



Sep 29th, 2023

16th NCGM International Infectious Diseases Forum
(NCGM-IIDF)



AMR pathogen surveillance and Antimicrobial Resistant Bacterial Bank in Japan

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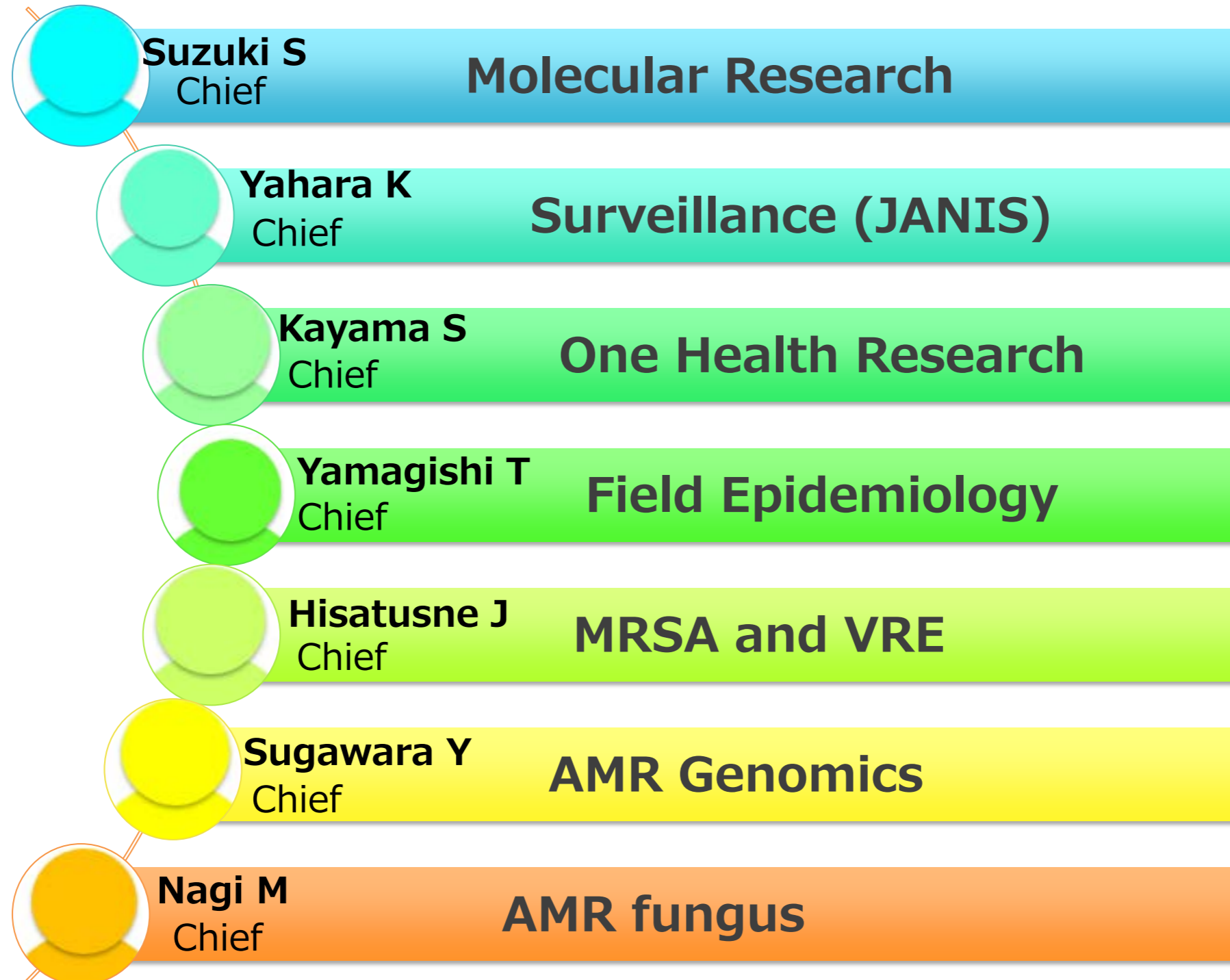
Antimicrobial Resistance Research Center (AMR-RC)

Established in April 2017

National Research Center aimed to carry out comprehensive research of basic science, surveillance and epidemiology. Think tank which provides scientific evidences in collaboration with clinical sectors, contributing to reducing AMR. National focal point of Global Surveillance of WHO (WHO AMR CC for surveillance and research since 2021).



Sugai M
Director



Our activities

✓ AMR Surveillance systems in Japan (Human)

■ NESID: National Epidemiological Surveillance on AMR Infectious Diseases

✓ A Case-based surveillance

based on the **mandatory** patient reporting under the Infectious Disease Control Law.

