2024

한국미생물학회
분자세포생물·유전학 분과
심포지엄

일시 2024. 2. 26 (금) 13:30 – 19:30

장소 강원대학교 미래도서관 5층 대회의실

주최 한국미생물학회

2024

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분자세포생물·유전학 분과
심포지엄

일시 : **2024**년 **2**월 **26**일 (월) **장소**: 강원대학교 미래도서관 5층 대회의실

Program

13:30-13:50	Registration	
13:50-14:00	Opening remarks	이은진 교수 (고려대학교)
14:00-15:00	**Short-talk Session**	좌장: 조용준 교수 (강원대학교)
14:00-15:00	강원대학교 김동현 외 16명	
15:00-16:00	**Symposium Session**	좌장: 반연희 교수 (강원대학교)
15:00-15:10	The Lipid A Hydroxylation and Palmitoylation are mediated by MgtC in Salmonella Typhimurium	최낙준 (고려대 이은진 교수 연구실)
15:10-15:20	Structure and Functional Analysis of MntP in *Salmonella enterica* serovar Typhimurium	하나경 (고려대 이은진 교수 연구실)
15:20-15:40	Analysis of Mycobiome in Healthy Individuals and Ulcerative Colitis Patients	김주희 (강원대 조용준 교수 연구실)
15:40-16:00	Fine-Tuning Histone Acetylation by Rpd31 and Rpd32 for Precision Control of *Candida albicans* Virulence	김주은 박사 (강원대 이정신 교수 연구실)
16:00-16:20	**Break**	
16:20-17:00	**Keynote Session**	좌장: 조유희 교수 (차의과대학)
16:20-17:00	The eukaryotic formyl-methionine ribosome quality control pathway	황철상 교수 (고려대학교)
17:00-17:10	Concluding remarks	이은진 교수 (고려대학교)

Short talk session

14:00~15:00

좌장: 조용준 교수

김동현(강원대)
홍혜진(강원대)
이경민(강원대)
박건우(강원대)
최연우(강원대)
남지윤(강원대)
정헌준(강원대)
방지원(강원대)
권민정(강원대)

김동욱(고려대)
김민정(고려대)
김민지(고려대)
김서연(고려대)
김성규(고려대)
백승우(고려대)
윤민지(고려대)
조규상(고려대)

Title: Searching for marker genes to identify the telomeric silencing regulators in Saccharomyces cerevisiae

Donghyun Kim[1], Junsoo Oh[1], Seho Kim[1], Jung-Shin Lee[1]*

[1]Department of Molecular Bioscience, College of Biomedical Science, Kangwon National University, Chuncheon 24341, Republic of Korea

Telomeres have served as a valuable model for investigating heterochromatin structure. Position effect is a gene silencing phenomenon that is affected by heterochromatin blocks that are distributed across the chromosome. Because telomeres are also heterochromatin blocks, they exhibit a position effect, termed telomere position effect (TPE) or telomeric silencing. The Sir complex, a group of proteins including Sir2, plays a key role in forming heterochromatin near telomeres in Saccharomyces cerevisiae. When Sir2 is absent, telomeric silencing is defective. The URA3 assay, using expression of a uracil biosynthetic gene inserted into the subtelomere of ChrVII-L causing lethality in 5-FOA medium, is traditionally considered a useful experiment for gaining insight into TPEs. However, it comes with significant costs and raises critical questions such as the potential for false positives. Thus, there arises a pressing need to explore alternative or complementary methodologies to detect telomeric silencing efficiently. In our study, we select 6 marker genes that have significantly altered gene expression when changes Sir complex from RNA sequencing data of WT and Δsir2. These six markers offer a convenient and efficient means to screen for genes influencing TPE using qRT-PCR, a widely accessible technique in research laboratories.

