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科学研究費助成事業　　研究成果報告書

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研究課題名（和文）Identification and characterization of novel virulence factors of Staphylococcus aureus USA300 using silkworm model.

研究課題名（英文）Identification and characterization of novel virulence factors of Staphylococcus aureus USA300 using silkworm model.

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研究成果の概要（和文）：我々はカイコを用いて8つの新規 Staphylococcus aureus病原性因子を発見した。そのうちの1つyjbHは、黄色ブドウ球菌の病原性遺伝子群の発現を制御し、菌体の表面タンパク質を変化させる。その結果、宿主内で黄色ブドウ球菌は酸化ストレスに対して抵抗性を獲得し病原性を発揮することを明らかにした。さらに、カイコを用いて Bacillus anthracis および Bacillus cereus の病原性評価が可能であることを示した。

研究成果の学術的意義や社会的意義
The research identified novel virulence factors of a Gram-positive bacteria, methicillin-resistant Staphylococcus aureus, using silkworm infection model and deepened our understanding of its pathogenicity.

研究成果の概要（英文）：We screened Nebraska Transposon Mutant Library of USA300 and found that 8 mutants with reduced virulence in silkworm and mice infection models. The pathogenicity was not restored by introduction of one of the genes: yjbI, while the introduction of the downstream gene yjbH complemented the pathogenicity in silkworms and mice. RNA-seq analysis of yjbI::Tn and yjbH::Tn mutants revealed that disruption of both genes significantly affected the expression of > 200 genes including downregulation of several virulence genes. We,theb, established silkworm infection models of Bacillus anthracis and B. cereus. Constructing a mutant library of Bacillus cereus, we found one gene X to have role in virulence in silkworm. We then used the mutants with transposon inserted in the gene X from the NTML library of S. aureus and found that the disruption of the gene X made S. aureus hyper virulent. Thus, we found that although the gene was conserved among S. aureus and B. cereus and had role in virulence.

研究分野：Bacteriology

キーワード：pathogenesis　virulence　virulence factor　silkworm　infection　Bombyx mori　Bacillus cereus

１．研究開始当初の背景

Development of novel antimicrobial agents has been a challenge as microbes acquire ways to resist the drugs. One of the major causes of such emergence of resistance is the overuse and misuse of antimicrobial agents. The antimicrobial agents that kill or suppress the growth of microbes exert huge pressure to the microbes (both the pathogen and microbiota). In order to counteract the pressures, microbes find ways to resist the antimicrobial agents leading to the emergence of drug resistance. *Staphylococcus aureus* accounts for a large number of infections and deaths every year. On the top of it, emergence of *S. aureus* strains resistant to all the clinically used antibiotics including the last resort of treatment, vancomycin, has urged the need of discovery and development of novel antimicrobial/anti-infective agents effective against such multidrug-resistant strains. *S. aureus* exists as a commensal-bacteria which upon favorable conditions, turn into a deadly pathogen by production of virulence factors. Virulence is the degree of pathogenicity of a microorganism that is largely affected by host environment and host-pathogen interaction. In order to establish infection within the host, *S. aureus* produces virulence factors such as cytolysins, hemolysins, leukocidins, proteases, enterotoxins, exfoliative toxins and immune-modulatory factors. Although some of the pathways of virulence factor expression and regulation such as sarA, agr, srrAB, saeRS systems in *S. aureus* are well-studied, many genes with unknown functions are present in *S. aureus* genome that might have roles in virulence and pathogenicity.

Since virulence is due to the interplay between the host and pathogen, a suitable model that reflects the actual clinical condition of infection is required for the purpose of identification of novel virulence factors. Here, we used silkworms (*Bombyx mori*) for this purpose. We previously showed that injection of *S. aureus* kills the silkworms, activates innate immunity, and the ED_{50} values of clinically used antibiotics were similar between silkworms and mammals. We discovered antibacterial agents lysocin E, GPI0363, compound 5 and antifungal agent ASP2397 using silkworm infection models. Using silkworm, we previously identified three novel *S. aureus* virulence factors: CvfA, CvfB and CvfC which also have roles in pathogenicity to mammals. In this regard, use of silkworm as a model is the unique way for the identification of novel virulence factors of *S. aureus* that have roles in pathogenicity to mammals.