Notifiable diseases: VRSA, VRE, MDRA, CRE

Sentinel surveillance: MRSA, PRSP, MDRP

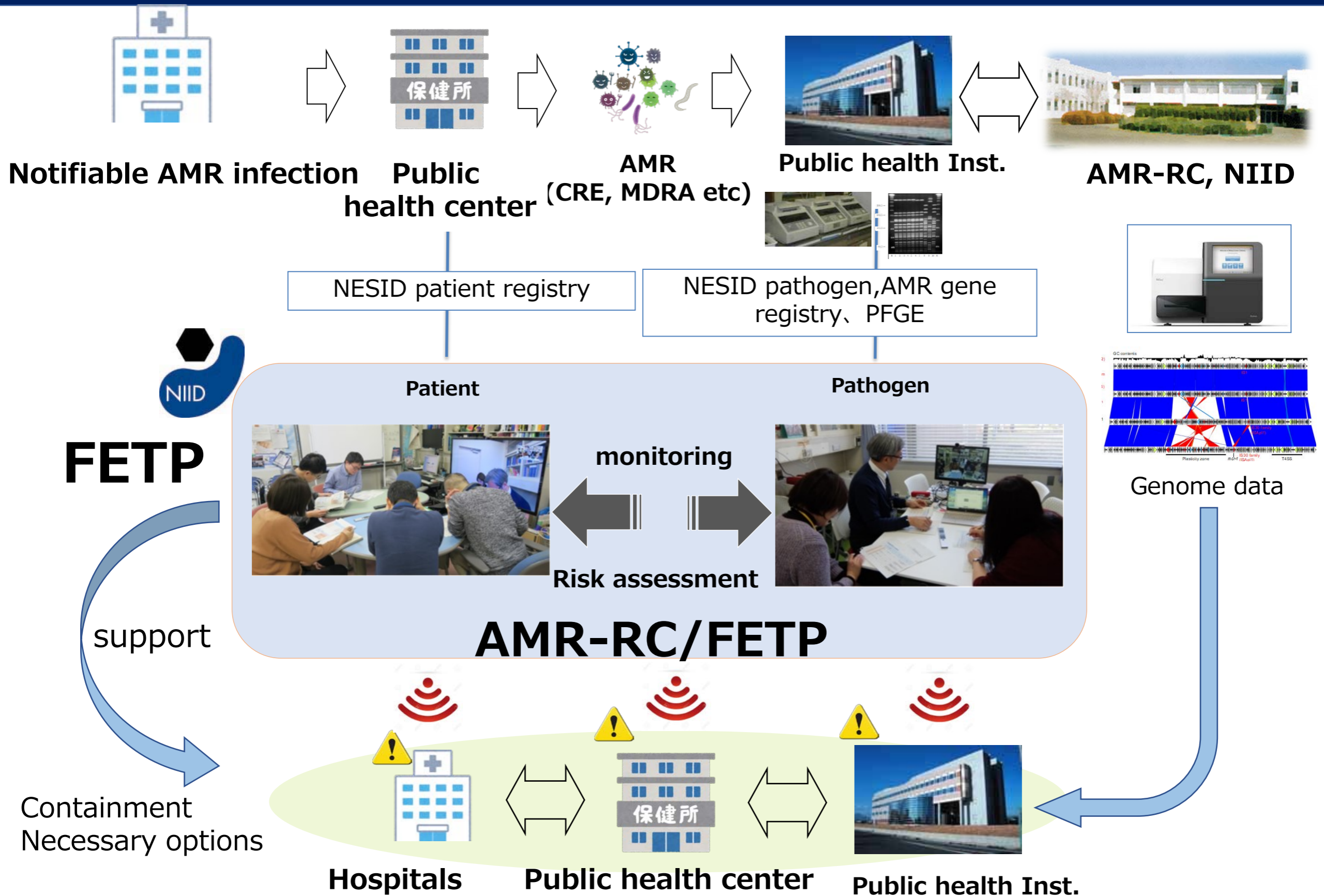


■ **JANIS: Japan Nosocomial Infection Surveillance**

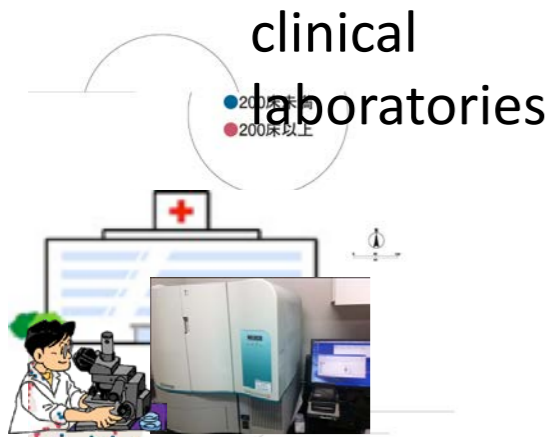
✓ A laboratory-based surveillance

Voluntary surveillance covering more than 2,000 hospitals across the country since 2000 and provide a hospital feedback report as well as national report, contributing to infection control activities.

NESID and AMR outbreak response



JANIS (Japan Nosocomial Infections Surveillance)



All bacterial data
(both positive and negative,
all sample types)

automatic conversion

JANIS data file

| | | | | |
|-----------------|------------------|---|-------------|-------------|
| 190426041314369 | M200201131401 | 2 | 0000.002009 | 0000.002009 |
| 190426015631002 | F200205301401 | 2 | 0000.002009 | 0000.002009 |
| 190425101726131 | F200211211401 | 2 | 0000.002009 | 0000.002009 |
| 189888047714175 | F199907112401FR1 | 2 | 0000.002009 | 0000.002009 |
| 180945141509869 | F200411031401 | 2 | 0000.002009 | 0000.002009 |
| 180935014823642 | M200304261401 | 2 | 0000.002009 | 0000.002009 |
| 180954004805530 | M200504051401 | 2 | 0000.002009 | 0000.002009 |
| 180952058227874 | M200508291401 | 2 | 0000.002009 | 0000.002009 |
| 180941089123816 | F200409281401 | 2 | 0000.002009 | 0000.002009 |
| 189891182324063 | F199912201401 | 2 | 0000.002009 | 0000.002009 |
| 180951003228800 | M200503281401 | 2 | 0000.002009 | 0000.002009 |

>4,000 / 8,300
Voluntarily participating hospitals

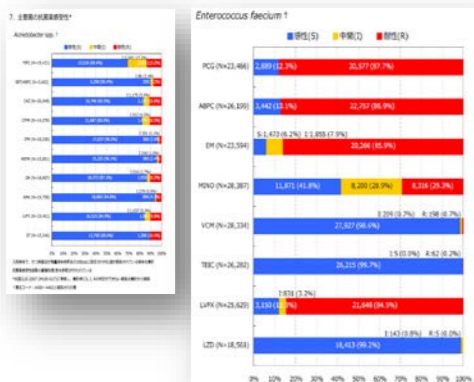


uploaded
to a secure
cloud

8 millions of
samples per
year



AMR reports
periodically



National report

Feedback report
to each hospital

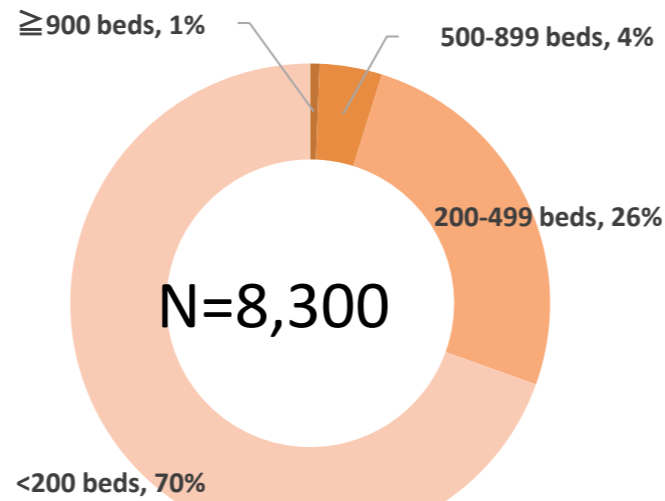
- data check
- R-I-S interpretation
- De-duplication