Title: Histone H2B ubiquitination controls morphology in Candida albicans

Hyejin Hong[1], Hyojeong Koo[1], Jueun Kim[1,2], Shinae Park[2] and Jung-Shin Lee[1]

[1]Department of Molecular Bioscience, College of Biomedical Science, Kangwon National University, Chuncheon-si, 24341, Republic of Korea

[2]Kangwon Institute of Inclusive Technology, Kangwon National University, Chuncheon-si, 24341, Republic of Korea

Candida albicans, the human fungal pathogen, is part of the normal flora. The morphological change from yeast to hypha is a critical factor in regulating the virulence of C. albicans and is caused by changes in the expression of many genes. Enzymes of histone modification regulate this morphological transition, but it is still unclear how histone modifications regulate the pathogenic mechanism of C. albicans. In our study, we observed that the deletion of Rad6 or Bre1, components of the histone H2B ubiquitination machinery, reduced pathogenicity in a mouse infection model. Surprisingly, we observed that both mutant strains formed hyphae more rapidly compared to the wild-type strain. Our findings suggest that the absence of histone H2B ubiquitination attenuates pathogenicity by mechanisms other than filament formation.

Title: The Role of Chromatin Regulators in Sterol Metabolism

Kyungmin Lee[1], Shinae Park[1], Jung-Shin Lee[1*]

[1]Department of molecular bioscience, Kangwon National University, Chuncheon 24341, Korea

In eukaryotes, sterols are crucial components of cell membrane structures, significantly influencing membrane permeability, fluidity, and the functionality of cellular proteins. The regulation of sterol metabolism is vital because its dysregulation can lead to diseases such as atherosclerosis and myocardial infarction. Furthermore, chromatin structure, which is modulated by histone modification, has been linked to atherosclerosis. In our previous research, we found that the absence of Leo1, a component of the Paf1 complex, led to the upregulation of *UPC2* and its target genes, which are vital for sterol biosynthesis in yeast. This finding suggests a new cellular function of Leo1 in sterol metabolism. Moving forward, we plan to identify chromatin regulators that influence sterol metabolism in *Saccharomyces cerevisiae* using the yeast gene knockout collection library. We also aim to discover target genes affected by chromatin regulators through transcriptome analysis, further clarifying the role of chromatin regulators in sterol metabolism.

Title: Discovery for the bioactive natural products from cave-derived *Streptomyces* sp. OG2-3

Geonwoo Park[1], Yeon Hee Ban[1*]

[1]Department of Molecular Bioscience, College of Biomedical Science, Kangwon National University, Chuncheon 24341, Republic of Korea

Through genome sequencing analysis, we performed structure comparison analysis with known compounds and selected biosynthetic gene clusters that are expected to produce unknown compounds. Through LC/MS analysis, compounds of various molecular weights were detected, and we predicted a biosynthetic gene cluster that can biosynthesize a large molecular weight compound corresponding to 1482.9. Among the predicted biosynthetic gene clusters, we will disrupt essential genes including NRPS (Nonribosomal peptide synthetase) or PKS (Polyketide synthase) genes to check the changes in the substances produced. We will conduct various analyses, including NMR analysis, to analyze the structure of the novel compounds.

Title: Characterization of Kasugamycin Biosynthesis: Optimization of Expression and Purification of Biosynthetic Enzyme

Yeonwoo Choi[1] and Yeon Hee Ban[1]

[1]Department of Molecular Bioscience, College of Biomedical Science, Kangwon National University, Chuncheon 24341, Republic of Korea

Kasugamycin, an aminoglycoside antibiotic isolated from *Streptomyces kasugaensis*, is composed of *D*-chiro-inositol, kasugamine, and amidine moiety. While traditionally used to treat rice blast disease, recent investigations have revealed potential anti-*Mycobacterium tuberculosis* activity. However, the biosynthesis pathway remains unidentified. In this study, we hypothesized UDP-*N*-acetylglucosamine or UDP-glucosamine as the starting material. We also predicted that three enzymes, KasQ (UDP-*N*-acetylglucosamine 2-epimerase), KasD (dNDP-hexose 4,6-dehydratase), and KasE (hydrolase), would be responsible for the early steps of the kasugamycin biosynthetic pathway. We aim to elucidate the kasugamycin biosynthetic process through in vitro reconstitution.

Title: Development of aminoglycoside analogs with antibacterial activity against multidrug-resistant pathogens.

