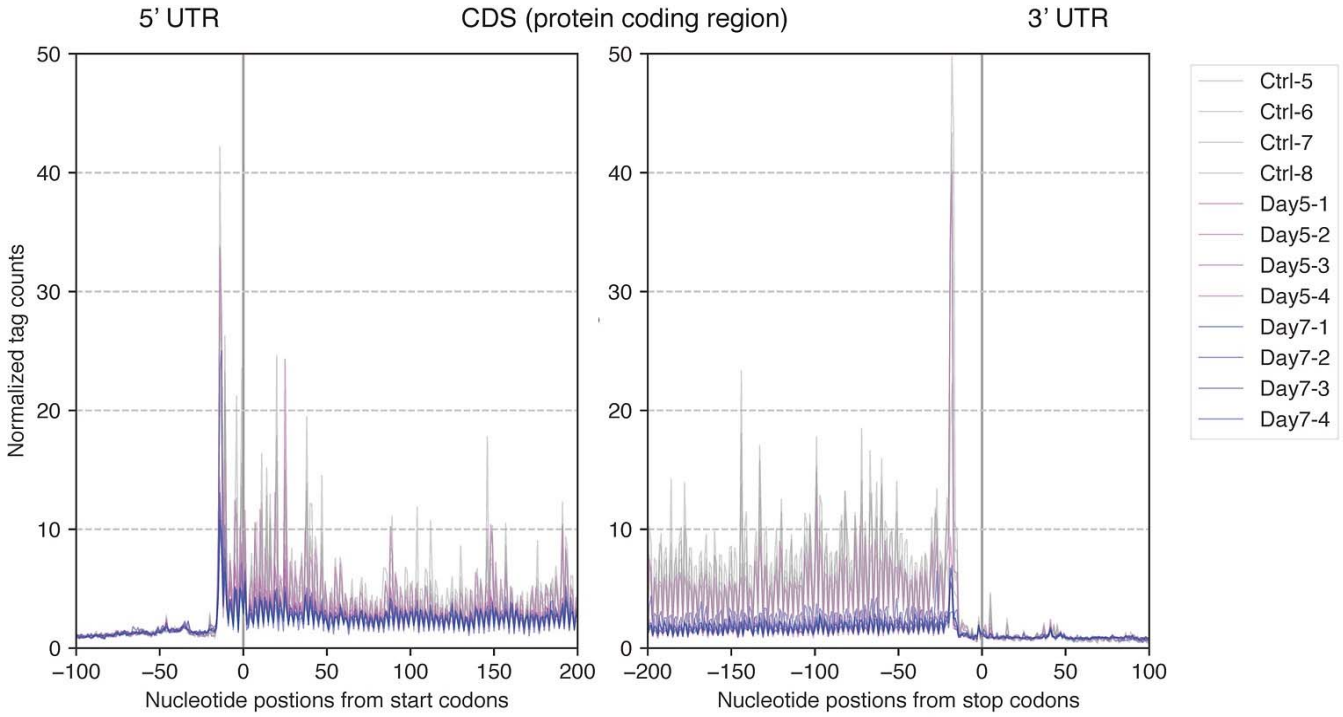
Metagene alignment around start and stop codons

The early phase (set 1)