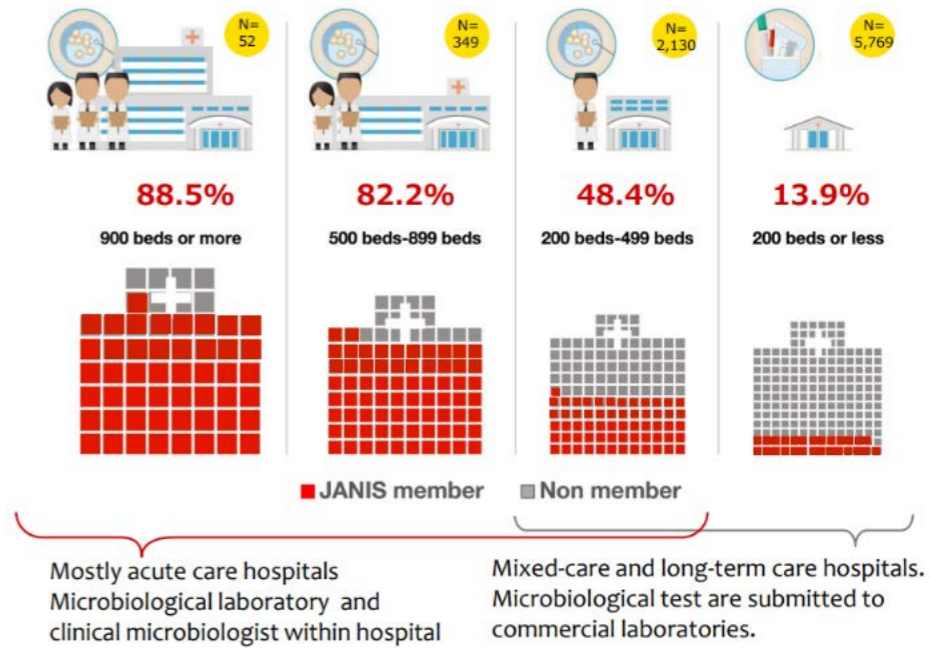
JANIS

JANIS

Japan Nosocomial Infection Surveillance

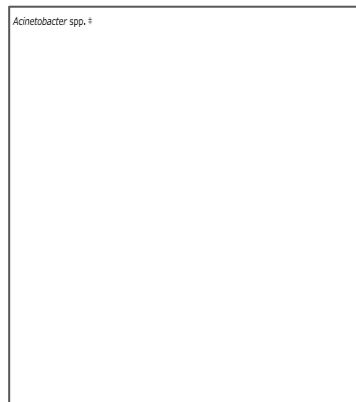
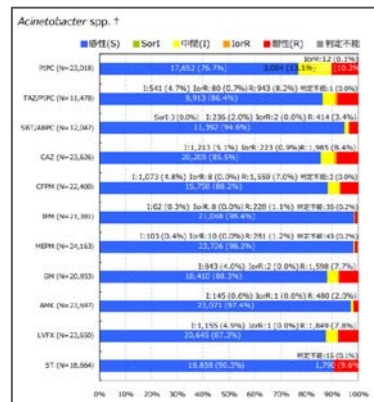


Number of Medical Facility



Feedback Report

National AMR reports

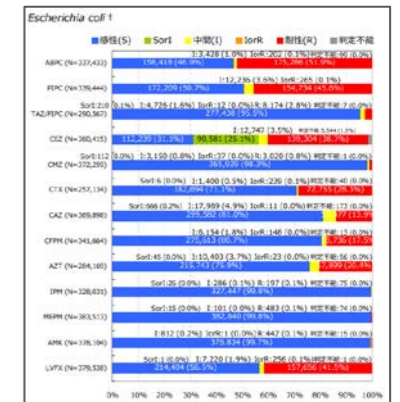
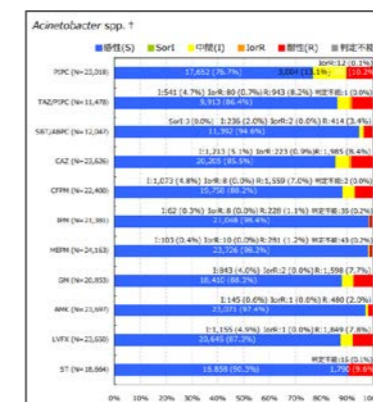


National data

Hospital X

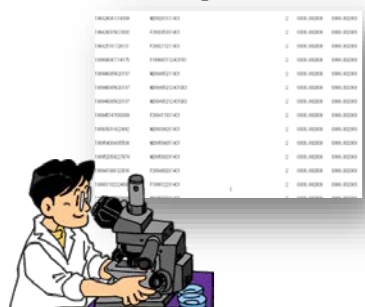


AMR Research Center, NIID



Laboratory MIC data

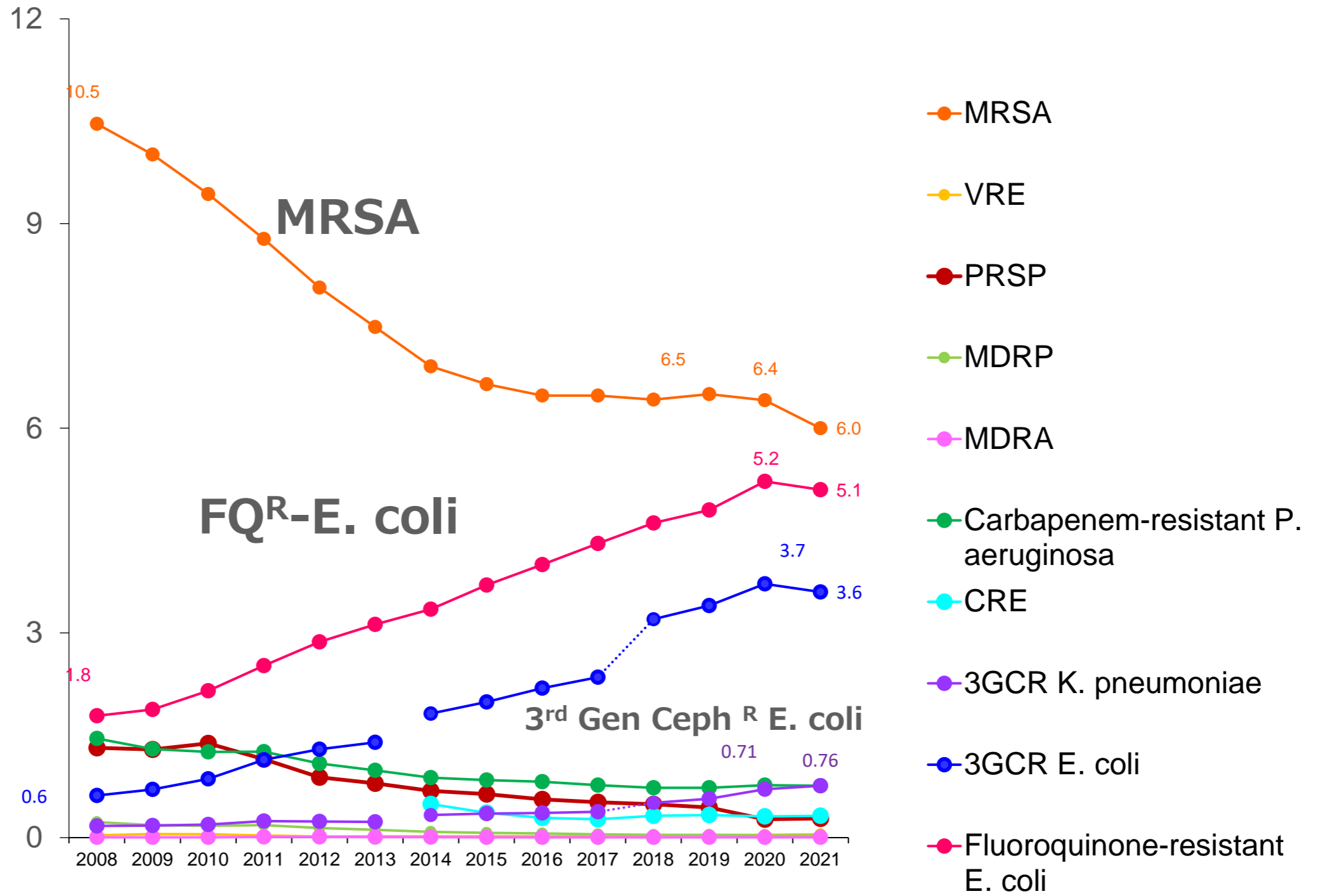
8,000,000 samples from 2,168 Medical Facilities
5,430,000 isolates