Jiyoon Nam[1], Yeon Hee Ban[1*]

[1]Department of molecular bioscience, Kangwon National University, Chuncheon 24341, Korea

Aminoglycosides (AGs), one of the oldest classes of antibiotic agents, exhibit strong antimicrobial activity against a wide range of Gram-negative and Gram-positive pathogens. The prolonged and extensive use of AGs has led to the emergence of resistant strains. A prominent resistance mechanism involves the action of aminoglycoside-modifying enzymes (AMEs), which modify the structure of AGs, thereby acquiring resistance against antibiotics. To overcome the challenge of AG inactivation by AMEs, the development of new AG antibiotics has been required. In the previous study, the AG acetyltransferase, AAC(6′)-APH(2″), one of the most typical AMEs, was employed to enzymatically synthesize new 6′-*N*-acylated amikacin. The antibacterial activity of enzymatically synthesized amikacin analogs will be evaluated against AG-resistant pathogens such as *Acinetobacter baumannii*. These structural modifications through enzymatic synthesis could be utilized for the generation of novel AG analogs, and these findings could be suggested the AG structure-activity relationship.

Title: Genomic and metabolomic analysis of a cave-derived *Streptomyces* sp. OG석고3 for discovery of novel bioactive compounds

Heon-jun Jeong[1,2], Yeon Hee Ban[1,*]

[1]Department of Molecular Bioscience, College of Biomedical Science, Kangwon National University,

Microorganisms can produce various bioactive compounds, and *Streptomyces* is particularly well known for producing medically useful bioactive compounds. In addition, microorganisms found in unique environments are well-suited for mining novel bioactive compounds. Recent advances in genome sequencing technologies and databases have enabled us to predict biosynthetic gene clusters (BGCs) that encode enzymes responsible for biosynthesizing bioactive compounds. In this study, we predicted BGC regions with non-ribosomal peptide synthetase (NRPS) and polyketide synthase (PKS) that are likely to biosynthesize novel bioactive compounds in *Streptomyces* sp. OG석고3. We also predicted the molecular weights of the compounds produced by the culture extract of OG석고3 using LC/MS analysis. Through comparative analysis with the BGCs of known compounds, we can expect to discover novel BGCs and bioactive compounds from OG석고3.

Title: Antifungal drug-associated genomic analysis of *Candida auris*

Jiwon Bang, Yong-Joon Cho

Department of Molecular Bioscience, Kangwon National University

This study investigates the genomic differences between drug-sensitive and drug-resistant strains of *Candida auris*. *Candida auris*, a fungal pathogen that causes candidiasis in patients with weakened immune systems, has a high rate of resistance to antifungal drugs. We wanted to find out how the two strains differ genomically, using a drug-sensitive strain as a control. To do this, we extracted DNA from two drug-sensitive strains and two drug-resistant strains. And we obtained the data using next-generation sequencing (NGS) and analyzed. We found that the drug-sensitive strains had similar genomes, and that they differed in amino acid types from the drug-resistant strains. Further analysis to identify which genes differed between the two strains, and if they are indeed the genes that contribute to drug resistance, could help develop new drugs to combat antifungal resistance in *Candida auris*.

Title: Genome Analysis of Cave-derived Streptomyces

Minjeong Kwon, Yong-Joon Cho

Department of Molecular Bioscience, Kangwon National University

This study investigates how four species of Streptomyces from moonmilk in cave differ from existing species in order to find new antibiotic properties. Many antibiotics from the Streptomyces family have been developed so far, but the emergence of antibiotic-resistant bacteria has caused many difficulties in treatment. To develop new antibiotics, DNA was extracted from Streptomyces and the V3-V4 region of 16s rRNA was amplified by next-generation sequencing (NGS) and data was obtained. After data assembly, the genomes were subjected to antiSMASH and several antimicrobial biosynthetic gene clusters were identified that are expected to produce secondary metabolites. We believe that this analysis will facilitate the development of new Streptomyces antibiotics to treat antibiotic-resistant bacteria.

Target Screening and Function Analysis of SpoT in Uropathogenic *Escherichia coli*