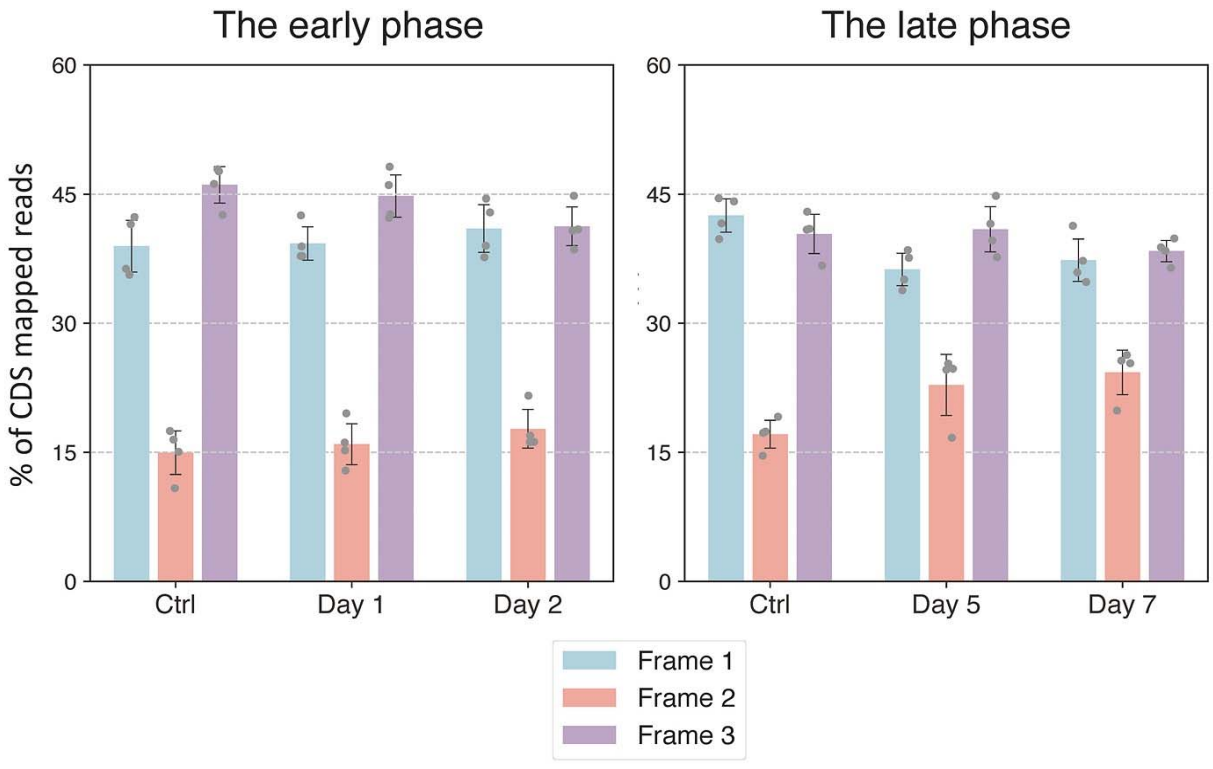


Metagene alignment around start and stop codons

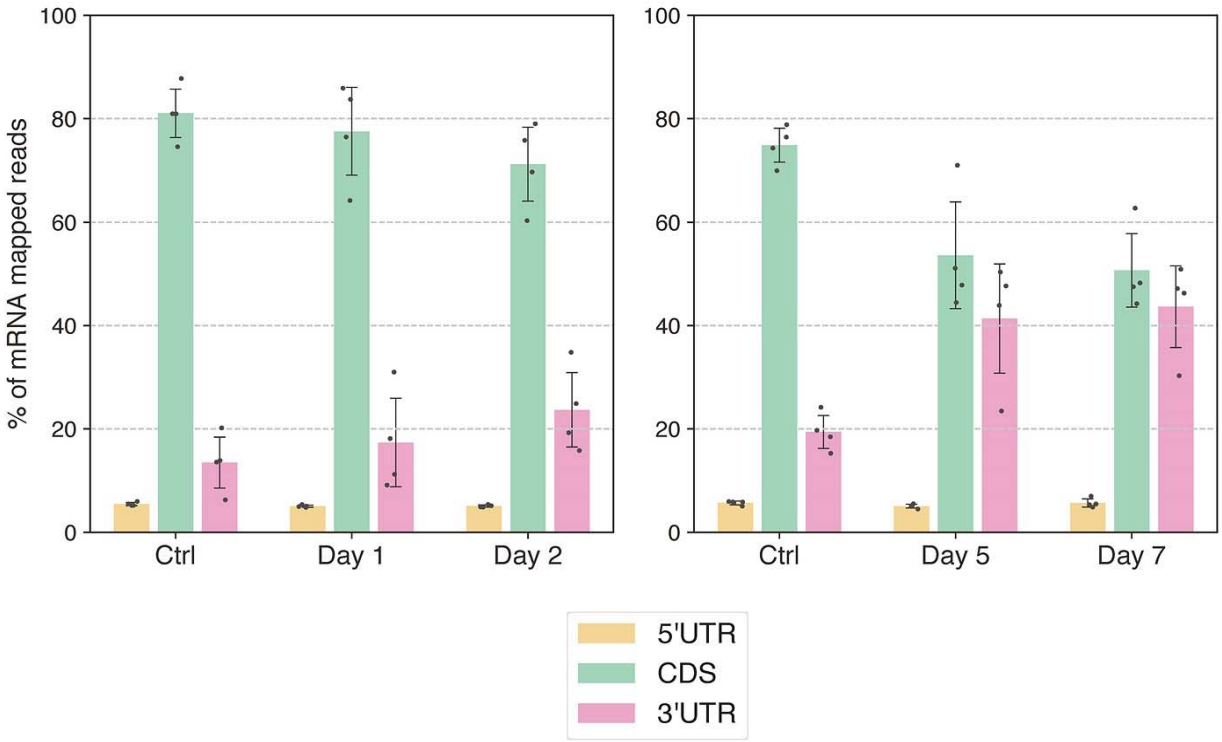
The late phase (set 2)