Reviewed in
Kajihara (2020), JJID

Trends of the AMRB isolation rate in Japan

Ratio (%) = AMRO detected PT ÷ Sample Submitted PT X 100



AMR Surveillance linked to JANIS

JANIS data

Date
Place
Specimen
Origin
Sex
Age
Identification
AST results
patient ID number...

No genomic info

AMR genomic surveillance

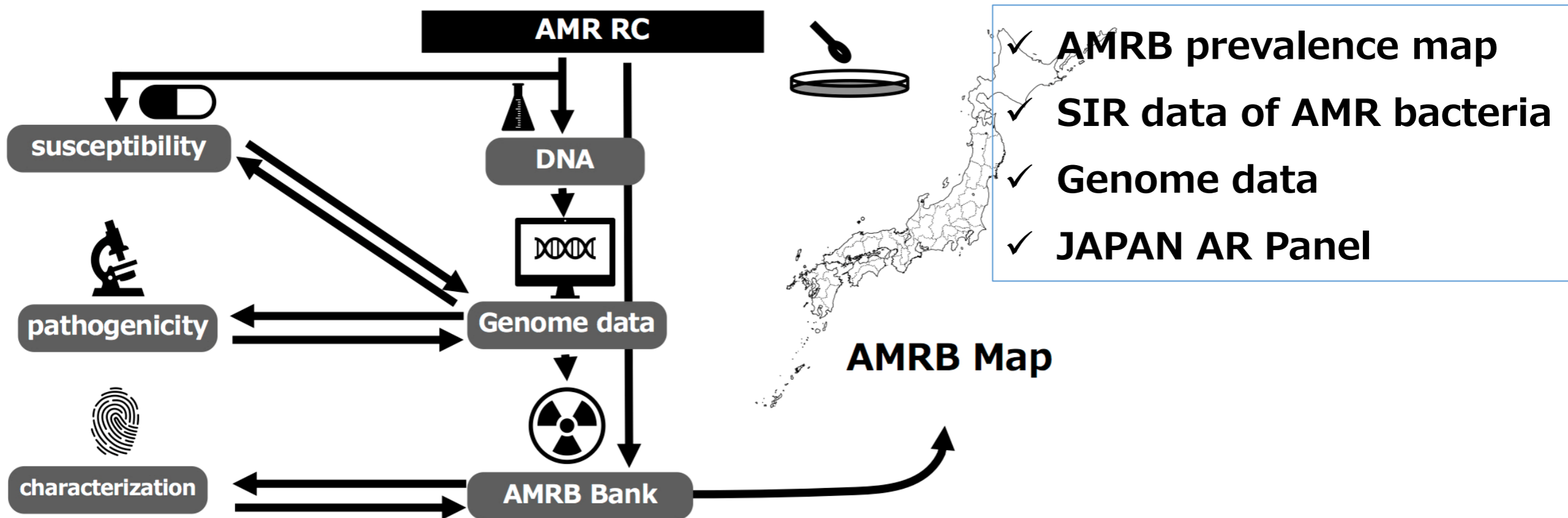
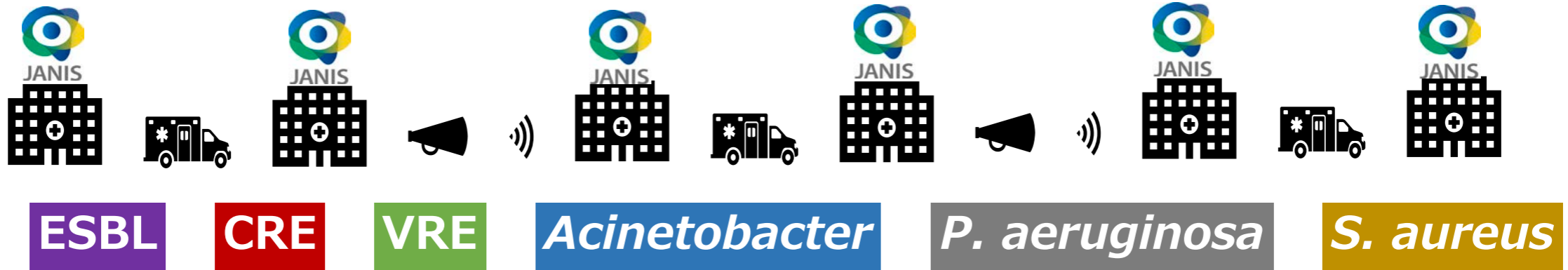
Resistance genes
Virulence genes
Plasmid profile
MLST
Genome data





JARBS

Japan **A**ntimicrobial **R**esistant **B**acterial **S**urveillanc
AMR pathogen **genomic** surveillance linked with JANIS





Japan Antimicrobial Resistant Bacterial Surveillance (JARBS) 2019 - 2020

Collected No.