２．研究の目的

The purpose of the research was to identify and characterize the novel factors of *S. aureus* involved in pathogenicity, which will be useful as novel targets for development of novel anti-infective agents and ultimately provide novel insights into the host-pathogen interaction during infection.

３．研究の方法

Screening of mutants for reduced pathogenicity in silkworms

We used the Nebraska Transposon Mutant Library (NTML) of *S. aureus* USA300 and perform the comprehensive screening by selecting the mutants harboring mutations in the genes whose roles in pathogenicity are not known. These genes include the ones which are not characterized as well as their roles in pathogenicity are not known. Out of a total of 1919 mutants from the NTML, we first, selected 480 genes encoding hypothetical protein according to TIGR (The Institute for Genomic Research) Microbial Database. We omitted 100 genes that were previously tested using silkworm model and used the remainder for screening purpose. The selection scheme is shown in **Figure 1.** The candidates obtained from the screening were, at first, confirmed for pathogenicity in silkworms and then tested for their pathogenicity in a mouse infection model. Phenotypic and genotypic analysis was performed for the candidate gene disruption mutants. RNA sequencing, surface protein and Fourier-Transform Infrared spectroscopic analysis were performed.

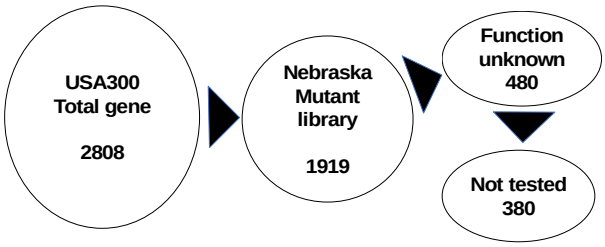

Figure 1: Selection of mutants for screening

４．研究成果

Identification of novel *S. aureus* gene-disrupted mutants with reduced pathogenicity in silkwormsWe found that 10 mutants had significantly lower virulence in silkworms than the wild-type strain as shown by their higher lethal dose fifty (LD_{50}) values (**Figure 2A**). Of the 10 strains, 8 had significantly reduced microbial survival in at mouse organs (**Figure 2B, 2C**), indicating that 80% of the virulence factors identified using

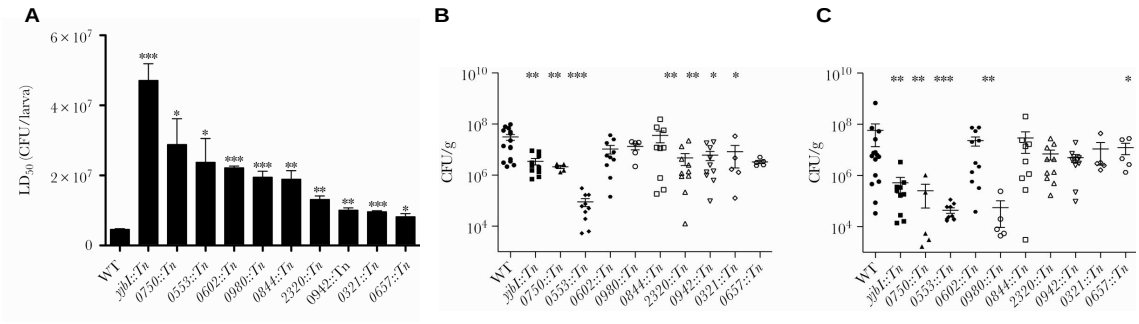

Figure 2. Screening and identification of novel candidate virulence factors of *S. aureus*.

silkworms exerted virulence in mice. This finding shows that the silkworm infection model efficiently identified bacterial factors with pathogenic roles in mice. We further confirmed that the transposon insertion point of each mutant strain was within the coding frame of the specified gene. To rule out the possibility of polar effect, we complemented the mutants with plasmids containing the intact genes and determining the pathogenicity of the complemented strains in silkworms. We found that complementation of 6 of the strains (0750::Tn, 0553::Tn, 0980::Tn, 2320::Tn, 0321::Tn, and 0657::Tn) restored pathogenicity, suggesting the absence of any polar effects. Complementation of 0942::Tn resulted in a further loss of pathogenicity and yjbI::Tn did not recover the pathogenicity. As organization of the *yjbI* gene suggests that it forms an operon along with the *yjbH* gene, we complemented the yjbI::Tn mutant with *yjbH* gene, which recovered the virulence in the silkworms (**Figure 3**), suggesting YjbH was the actual factor involved in pathogenicity.