Dong-Uk Kim, and Eun-Jin Lee*

Division of Life Sciences, Korea University, South Korea

Urinary Tract Infections (UTI) are most commonly caused by a certain strain of *Escherichia coli* now classified as Uropathogenic *Escherichia coli*, or UPEC for short. In 2019, there have been an estimated 400 million cases of UTIs worldwide, and the bacterial pathogenesis in which the infection is caused by is still being widely studied. Previous research has shown that several key functions of the pathogenesis widely rely on several virulence factors, ranging from secreted toxins to iron acquisition systems. The SpoT regulatory enzyme is a key protein of interest because of its ability to synthesize and hydrolyze (p)ppGpp under certain conditions of environmental stress. Several studies have emphasized the importance of the alarmone ppGpp and its role in the stringent response for survivability. It also highlights several results that indicate the importance of the SpoT protein in bacterial pathogenicity. Utilizing screening methods such as the Bacterial Adenylate Cyclase Two-Hybrid (BACTH) System, this study will be focusing on target screening for the protein SpoT in Uropathogenic *E. coli,* specifically the CFT073 strain. Making use of the two complementary fragments T18 and T25 from the catalytic domain of adenylate cyclase, spoT and other several key genes of interest will be fused onto the fragments and hybridized into competent cells. The transformed cells will then be cultured on selected media and differentiated between the samples that signify protein-protein interaction and samples that do not. Further research utilizing several other screening methods, such as qRT-PCR, co-immunoprecipitation, and Western Blotting, would be conducted to identify key proteins and their relevance to bacterial pathogenesis.

Title: YadQ functions as a ClC chloride antiporter of amino acid-mediated acid resistance systems in *Salmonella* Typhimurium

Minjeong Kim, and Eun-Jin Lee*

Division of Life Sciences, Korea University, South Korea

Salmonella, a Gram-negative pathogenic bacterium, colonizes the human intestine, need to traverse through a spectrum of pH ranges within the gastrointestinal tract. In order to increase their survival in the presence of acidic environments like the stomach, these bacteria have evolved distinct defense mechanisms, including acid resistance systems mediated by amino acids. One of the components of these protective strategies is the ClC chloride antiporter, which facilitates the exchange of extracellular protons with negatively charged intracellular chloride ions, thereby preventing excessive inner membrane hyperpolarization. Here we demonstrate that YadQ contributes to acid resistance in Salmonella. Notably, YadQ exhibits increased expression levels in acidic conditions and the *yadQ* deletion renders Salmonella sensitive to acidic challenge. These data suggest that *Salmonella* YadQ acts as a ClC chloride antiporter, serving as an electrical shunt for the amino acid-mediated acid resistance systems.

Title: Investigation of the correlation between acetylation and PhoP protein stabilization in *Salmonella*

Minji Kim, and Eunjin- Lee*

Division of Life Sciences, Korea University, South Korea

Salmonella Typhimurium is a facultative intracellular pathogen. S.Typhi PhoP is a response regulator of PhoP/PhoQ two-component signal transduction system that plays a critical role in adaptation of the pathogen. PhoQ is an inner membrane sensor that is activated by environmental signals such as low Mg^{2+}, acidic pH, antimicrobial peptide. PhoP is a DNA binding regulator that binds to the promoters of various genes that are important for the pathogenicity and survival of S.Typhi. Activated PhoQ induce phosphorylation of PhoP and phosphorylated PhoP regulates the expression of genes required for pathogenicity, magnesium transport, protein post-translational modification (PTM), invasion into epithelial cells, and survival within macrophages. Previous research has confirmed that acetylation of lysine residues located at 102 and 201 of PhoP has significant impact on PhoP stabilization. Thus, we made a mutant strain where 102 and 201 lysine residues of PhoP are replaced with arginine, glutamine, and alanine. The acetylation of 102 and 201 lysine residues made PhoP stability decrease leading to the growth inhibition in low Mg2+ environment. This result suggests that other genetic factors that regulates PhoP stability may exist in mutant strains where the lysine residue of PhoP is acetylated. Therefore, we created a reverse mutant strain that restores PhoP stability from PhoP mutant in laboratory environment and found which genes contributed to the recovery of PhoP stability through whole genome sequencing. Then, we aim to determine whether that specific gene directly contributed to the recovery of PhoP stability by producing strains with specific gene deletion using one-step inactivation method of chromosomal genes and verifying the PhoP expression level using qRT-PCR and western blot. Through this, we aim to reveal the molecular regulatory mechanisms of acetylation and PhoP stabilization.