JARBS-GNR

ESBL CRE

ESBL Hmv *K. pneumoniae*

23,119

JARBS-Acineto

Acinetobacter

39

JARBS-PA

P. aeruginosa

639

JARBS-hmv KP

Hmv *K. pneumoniae*

707

JARBS-SA

S. aureus Blood isolates

796

JARBS-VRE

VRE

34



Japan Antimicrobial Resistant Bacterial Surveillance (JARBS) 2019-2020

JARBS-GNR:

- Genomic surveillance of Enterobacterales resistant to 3GCs and those insusceptible to carbapenems from 175 hospitals.
- 5,143 isolates were sequenced and AST was conducted for 4,195 isolates using the same panel.



Kayama et al., in revision

Bacterial culture and DNA
extraction: manual



Library preparation for NGS:
Biomek i7 system

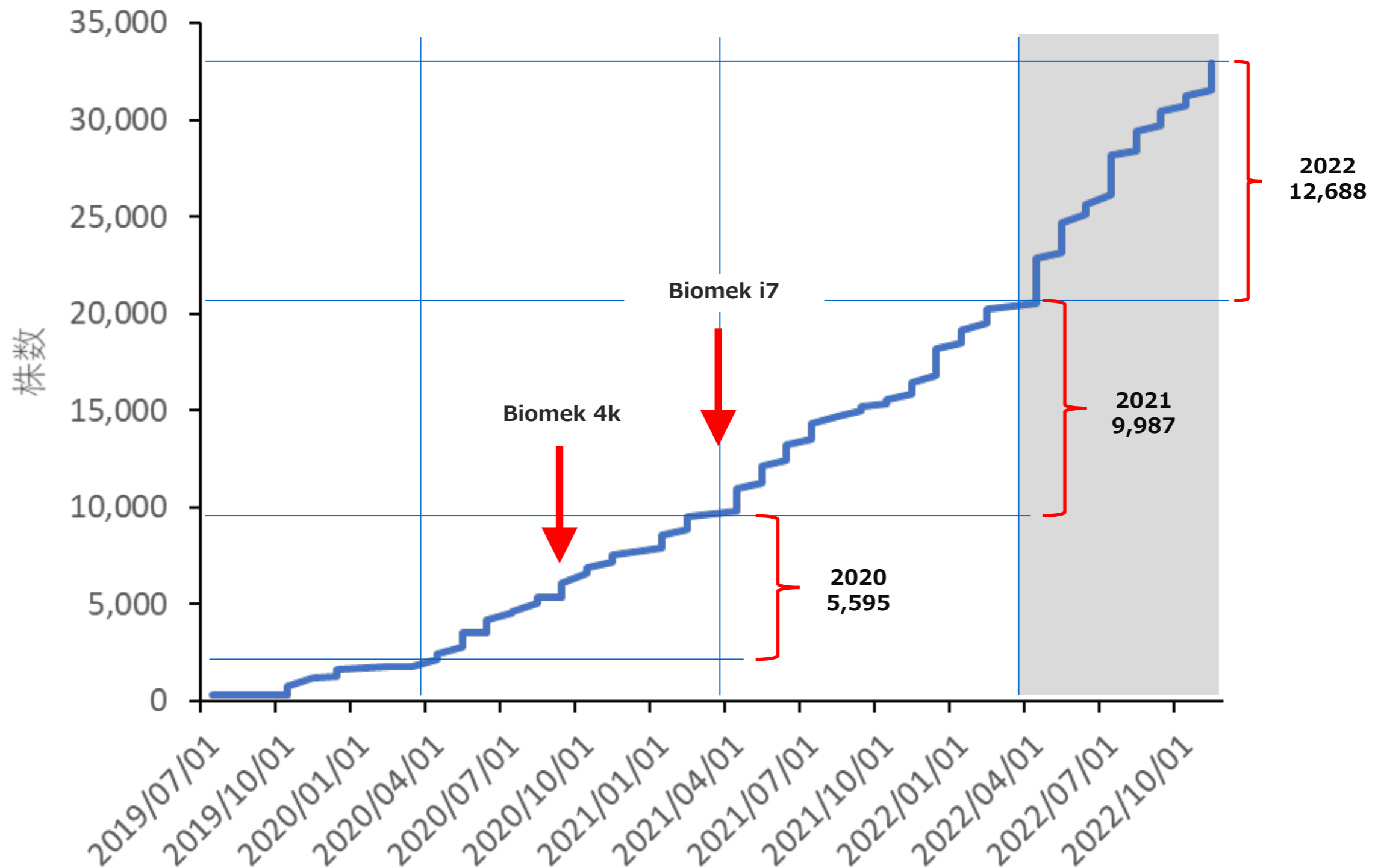


NGS:
HiSeq X (outsourcing)