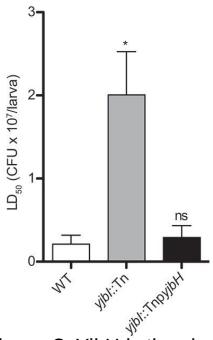

Figure 3. YjbH is the virulence factor.

In vitro phenotypes of the mutants

We examined the growth rates of all the mutants in vitro in TSB medium at 37°C. The doubling times did not differ significantly between the mutants and the wild type, suggesting that the differences in pathogenicity could not be attributed to differences in the growth rates of the strains. To further check whether the phenomenon of low pathogenicity was related to reduced toxin production, we compared the hemolytic and proteolytic activities between the mutants and the wild type. We found that 3 strains (yjbI::Tn, 0750::Tn, and 0657::Tn) had reduced hemolytic activity as determined by a clear zone surrounding the colony on sheep blood (**Figure 4**) and that yjbI::Tn had reduced proteolytic activity as evaluated by a clear zone surrounding the colony on skimmed milk agar plates (**Figure 4**). Next, we checked the survival of the identified strains in murine monocyte-macrophage RAW 264.7 cells. We determined the intracellular bacterial survival by a gentamicin protection assay followed by lysis of macrophage cells. The results indicated that 2 of the 8 strains (0980::Tn and 0942::Tn) had significantly reduced survival, while 1 of the strains (yjbI::Tn) had increased survival compared with the wild type (**Figure 5**). This finding suggests that the mechanisms involved in the pathogenesis of most of these mutants are independent of macrophage resistance.

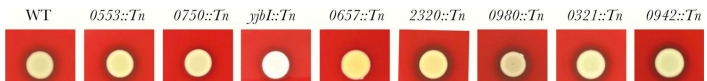

Figure 4. Hemolytic and proteolytic activities of the strains.

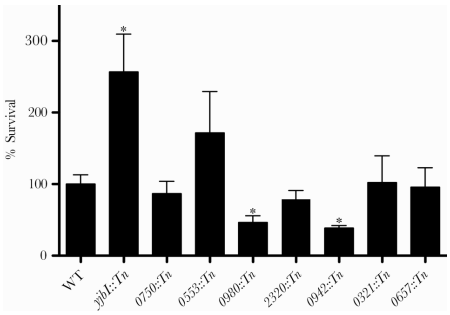

Figure 5. Intracellular survival of the strains within murine macrophages.

Surface protein and cell envelope glycopolymer structure were altered by disruption of the yjbI and the yjbH genes

To get insight into the mechanism of reduced virulence by YjbH, we sought to analyze the surface protein

profiles. We found that the yjbH and the *yjbI* genes-disrupted mutants had reduced surface proteins compared to that of the wild-type, which was complemented by the introduction of the mutants with the yjbIH operon and the *yjbH* gene but not the yjbI gene (**Figure 6A**). Next, we performed spectroscopic fingerprinting using Fourier-transform infrared (FTIR) spectroscopy for the yjbI::Tn, yjbH::Tn, and the wild-type strains to investigate changes in the cell envelope glycopolymer structure. We found that both the yjbI::Tn and yjbH::Tn mutants clustered distinct from the wild-type, but they could not be discriminated from each other using the highly discriminatory polysaccharide spectral region (**Figure 6B, upper**). Disruption of the *yjbI* and the *yjbH* genes caused a large number of prominent spectral differences at wavenumbers between 1190–890 cm−1, which can be assigned to strong perturbations in the bacterial surface/cell wall-glycopolymer composition (**Figure 6B, lower**). Here, the absence of YjbH led to an alteration in surface protein and cell envelope glycopolymer composition that could likely contribute to the virulence of S. aureus.