Title: A bacterial toxin promotes virulence by enhancing persistence of *Salmonella* inside macrophages

Seoyeon Kim and Eun-Jin Lee*

Department of Life Sciences, School of Life Sciences and Biotechnology, Korea University, Seoul 02841, Republic of Korea

Bacteria have evolved their own survival strategies against host immunity. Intracellular pathogen *Salmonella enterica* serovar Typhimurium can survive within a macrophage phagosome by forming non-replicating persisters, which are also non-responsive to antibiotics. Toxin-antitoxin (TA) system is one of the molecular mechanisms that are required for the formation of persisters and pathogen's survival inside host immune cells, although biological targets of toxins are largely hidden. Here, we report that IbsA, a 19 amino acid-long type I toxin from *Salmonella* Typhimurium, induces bacterial growth arrest and decreases intracellular ATP levels. A large-scale unbiased bacterial two-hybrid screening identifies 54 IbsA-interacting targets, including proteins involved in oxidative phosphorylation and multidrug resistance. Bacteria overexpressing IbsA inhibits ATP synthesis via oxidative phosphorylation and promotes *Salmonella* antibiotic persistence, which supports and validates the results of target screening. IbsA-mediated decrease in ATP levels causes bacteriostatic effect and leads *Salmonella* to form persister cells inside macrophages. Deletion of the entire *ibsA* locus attenuates mouse virulence, implicating that *Salmonella* IbsA toxin promotes the pathogenicity of this pathogen.

Title: Characterization of IbsC toxin in *Salmonella* Typhimurium

Seonggyu Kim, Seoyeon Kim, and Eun-Jin Lee*

Division of Life Sciences, Korea University, South Korea

Salmonella enterica is a Gram-negative bacterium that causes typhoid fever and food poisoning. Infection by *Salmonella* occurs mainly through invasion in the small intestinal epithelial cells.
Intracellular pathogen *Salmonella enterica* utilizes several strategies to evade various host immune systems and cause systemic infection. Toxin-antitoxin (TA) system is one of the mechanisms that induce non-growing/dormant cells that are tolerant to antibiotic treatment. Here, we focus on IbsC toxin in *Salmonella enterica* serovar Typhimurium, which belongs to the type I TA system. In normal conditions, sibC antitoxin RNA represses *ibsC* expression by base-pairing with *ibsC* mRNA. As Ibs toxin family is not well annotated in *Salmonella enterica* serovar Typhimurium 14028s, we first clarified the location and sequence of *ibsC* gene and its antitoxin, *sibC*. The *ibsC* gene encodes a 19 amino acid-long toxin which brings bacterial growth arrest when overexpressed. Site-directed mutagenesis revealed several key residues required for IbsC's toxin activity. In order to reveal the function of the IbsC toxin, we created the chromosomal *ibsC* deletion and found that IbsC toxin in required for *Salmonella* pathogenesis.

Title: EF-P mediated Frameshift regulation in *Salmonella* Typhimurium.

Seungwoo Baek [1,4], Yong-Joon Cho [2,4], Fuad Mohammad [3], Eunna Choi [1], Soomin Choi [1], Allen R. Buskirk [3], Eun-Jin Lee [1*]

[1] Department of Life Sciences, School of Life Sciences and Biotechnology, Korea University, Seoul, South Korea,

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[4] These authors contributed equally to this work

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Elongation factor P(EF-P) is required to enhance peptidyl transferase on pausing ribosomes, which can be induced by certain codons on mRNA. Therefore, to search EF-P mediated ribosome stalling motif, ribosome profiling has been used. However, it has not been addressed on the intracellular pathogen *Salmonella* Typhimurium. To investigate EFP mediated ribosome stalling motif and its relevance on the virulence of *S*. Typhimurium, we conducted ribosome profiling in wild-type and Δ*efp* strain. 135 sites in 128 genes were identified as EFP dependent sequences and many of these sites had consecutive proline codons. As a motif level, PPG was the most abundant amino acid motif at EPA site. Also, our findings revealed that a *Salmonella*-specific gene is regulated by frameshifting caused during translation as ribosome stalled in the DPP motif. And we showed that both proline motif and EF-P are engaged in this regulation, which affects the antimicrobial peptides resistance. In conclusion, this study emphasized the importance of poly proline motif on EFP and suggested a possible mechanism how EF-P affects the physiology of *Salmonella*.