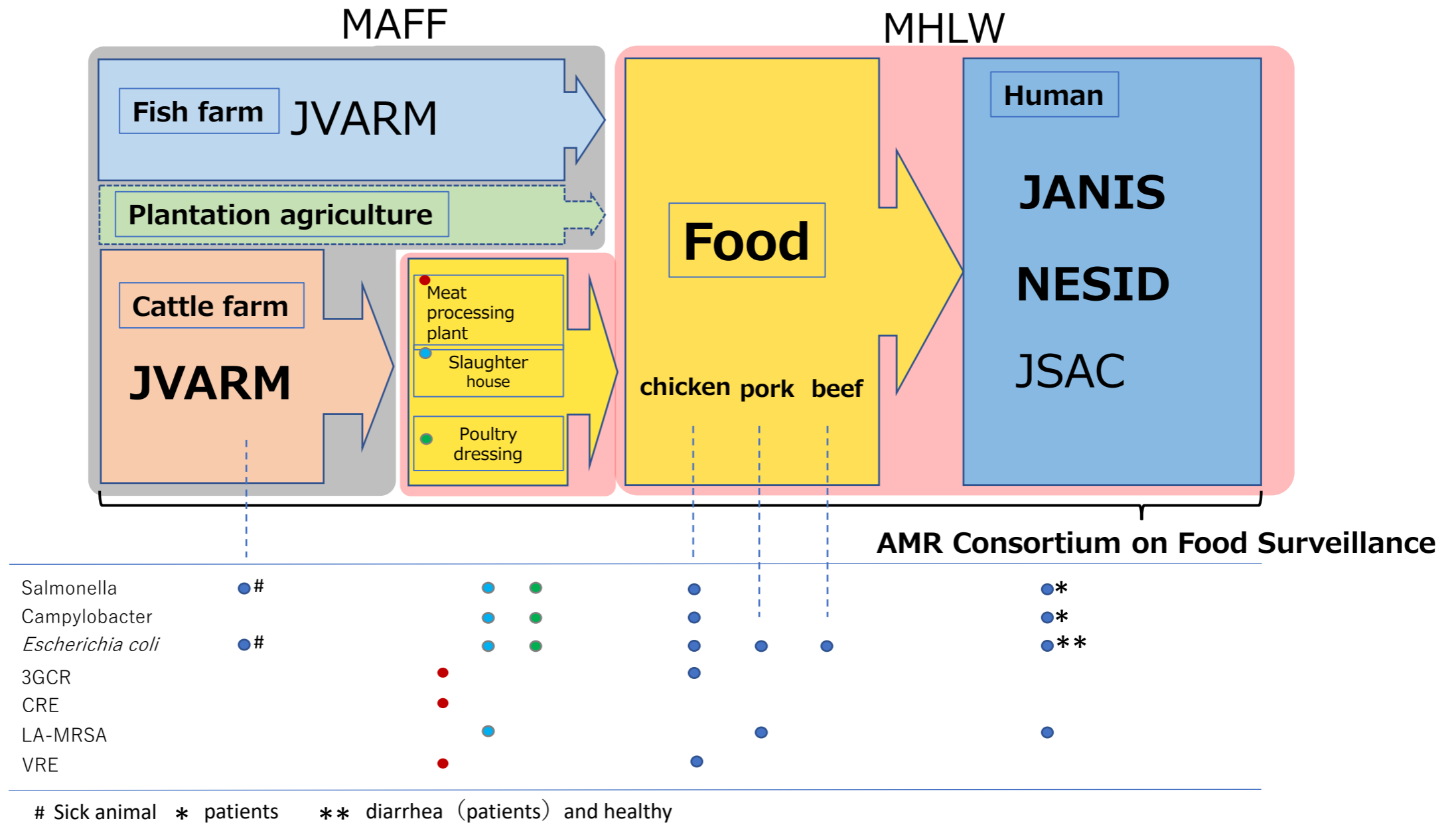
**>2,400
isolates/month**

Sequence reads (Short read, cumulative)



AMR surveillance on food

AMR Consortium on Food Surveillance



JVARM: Japanese Veterinary Antimicrobial Monitoring Program

JANIS: Japan Nosocomial Infection Surveillance

NESID: National Epidemiological Surveillance of Infectious Diseases

JSAC: Japan Surveillance of Antimicrobial Consumption

Tripartite Global Survey on ESBL-producing *E. coli* using a “One Health” approach, “The Tricycle Project”

Epidemiology statics = $ESBL^+ E. coli / E. coli$



Surveillance in humans

Bacteremia $ESBL^+ E. coli / E. coli$

Pregnant women rectal swab $ESBL^+ E. coli / E. coli$

Surveillance in the food chain

Chicken caecum $ESBL^+ E. coli / E. coli$

Surveillance in the environment

River and sewage $ESBL^+ E. coli / E. coli$

Japan Antimicrobial Resistant Bacterial Bank

AMR Bacterial Bank

JAPAN AR Panel

Bacteria 220,000 isolates
+
Clinical Info
+
Genome



Database

Antimicrobials

Drug Discovery

Pharma / Clinical Laboratory

Basic Res

Research & Develop

Academia Pharma

Quality control

Quality control

Hospital Clin Lab

Sharing AR Panel With other countries

International Collaboration & Research

US CDC AR Panel

Overseas AR Panel

NIID AMRRC JARBS

NESID AMR Bacteria

AMR Bacteria from Local Public Health Institute

AMRB from Human

AMRB from Food

AMRB from environment





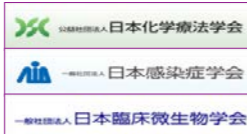
Tricycle Surveillance

Strain collection at JARBB

~220,000 strains (As of July 2023)

Surveillances conducted by AMR-RC, NIID

Donations from external organizations

| | |
|---|---|
|  | JARBS National surveillance 30,862 strains |
|  | WHO Tricycle surveillance 19,418 strains |
| | Ministry of Health Labour Welfare Food Surveillance 971 strains |
|  | Daiichi Sankyo strains (YK strains) 106,918 strains |
| | Hiroshima Univ/Juntendo Univ/Osaka Univ strains 19,372 strains |
|  | Animal hospital strains (VDT strains) 32,295 strains |
|  | Three Academic Societies Joint Antimicrobial Susceptibility Surveillance Program strains 5,680 strains |

Sharing AMR panels from other countries



US CDC-FDA AR Isolate Panel

Distribution of AMR bacterial panels via JARBB website



Contents

すべての薬剤耐性パネル
Browse All Panels

| Panel | Action |
|---------------------------------------|-----------------------------------|
| MRSA SCCmec panel | Go to detail page |
| Staphylococcal enterotoxin type panel | Go to detail page |

<https://jarbb.jp/en/>

Antimicrobial-Resistant Bacterial Panels from JARBB

- **Basic Research Panel:**

For basic research such as the analysis of properties and development of detection methods for antimicrobial-resistant bacteria

- **Drug Development Research Panel:**

For the development of diagnostics, prophylaxis, and therapeutics for antimicrobial-resistant bacterial infections.

- **Quality Control Panel:**

For quality control in hospital laboratories

Staphylococcus aureus panel

MRSA SCCmec Panel

The strains were curated and stored by the late Dr. Keiichi Hiramatsu, the late Dr. Teruyo Ito, and Dr. Yuki Uehara at Juntendo University.

| ID | Strain name | SCCmec type |
|-------------|----------------|----------------|
| JARB-OU2307 | COL | Type I |
| JARB-OU2308 | NCTC10442 | Type I (1B) |
| JARB-OU2309 | N315 | Type IIa (2A) |
| JARB-OU2310 | 036-1 | Type IIb |
| JARB-OU2311 | BK351 | Type IIA |
| JARB-OU2312 | RN7170 | Type II.4 |
| JARB-OU2313 | 85/2082 | Type III (3A) |
| JARB-OU2314 | CA05 | Type III (2B) |
| JARB-OU2315 | USA300_FPR3757 | Type IVa |
| JARB-OU2316 | MW2 | Type IVa |
| JARB-OU2317 | 8/6-3P | Type IVb |
| JARB-OU2318 | MR108_81/108 | Type IVc |
| JARB-OU2319 | MS13167 | Type IVd |
| JARB-OU2320 | JCSC8990 | Type IVl |
| JARB-OU2330 | JCSC8843 | Type IVm |
| JARB-OU2321 | WIS_WBG8318 | Type V |
| JARB-OU2322 | TSGH17 | Type V (5C2) |
| JARB-OU2324 | HDE288 | Type VI |
| JARB-OU2325 | P57412002 | Type VII (5C1) |
| JARB-OU2326 | C10682 | Type VIII (4A) |
| JARB-OU2327 | JCSC6943 | Type IX (1C2) |
| JARB-OU2328 | JCSC6945 | Type X (7C1) |
| JARB-OU2329 | LGA251 | Type XI (8E) |
| JARB-OU2331 | SC792 | Type XIV |
| JARB-OU2528 | 55-99-44 | Type XIII (9A) |

Detailed of the SCCmec strains are available at IWG SCCmec website.