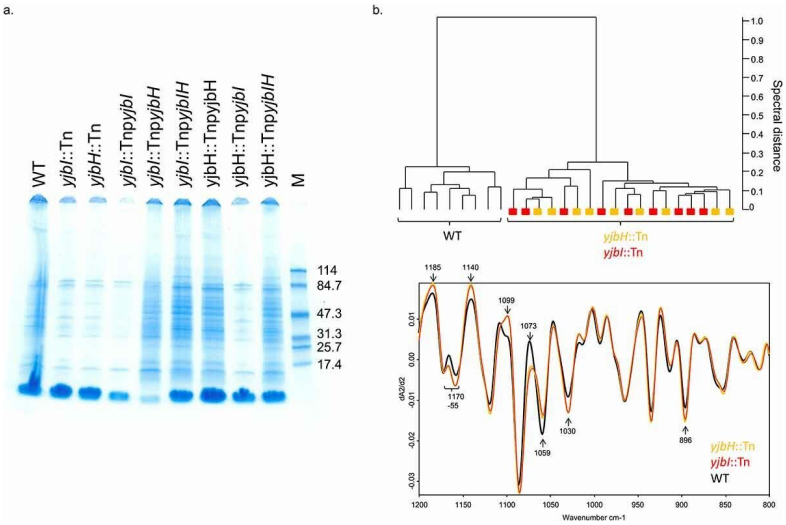

Figure 6. Alteration in surface structure due to the *yjbI* and the *yjbH* genes disruption.

RNA-seq analysis reveals downregulation of virulence and oxidative stress-related genes

With the involvement of the *yjbI* and the *yjbH* genes in protease and pigment production, surface protein production and pathogenicity of *S. aureus*, we speculated YjbH might be involved in regulating the expression of various genes. Therefore, we performed RNA-seq analysis. We found that disruption of both the genes led to significant changes in the expression of the genes from diverse pathways that included virulence genes, surface proteins, and genes involved in oxidative stress. From the RNA-seq analysis results, we were intrigued to test whether YjbH is involved in virulence by protecting *S. aureus* against oxidative stress in the host. For this purpose, we determined LD_{50} values of the strains in the presence and absence of N-acetyl-L-cysteine (NAC). NAC is a free radical scavenger; it eliminates reactive oxygen species (ROS) such as OH•, HOX, NO_2, and H_2O_2. We found that by the pre-injection of NAC into silkworm hemolymph, LD_{50} values were significantly decreased, rendering the strains more effective in killing the silkworms (**Figure 7**). These results suggested that YjbH functions in protecting *S. aureus* from oxidative stresses in the host.

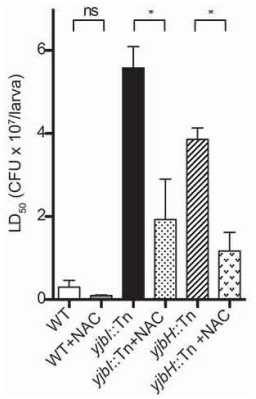

Figure 7. Effect of NAC upon pathogenicity

Virulence determination of other Gram-positive bacteria using silkworms

We, then, expanded our study to other Gram-positive bacteria of *Bacillus cereus* group. We established silkworm infection model of *Bacillus anthracis* Sterne strain. We found that that it was pathogenic to silkworms and killed them with an LD_{50} of $8.1x10^2$ CFU/larva at 19 hours post infection. We further found that antibiotic treatment protected silkworms from the infection. Using fluorescent protein Amcyan1 expressing *B. anthracis*, we showed that the bacteria proliferated in silkworm hemolymph after injection into the hemolymph and antibiotic treatment halted this proliferation (**Figure 8**). Furthermore, we found that the virulence gene knockout mutants of *B. anthracis* had attenuated virulence in silkworms as observed by the survival of