Title: Molecular mechanism of the motor protein of flagella in *Salmonella* Typhimurium

Minji Youn, and Eun-Jin Lee*

Department of Life Sciences, Korea University, South Korea

Flagella is necessary for motility in Salmonella. The flagella is composed of several proteins, and the most important proteins in the motility of the flagella are the motor proteins. In the Salmonella, there are two motor proteins called MotA and MotB. When proton passes through the H^+ channel between MotA and MotB, the flagella's tail, filament, rotates by the flagella's torque. Previous studies have mainly focused on MotA, but not much research has been done. Therefore, experiments are underway to find out the mechanism of the motor protein. We observed that MotA and MgtC, a pathogenic protein of Salmonella, interact by BACTH. In order to find out which domain of MotA and MgtC interact, MotA was divided into two domains and MgtC was divided into each transmembrane and we found that MotA and the third transmembrane(TM3) of MgtC interact. Also in order to find out which amino acid of TM3 has an important role, a strain produced by point mutation of TM3 is used to find out the interaction with MotA. In addition, to find out how important MotA and MotB have an important role in the motility of Salmonella, the motA and motB genes were deleted and spotted on 0.3%, high Nmm, and low Nmm agar medium. The importance of motA and motB is observed by qRT PCR of the deletion strain to confirm the difference in the degree of mRNA expression. Through additional experiments, we will find the mechanism of the flagella motor protein to regulate the motility of Salmonella and to regulate the expression of Salmonella in the host.

Title: The Characterization of Oligoribonuclease in Salmonella Typhimurium

Kyu Sang Cho and Eun-Jin Lee*

Division of Life Sciences, Korea University

RNA degradation is a central role in the RNA metabolism of bacteria. There is a multistep process from long RNA polymers to short oligonucleotides, catalyzed by endoribonucleases and exoribonucleases. In the final stage of the RNA degradation pathway, oligoribonuclease (Orn) is the only diribonucleotidase to produce the nucleotide monophosphate. Therefore, orn is the essential gene for the survival of bacterial cells. In this study, we investigated the Orn from the intracellular bacterial pathogen Salmonella enterica serovar Typhimurium. When the orn gene is deleted by the FLP-FRT recombination system, it shows a slow-growing defect but remains viable in the LB medium. Furthermore, its slow growth rate can return to a normal state when the Orn is overexpressed by ectopic production. Using site-directed mutagenesis and hydrolysis of the pNP-TMP assay, an artificial nucleoside 5′-phosphodiester substrate, critical residues of Orn that are directly involved in hydrolyzing the phosphodiester bond of diribonucleotide were identified. In addition, the orn deletion mutant affects Salmonella pathogenicity inside macrophages. Understanding the role of the orn within Salmonella RNA metabolism will provide a new perspective on Salmonella pathogenicity.

Symposium session

15:00~16:00

좌장: 반연희 교수

15:00~15:10 최낙준 (고려대)

15:10~15:20 하나경 (고려대)

15:20~15:40 김주희 (강원대)

15:40~16:00 김주은 박사 (강원대)

영문명 : Nakjun Choi

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Educational Experience:

2020.9 – Present: M.S./PhD. Department of Life Sciences, Korea University

2014.3 – 2020.8: B.S. Department of Biology, KyungHee University

Selected Publications (5 maximum)

1. Kim M, Choi N, Choi E, **Lee EJ*.** ClC Chloride Channels in Gram-Negative Bacteria and Its Role in the Acid Resistance Systems. ***J Microbiol Biotechnol***. 2023 Jul 28;33(7):857-863. doi: 10.4014/jmb.2303.03009. Epub 2023 Apr 14.

Title: The Lipid A Hydroxylation and Palmitoylation are controlled by a *Salmonella* virulence protein

Nakjun Choi1, and Eun-Jin Lee1*

1Department of Life Sciences, Korea University

Abstract:

Salmonella enterica serovar Typhimurium is a representative of an intracellular pathogen, but understanding its intracellular survival within host cells is challenging. The PhoP/PhoQ two-component system is a pivotal player in adaptation to host environments, regulating stress responses and lipid A modification enzymes. LpxO is one of the lipid A modification enzymes that hydroxylate the 3`-myristate chain of hexa-acylated lipid A and is associated the resistance to cationic antimicrobial peptides. The virulence protein MgtC is positively regulated by the PhoP/PhoQ system under magnesium depletion, however, has less information about its functions. In our study, we identified an interaction between MgtC and LpxO, highlighting the significance of the L287 residue of LpxO for this interaction rather than its function. This interaction was found to enhance the hydroxylation of lipid A. Furthermore, under low magnesium conditions, the deletion of mgtC led to a significant increase in the palmitoylation of lipid A. In conclusion, our findings suggest that the virulence protein MgtC plays a crucial role in finely tuning the modification of lipid A, providing insight into its involvement in Salmonella's adaptation within the host environments.