<https://www.sccmec.org/index.php/en/>
created by Dr. Uehara
(present affiliation: Fujita Health Univ.)

The screenshot displays the SCCmec website interface. The header includes the title 'SCCmec' and the subtitle 'International Working Group on the Staphylococcal Cassette Chromosome elements'. A search bar is located at the top left. The main content area is divided into a left sidebar with navigation links (Overview, Search, Identification, Database English, New Menu) and a main content area. The main content area shows the 'Background' section, which includes a 'Background' sub-section with a publication date of 01 February 2012 and 3595 hits. Below this, the 'Identification of the first SCCmec' section describes the element's characteristics. A diagram at the bottom illustrates the N315 SCCmec structure, highlighting the class A mec gene complex, the ccr gene complex, and the integration site at the 3' end of orfX.

SCCmec
International Working Group on the Staphylococcal Cassette Chromosome elements

You are here: Home > Background

Background

Background
Published: 01 February 2012 | Hits: 3595

Background

Identification of the first SCCmec

The SCCmec element carried by preMRSA N315 was characterized first by cloning the chromosomal region surrounding *mecA* sequence and subsequent comparison with the corresponding region of methicillin-susceptible *S. aureus* strain revealed that:

- (1) It carries the class A *mec* gene complex, consisting of *mecA*, its regulatory genes, *mecI* and *mecR1*, and the insertion site *IS431*.
- (2) It carries two site-specific recombinase homologues, *ccrB1* and *ccrB2*.
- (3) It has characteristic direct repeats and inverted repeats at both ends.
- (4) It is located at the 3' end of *orfX*.

Subsequent experiments showed that the island was precisely excised from the N315 chromosome and integrated into the cassette chromosome *mec* (SCCmec) as a new family of staphylococcal genomic islands and its recombinases as cassette chromosome integrase.

N315 SCCmec

1. class A *mec* gene complex
2. *ccr* gene complex
3. Direct repeats/ Inverted repeats
4. Integrated at the 3' end of *orfX*

Staphylococcus aureus panel

Other MRSA Panels

The strains are selected from our own collections (Hiroshima Univ. and NIID) and includes those taken over from the late Dr. Katsuhiko Omoe (Iwate Univ.) .

• Staphylococcal enterotoxin type panel

| ID | Gene ID | MLST |
|----------------|--|-------|
| RN4220 | <i>selx</i> | ST8 |
| Newman | <i>sea, selx</i> | ST254 |
| N315 | <i>sec3, seg, sei, sel, sem, sen, seo, sep, tst1, selx</i> | ST5 |
| Mu50 | <i>sea, sec3, seg, sei, sel, sem, sen, seo, tst1, selx</i> | ST5 |
| MW2 | <i>sea, sec4, seh, sek1, sel, seq, selx, lukS-PV, lukF-PV</i> | ST1 |
| COL | <i>seb, sek2, seq, selx</i> | ST250 |
| 326 | <i>see, seq, selx, selz</i> | ST395 |
| 196E | <i>sea, sed, selj, ser, selx</i> | ST8 |
| Fukuoka5 | <i>selj, ser, ses, set</i> | ST8 |
| FRP3757_USA300 | <i>sek2, seq, selx</i> | ST8 |
| JP197 (TY2037) | <i>seg, sei-arg, sem-arg, sen, seo, seu, selx, sey1, selz, se1</i> | ST121 |

• Staphylococcal coagulase type panel

| ID | Coagulase type | MLST |
|----------------|----------------|-------|
| JP008 (TY825) | I | ST509 |
| N315 | II | ST5 |
| COL | III | ST250 |
| JP029 (TY730) | IV | ST30 |
| JP197 (TY2037) | V | ST121 |
| JP099 (TF2772) | VI | ST97 |
| MW2 | VII | ST1 |
| JP058 (TF2876) | VIII | ST20 |
| JP072 (TY991) | X | ST15 |