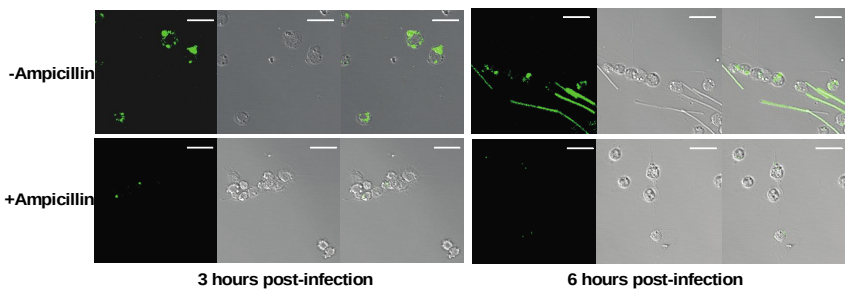

Figure 8. Proliferation of B. anthracis in silkworm hemolymph is halted by antibiotic

silkworms (**Figure 9A**) and microbial burden in silkworm hemolymph 6 hours post infection (**Figure 9B**). We, similarly, established a silkworm model of *Bacillus cereus* infection and used silkworms to screen for less virulent mutants from a random mutant library of *B. cereus* obtained by treatment with a mutagen. We found several mutants with reduced virulence in silkworms and performed their whole genome sequencing to identify genes with mutations. We found that one mutant had a point mutation in a gene that led to amino acid change. This gene, gene X, was conserved among *S. aureus* and *B. cereus* group of bacteria. When we checked the pathogenicity of gene X-disruption mutant of *S. aureus* from the NTML library, we found that the mutant was hypervirulence to silkworms. Thus, we found that gene X had roles in pathogenicity of both *B. cereus* and *S. aureus*, which needs to be further verified and mechanism of virulence needs to be elucidated.

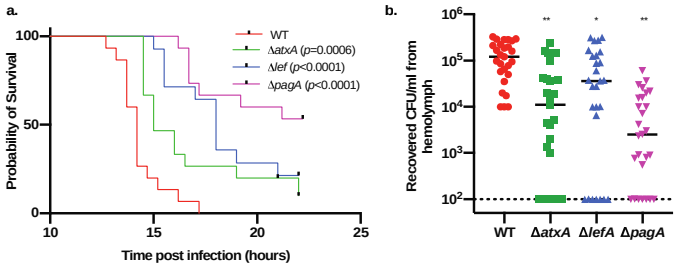

Figure 9. Assessment of virulence of *B. anthracis* mutants using silkworms

５．主な発表論文等

〔雑誌論文〕　計19件（うち査読付論文　11件／うち国際共著　11件／うちオープンアクセス　11件）

１．著者名 Atmika Paudel, Hiroshi Hamamoto, Suresh Panthee, Yasuhiko Matsumoto, Kazuhisa Sekimizu	４．巻 221
２．論文標題 Large-Scale Screening and Identification of Novel Pathogenic Staphylococcus aureus Genes Using a Silkworm Infection Model	５．発行年 2020年
３．雑誌名 The Journal of infectious diseases	６．最初と最後の頁 1795-1804
掲載論文のDOI（デジタルオブジェクト識別子） 10.1093/infdis/jiaa004	査読の有無 有
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 該当する

１．著者名 Atmika Paudel, Suresh Panthee, Hiroshi Hamamoto, Kazuhisa Sekimizu	４．巻 14
２．論文標題 A simple artificial diet available for research of silkworm disease models	５．発行年 2020年
３．雑誌名 Drug Discoveries & Therapeutics	６．最初と最後の頁 177-180
掲載論文のDOI（デジタルオブジェクト識別子） 10.5582/ddt.2020.03061	査読の有無 有
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 該当する

１．著者名 Bimala Panthee, Saraswati Dhungana, Nirmal Panthee, Atmika Paudel, Saroj Gyawali, Suresh Panthee	４．巻 37
２．論文標題 COVID-19: the current situation in Nepal	５．発行年 2020年
３．雑誌名 New microbes and new infections	６．最初と最後の頁 100737
掲載論文のDOI（デジタルオブジェクト識別子） 10.1016/j.nmni.2020.100737	査読の有無 有
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 該当する

１．著者名 Suresh Panthee, Atmika Paudel, Hiroshi Hamamoto, Anne-Catrin Uhlemann, Kazuhisa Sekimizu	４．巻 11
２．論文標題 The Role of Amino Acid Substitution in HepT Toward Menaquinone Isoprenoid Chain Length Definition and Lysocin E Sensitivity in Staphylococcus aureus	５．発行年 2020年
３．雑誌名 Frontiers in microbiology	６．最初と最後の頁 2076
掲載論文のDOI（デジタルオブジェクト識別子） 10.3389/fmicb.2020.02076	査読の有無 有
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 該当する