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Educational Experience:

2021.3 - M.S./PhD. Department of Life Sciences, Korea University
2015.3 – 2021.2 B.S., Department of Life Sciences, Korea University

Selected Publications (5 maximum)

1. Korean Journal of Microbiology (2021) '병원성 *Escherichia coli*에서 toxin-antitoxin system의 분포 및 역할'
2. Journal of Microbiology (2023) 'Manganese Transporter Proteins in *Salmonella enterica* serovar Typhimurium'

Title: Structure and Functional Analysis of MntP in *Salmonella enterica* serovar Typhimurium

Nakyeong Ha, and Eun-Jin Lee*

Department of Life Science, Korea University, Seoul 02841, Korea

Salmonella is an intracellular pathogen which has an ability to surive and reproduce inside the host macrophage. Therefore, *Salmonella* has to face an unfavorable environment such as low pH, oxidative stress, nitrosative stress, and nutritional shortage. Manganese plays an important role in proper functioning of enzymes needed for overcoming the harsh environment. However, the host restricts the manganese acquisition in a way called 'nutritional immunity'. *Salmonella* has evolved several ways to maintain manganese homeostasis. There are three importer proteins, MntH, SitABCD, and ZupT, and two exporter proteins, MntP and YiiP, identified to take part in manganese transport. Here, we analyzed the structure and functional mechanism of MntP. Beta-galactosidase and alkaline phosphatase assays were used for confirming the predicted six transmembrane domain model. Western blotting and qRT PCR method was used for observing upregulation of *mntP* in presence of excessive manganese.

영문명 : Kim, Jueun

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Educational Experience: (최근순서)

2014.3 – 2020.8 Ph.D., Department of Biomedial Science, Kangwon National University
2010.3 – 2014.2 B.S., Department of Molecular Bioscience, Kangwon National University

Professional Experience: (최근순서)

2020.9 – Present Post-doc, Kangwon Institute of Inclusive Technology, Kangwon National University

Selected Publications (5 maximum)

1. Yang SM*, ~~Kim J~~*, Lee JY*, Lee JS and Lee JM (2023) Regulation of glucose and glutamine metabolism to overcome cisplatin resistance in intrahepatic cholangiocarcinoma. BMB Rep 56, 600-605 (*co-firsts)

2. ~~Kim J~~, Park S, Kwon SH, Lee EJ and Lee JS (2021) Set1-mediated H3K4 methylation is required for Candida albicans virulence by regulating intracellular level of reactive oxygen species. Virulence 12, 2648-2658

3. ~~Kim J~~ and Lee JS (2020) Rapid method for chromatin immunoprecipitation (ChIP) assay in a dimorphic fungus, Candida albicans. J Microbiol 58, 11-16

4. ~~Kim J~~, Park S and Lee JS (2018) Epigenetic Control of Oxidative Stresses by Histone Acetyltransferases in Candida albicans. J Microbiol Biotechnol 28, 181-189

5. ~~Kim J~~, An YK, Park S and Lee JS (2018) Bre1 mediates the ubiquitination of histone H2B by regulating Lge1 stability. FEBS Lett 592, 1565-1574

Title: Fine-Tuning Histone Acetylation by Rpd31 and Rpd32 for Precision Control of *Candida albicans* Virulence

Jueun Kim[1,2], Shinae Park[1], and Jung-Shin Lee[1,*]

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Rpd3 is a well-known Class I histone deacetylase identified in yeast. Although Candida albicans possesses two distinct orthologous proteins, Rpd31 and Rpd32, the reason for their coexistence remains unclear despite previous studies on their physiological roles. Additionally, the transcriptional regulatory mechanisms orchestrated by Rpd31 and Rpd32 through their catalytic functions remain elusive. In this study, we observed that the absence of Rpd31/32 resulted in impaired hyphal formation and complete loss of pathogenicity in mice. We observed a complementary relationship between Rpd31 and Rpd32 in orchestrating gene expression in C. albicans. Interestingly, their absence did not globally increase histone acetylation but rather redistribution H3 acetylation from promoter-TSS regions into gene bodies. Genes with reduced expression in the absence of Rpd31/32 had extended upstream intergenic regions (IGRs) showing extensive H3 acetylation, which was depleted in the absence of Rpd31/32. Notably, numerous transcription factors in C. albicans have long IGRs and their transcription were regulated by Rpd31/32. These findings highlight the crucial role of Rpd31 and Rpd32 in regulating the precise positioning of H3 acetylation on key regulatory genes important for morphogenesis and virulence within host cells.