3nt periodicity



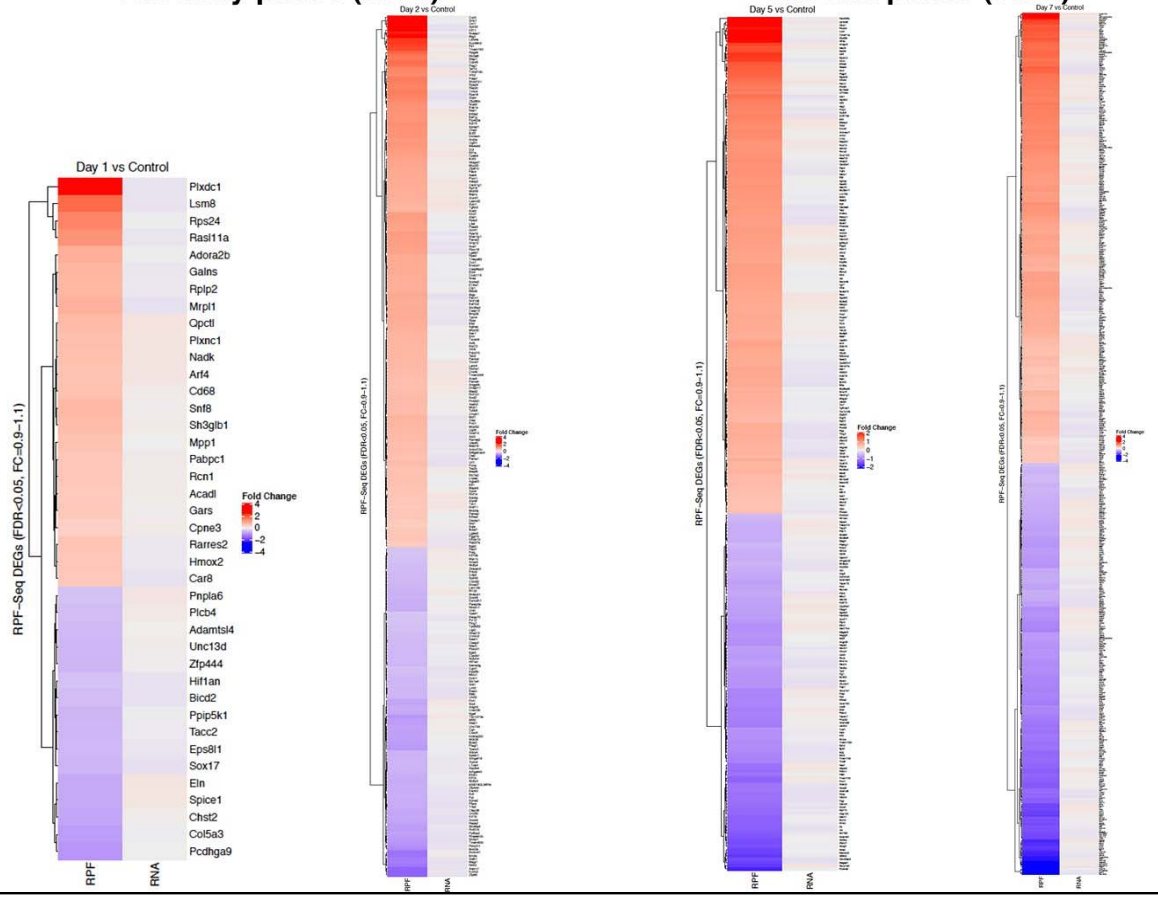
Ribosome distribution across mRNAs



Differentially expressed gene (DEG) analysis

The early phase (set 1)

The late phase (set 2)



BPS의 SERVICES

Screening & Profiling : 연구 대상 compound를 screening 하기 위해 400여 개 이상의 biochemical or cell based assay 가능

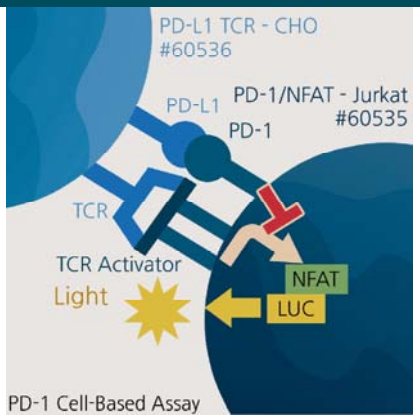
Protein Expression : 다양한 tag, host, species, 사용자 지정 가능한 QC

Cell Line Development : 70여 개 이상의 cell type/ 20여 개의 reporter gene 선택 가능

Screening & Profiling
Biochemical & Cell-Based Assays

BPS Advantages

- 수많은 고유 screening& profiling service 제공
- 200여 개 이상의 검증된 assay를 통해 시간 절약 및 문제점 해결
- 표준화된 screening protocol로 진행
- 고객 맞춤형 service 제공
- raw data와 분석된 data, 그래프, 세부 protocol을 report로 제공



Biochemical Assay Target Classes

- Acetyltransferase
- Apoptosis
- Bromodomain
- Cell Surface Receptor
- DNA Methyltransferase
- HDAC/Sirtuin
- Histone Demethylase
- Histone Methyltransferase
- HSP90
- Immune checkpoints
- Kinase
- Metabolic Enzymes
- Methyl-lysine Reader
- PARP
- PCSK9
- PDE
- Phosphatase
- Protease

Cell-Based Assays

- CAR T-Cell Screening
- Cytokine Assays
- Ion Channel Assays
- Tumor Proliferation Assays
- Reporter Gene Assays

Cell-Based Assay Target Classes

- Cell Signaling Pathways
- Hedgehog pathway
- Histone Deacetylases
- Immune Checkpoints
- Nrf2 Antioxidant Pathway
- NF-kB Pathway
- Phosphodiesterases
- T-Cell Activation
- Wnt/β-catenin pathway

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유전독성, 면역독성, 안전성약리 등

유효성(효능)평가
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4 Biomarker Discovery

질환별 miRNA 바이오마커 발굴

[원천 기술]

- 다양한 체액 내 추출이 용이하지 않은 small RNA를 고순도-고농도 추출-정제
- 추출된 small RNA 대상으로 나노센서를 이용한 신속-정확한 정량 분석

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