1．著者名 Yuri Takada, Hiroaki Itoh, Atmika Paudel, Suresh Panthee, Hiroshi Hamamoto, Kazuhisa Sekimizu, Masayuki Inoue	4．巻 11
2．論文標題 Discovery of gramicidin A analogues with altered activities by multidimensional screening of a one-bead-one-compound library	5．発行年 2020年
3．雑誌名 Nature communications	6．最初と最後の頁 4935
掲載論文のDOI（デジタルオブジェクト識別子） 10.1038/s41467-020-18711-2	査読の有無 有
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 該当する

1．著者名 Bimala Panthee, Saraswati Dhungana, Nirmal Panthee, Saroj Gyawali, Atmika Paudel, Suresh Panthee	4．巻 38
2．論文標題 Clinical and epidemiological features of COVID-19 deaths in Nepal	5．発行年 2020年
3．雑誌名 New Microbes and New Infections	6．最初と最後の頁 100797
掲載論文のDOI（デジタルオブジェクト識別子） 10.1016/j.nmni.2020.100797	査読の有無 有
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 該当する

1．著者名 Atmika Paudel, Suresh Panthee, Hiroshi Hamamoto, Tom Grunert, Kazuhisa Sekimizu	4．巻 12
2．論文標題 YjbH regulates virulence genes expression and oxidative stress resistance in Staphylococcus aureus	5．発行年 2021年
3．雑誌名 Virulence	6．最初と最後の頁 470-480
掲載論文のDOI（デジタルオブジェクト識別子） 10.1080/21505594.2021.1875683	査読の有無 有
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 該当する

1．著者名 Suresh Panthee, Atmika Paudel, Hiroshi Hamamoto, Akihiko Ano Ogasawara, Toshihiro Iwasa, Jochen Blom, Kazuhisa Sekimizu	4．巻 113
2．論文標題 Complete genome sequence and comparative genomic analysis of Enterococcus faecalis EF-2001, a probiotic bacterium	5．発行年 2021年
3．雑誌名 Genomics	6．最初と最後の頁 1534-1542
掲載論文のDOI（デジタルオブジェクト識別子） 10.1016/j.ygeno.2021.03.021	査読の有無 有
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 該当する

1．著者名 Misheck Shawa, Yoshikazu Furuta, Gillan Mulenga, Maron Mubanga, Evans Mulenga, Tuvshinzaya Zorigt, Christone Kaile, Manyando Simbotwe, Atmika Paudel, Bernard Hang ' ombe, Hideaki HIGASHI	4．巻 10
2．論文標題 Novel chromosomal insertions of ISEcp1-blaCTX-M-15 and diverse antimicrobial resistance genes in Zambian clinical isolates of Enterobacter cloacae and Escherichia coli	5．発行年 2021年
3．雑誌名 BMC Antimicrobial Resistance & Infection Control	6．最初と最後の頁 79
掲載論文のDOI（デジタルオブジェクト識別子） なし	査読の有無 有
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 該当する

1．著者名 Suresh Panthee, Atmika Paudel, Jochen Blom, Hiroshi Hamamoto, Kazuhisa Sekimizu	4．巻 10
2．論文標題 Complete genome sequence of Weissella hellenica 0916-4-2 and its comparative genomic analysis	5．発行年 2019年
3．雑誌名 Frontiers in microbiology	6．最初と最後の頁 1619
掲載論文のDOI（デジタルオブジェクト識別子） 10.3389/fmicb.2019.01619	査読の有無 無
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 —

1．著者名 Atmika Paudel, Suresh Panthee, Hiroshi Hamamoto, Kazuhisa Sekimizu	4．巻 9
2．論文標題 GPI0363 inhibits the interaction of RNA polymerase with DNA in Staphylococcus aureus	5．発行年 2019年
3．雑誌名 RSC Advances	6．最初と最後の頁 37889-37894
掲載論文のDOI（デジタルオブジェクト識別子） 10.1039/C9RA06844A	査読の有無 有
オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 該当する