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Title: Analysis of Mycobiome in Healthy Individuals and Ulcerative Colitis Patients

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This study investigates the differences in the gut mycobiome between patients with ulcerative colitis (UC) and healthy individuals. Ulcerative colitis, a chronic condition of unknown etiology, has been the subject of numerous studies aiming to elucidate its causes and develop effective treatments, yet success has been limited thus far. Given reports suggesting a potential association between gut fungi and inflammation, we sought to explore whether the mycobiome is related to ulcerative colitis. To this end, we extracted DNA from fecal samples of 157 healthy individuals and 80 UC patients. Subsequently, we amplified the ITS region and obtained data through next-generation sequencing (NGS) and analyzed. Our findings revealed that regardless of whether individuals were healthy or had UC, the gut mycobiome could be broadly categorized into four enterotypes, with age-related differences observed in the mycobiome. Further analysis may reveal significant differences between healthy individuals and those with ulcerative colitis, potentially shedding light on the etiology of UC and facilitating fundamental therapeutic advancements.

기조강연

16:20~17:00

좌장: 조유희 교수

발표자: 황철상 교수(고려대)

발표제목: The eukaryotic formyl-methionine ribosome quality control pathway

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Mun SH, Lee CS, Kim HJ, Kim J, Lee H, Yang J, Im SH, Kim JH, Seong JK, **Hwang C S.** (2023) Marchf6 E3 ubiquitin ligase critically regulates endoplasmic reticulum stress, ferroptosis, and metabolic homeostasis in POMC neurons. **Cell Reports**. 42(7):112746.
Nguyen KT, Mun SH, Yang J, Lee J, Seok OH, Kim E, Kim D, An SY, Seo DY, Suh JY, Lee Y, **Hwang CS**. (2022) The MARCHF6 E3 ubiquitin ligase acts as an NADPH senso r for the regulation of ferroptosis. **Nat Cell Biol**. 24(8):1239-1251.
Kim, J.-M., Seok, O.-H., Ju, S., Heo, J.-E., Yeom, J., Yoo, J.-Y., Varshavsky, A., Lee, C*. , and **Hwang., C.-S.*** (2018) Formyl-methionine as an N-degron of a eukaryotic N-end r ule pathway, **Science**, 30; 362(6418).
Park, S.-E.#, Kim, J.-M#., Seok, O.-H., Cho, H., Wadas, B., Kim, S.-Y., Varshavsky, A.* and **Hwang C.-S.*** (2015) Control of mammalian G protein signaling by N- terminal ac etylation and the N-end rule pathway, **Science**, 347(6227):1249-1252.
Kim, H.-K.#, Kim, R.-R.#, Oh., J.-H., Cho, H., Varshavsky, A.* and **Hwang, C.-S.*** (20 14) The N-terminal methionine of cellular proteins as a degradation signal, **Cell**, 156:15 8-169. (*corresponding authors, #co-first authors).

Title: The eukaryotic formyl-methionine ribosome quality control pathway

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Contrary to the prevailing assumption that eukaryotic ribosomes exclusively initiate protein synthesis with methionine (Met), our recent research reveals the capacity of cytosolic ribosomes to utilize formylmethionine (fMet) to some extent. Specifically, stress-induced up-regulation of cytosolic N-terminally formylated proteins, governed by the Gcn2 protein kinase, occurs in conditions such as undernutrition and low temperature in the budding yeast *Saccharomyces cerevisiae*. Furthermore, the Psh1 E3 ubiquitin ligase coordinates a eukaryotic N-degron pathway selectively degrading N-terminally formylated proteins. Despite the anticipated widespread presence of N-terminal fMet residues in the eukaryotic proteome due to pre-translational fMet-tRNA synthesis, our study also demonstrates a limited amount of N-terminal formylated proteins. Mechanistically, we uncovered a novel fMet-mediated ribosome quality control (fMet-RQC) mechanism that eliminates fMet-bearing polypeptides during translation. In this presentation, I will explore the intricacies of eukaryotic fMet protein synthesis, delve into associated fMet-RQC pathway, and discuss their implications in stress responses and age-associated diseases.