1．著者名 Hiroaki Itoh, Kotaro Tokumoto, Takuya Kaji, Atmika Paudel, Suresh Panthee, Hiroshi Hamamoto, Kazuhisa Sekimizu, Masayuki Inoue	4．巻 10
2．論文標題 Development of a high-throughput strategy for discovery of potent analogues of antibiotic lysocin E	5．発行年 2019年
3．雑誌名 Nature communications	6．最初と最後の頁 2992
掲載論文のDOI（デジタルオブジェクト識別子） 10.1038/s41467-019-10754-4	査読の有無 有
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 該当する

1．著者名 Furuta Yoshikazu、Tsujinouchi Mai、Shawa Misheck、Zorigt Tuvshinzaya、Miyajima Yuya、Paudel Atmika、Suzuki Satowa、Higashi Hideaki	4．巻 11
2．論文標題 Complete Genome Sequences of 24 Strains of Bacillus cereus Isolated from Nosocomial Infection and Bacteremia Cases in Japan	5．発行年 2022年
3．雑誌名 Microbiology Resource Announcements	6．最初と最後の頁 e0120321
掲載論文のDOI（デジタルオブジェクト識別子） 10.1128/mra.01203-21	査読の有無 無
オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 －

1．著者名 Shawa Misheck、Furuta Yoshikazu、Paudel Atmika、Kabunda O'Brian、Mulenga Evans、Mubanga Maron、Kamboyi Harvey、Zorigt Tuvshinzaya、Chambaro Herman、Simbotwe Manyando、Hang'ombe Bernard、Higashi Hideaki	4．巻 368
2．論文標題 Clonal relationship between multidrug-resistant Escherichia coli ST69 from poultry and humans in Lusaka, Zambia	5．発行年 2022年
3．雑誌名 FEMS Microbiology Letters	6．最初と最後の頁 21-24
掲載論文のDOI（デジタルオブジェクト識別子） 10.1093/femsle/fnac004	査読の有無 無
オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 －

1．著者名 Panthee Suresh、Hamamoto Hiroshi、Nishiyama Yayoi、Paudel Atmika、Sekimizu Kazuhisa	4．巻 7
2．論文標題 Novel Pathogenic Mucorales Identified Using the Silkworm Infection Model	5．発行年 2021年
3．雑誌名 Journal of Fungi	6．最初と最後の頁 995～995
掲載論文のDOI（デジタルオブジェクト識別子） 10.3390/jof7110995	査読の有無 無
オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 －

1．著者名 Hamamoto Hiroshi、Panthee Suresh、Paudel Atmika、Ishii Kenichi、Yasukawa Jyunichiro、Su Jie、Miyashita Atsushi、Itoh Hiroaki、Tokumoto Kotaro、Inoue Masayuki、Sekimizu Kazuhisa	4．巻 12
2．論文標題 Serum apolipoprotein A-I potentiates the therapeutic efficacy of lysocin E against Staphylococcus aureus	5．発行年 2021年
3．雑誌名 Nature Communications	6．最初と最後の頁 6364
掲載論文のDOI（デジタルオブジェクト識別子） 10.1038/s41467-021-26702-0	査読の有無 無
オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 －

１．著者名 GC Sulochan、Khanal Ashok、Paudel Atmika、GC Vijay S.、Khanal Aashis、Panthee Suresh	４．巻 16
２．論文標題 Comparative analysis of COVID-19 case fatality rate between two waves in Nepal	５．発行年 2021年
３．雑誌名 Influenza and Other Respiratory Viruses	６．最初と最後の頁 186～189
掲載論文のDOI（デジタルオブジェクト識別子） 10.1111/irv.12922	査読の有無 無
オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 －

１．著者名 Paudel Atmika、Furuta Yoshikazu、Higashi Hideaki	４．巻 12
２．論文標題 Silkworm model for Bacillus anthracis infection and virulence determination	５．発行年 2021年
３．雑誌名 Virulence	６．最初と最後の頁 2285～2295
掲載論文のDOI（デジタルオブジェクト識別子） 10.1080/21505594.2021.1965830	査読の有無 無
オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 －

１．著者名 Furuta Yoshikazu、Cheng Cheng、Zorigt Tuvshinzaya、Paudel Atmika、Izumi Shun、Tsujinouchi Mai、Shimizu Tomoko、Meijer Wim G.、Higashi Hideaki	４．巻 6
２．論文標題 Direct Regulons of AtxA, the Master Virulence Regulator of Bacillus anthracis	５．発行年 2021年
３．雑誌名 mSystems	６．最初と最後の頁 e0029121
掲載論文のDOI（デジタルオブジェクト識別子） 10.1128/mSystems.00291-21	査読の有無 無
オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 －

〔学会発表〕　計9件（うち招待講演　1件／うち国際学会　3件）

１．発表者名 浜本 洋　、石島 早苗、スレス パンシー、アトミカ パウデル、関水 和久
２．発表標題 Cryptococcus neoformans の病原性因子の網羅的探索
３．学会等名 第64回日本医真菌学会総会・学術集会
４．発表年 2020年

１．発表者名
Hiroshi Hamamoto, Sanae Ishijima, Suresh Panthee, Paudel Atmika, Kazuhisa Sekimizu

２．発表標題
Comprehensive gene expression analysis of Cryptococcus neoformans infected in mouse brain

３．学会等名
ASM Microbe 2019, 2019 Jun 20-24, San Francisco, CA (USA)（国際学会）

４．発表年
2019年

１．発表者名
Suresh Panthee, Hiroshi Hamamoto, Atmika Paudel, Kazuhisa Sekimizu

２．発表標題
Discovering novel roles of genes for virulence of Staphylococcus aureus USA300 using invertebrate model silkworm

３．学会等名
ASM Microbe 2019, 2019 Jun 20-24, San Francisco, CA (USA)（国際学会）

４．発表年
2019年

１．発表者名
浜本洋、Suresh Panthee、Atmika Paudel、関水和久

２．発表標題
黄色ブドウ球菌の宿主感染後の時間経過に伴う網羅的遺伝子発現変化の解析

３．学会等名
第64回　日本ブドウ球菌研究会、2019年8月30日-31日、佐世保市（長崎国際大学）

４．発表年
2019年

１．発表者名
浜本洋、Suresh Panthee、Atmika Paudel、石島早苗、関水和久

２．発表標題
Cryptococcus neoformansのマウス感染状態における網羅的遺伝子発現解析

３．学会等名
第63回 日本医真菌学会総会、2019年10月11日、千葉市（オークラ千葉ホテル

４．発表年
2019年

１．発表者名
Atmika Paudel, Yoshikazu Furuta, Hideaki Higashi

２．発表標題
An invertebrate animal model to study the host-pathogen interaction during the infection

３．学会等名
The 7th Hokkaido University Cross-Departmental Symposium

４．発表年
2021年

１．発表者名
Atmika Paudel, Yoshikazu Furuta, Suresh Panthee, Hiroshi Hamamoto, Kazuhisa Sekimizu, Hideaki Higashi

２．発表標題
Utilization of invertebrate animal model for anti-infective drug discovery

３．学会等名
The 19th Awaji International Forum on Infection and Immunity（国際学会）

４．発表年
2021年

１．発表者名
Atmika Paudel, Yoshikazu Furuta, Suresh Panthee, Hiroshi Hamamoto, Kazuhisa Sekimizu, Hideaki Higashi

２．発表標題
Host-based approach for identifying virulence factors of pathogens

３．学会等名
The 86th Annual Conference of Japanese Society for Bacteriology Hokkaido Branch

４．発表年
2021年

１．発表者名
Atmika Paudel, Yoshikazu Furuta, Suresh Panthee, Hiroshi Hamamoto, Kazuhisa Sekimizu, Hideaki Higashi

２．発表標題
Understanding bacterial pathogenesis using silkworms

３．学会等名
The 94th Annual Meeting of the Japanese Biochemical Society（招待講演）

４．発表年
2021年

〔図書〕　計0件

〔産業財産権〕

〔その他〕

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６．研究組織

	氏名 （ローマ字氏名） （研究者番号）	所属研究機関・部局・職 （機関番号）	備考

７．科研費を使用して開催した国際研究集会

〔国際研究集会〕　計0件

８．本研究に関連して実施した国際共同研究の実施状況

共同研究相手国	相手方研究機関