• Staphylococcal exfoliative toxin type panel

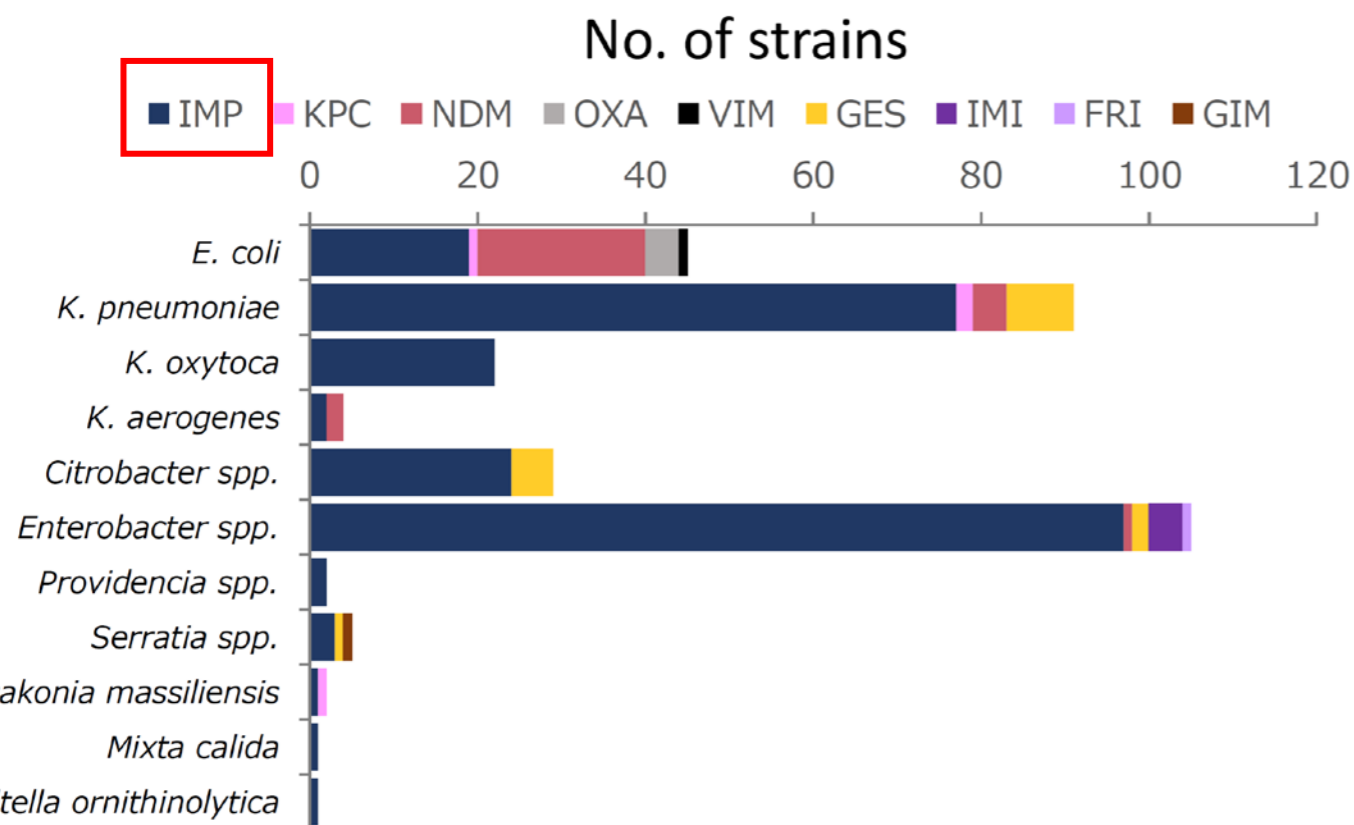
| ID | Gene ID | MLST |
|----------------|------------|-------|
| JP037 (TY34) | <i>eta</i> | ST88 |
| JP008 (TY825) | <i>etb</i> | ST509 |
| JP080 (TF2758) | <i>etd</i> | ST291 |

• Staphylococcal Agr type panel

| ID | Agr type | MLST |
|---------------|----------|-------|
| COL | I | ST250 |
| N315 | II | ST5 |
| MW2 | III | ST1 |
| JP083 (TY578) | IV | ST121 |

Isolate panel creation based on our surveillance

IMP-type carbapenemase is specifically endemic in Japan



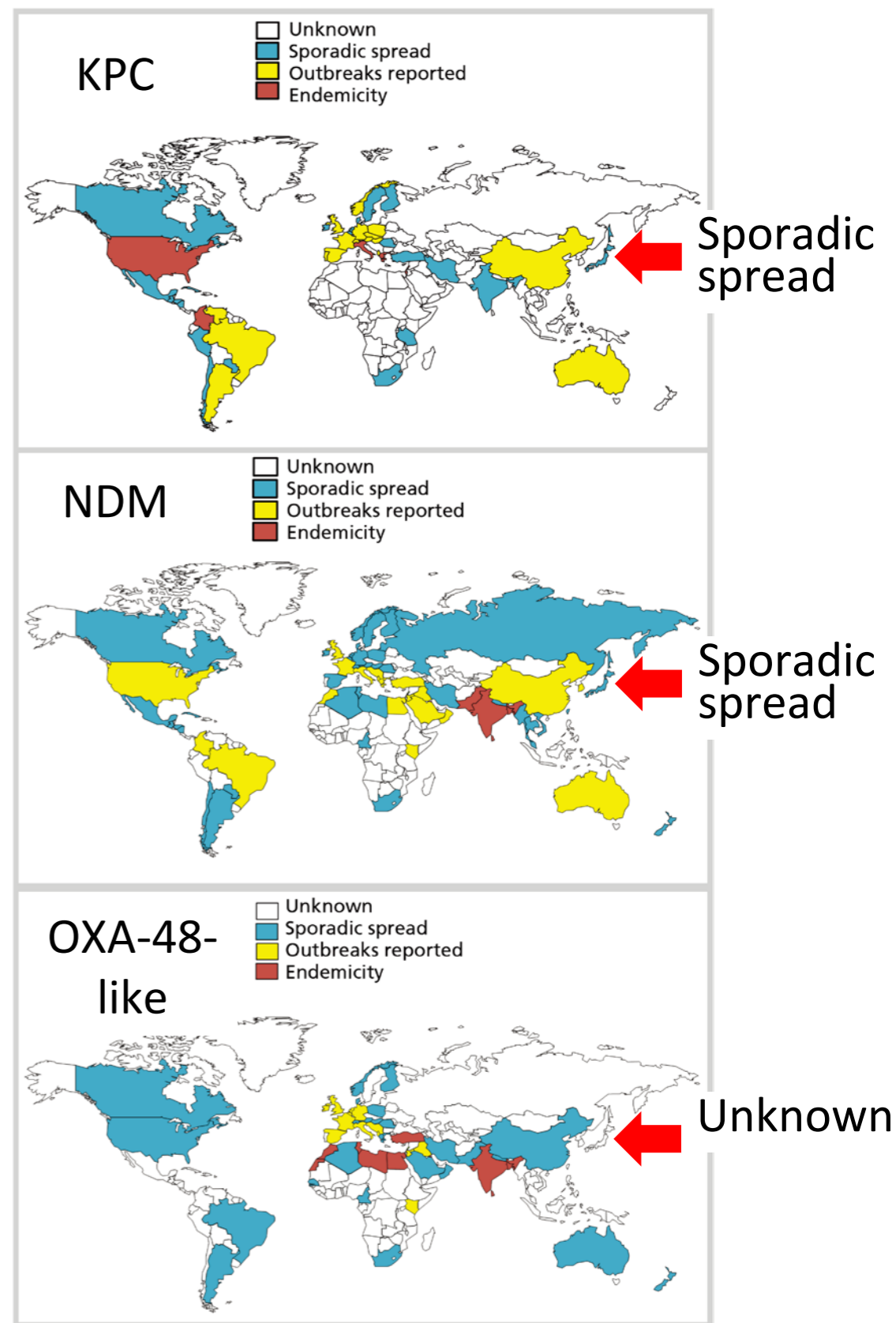
IMP: 81.1%
(IMP-1 : 62.9%, IMP-6 : 12.1%,)

***bla*_{NDM}: 8.7%**

(among the isolates positive for carbapenemase genes)

Kayama S. et al., in revision

Worldwide distribution of carbapenemases



Bonomo RA. et al. CID 2018.

Japan IMP Carbapenemase Panel

Various species

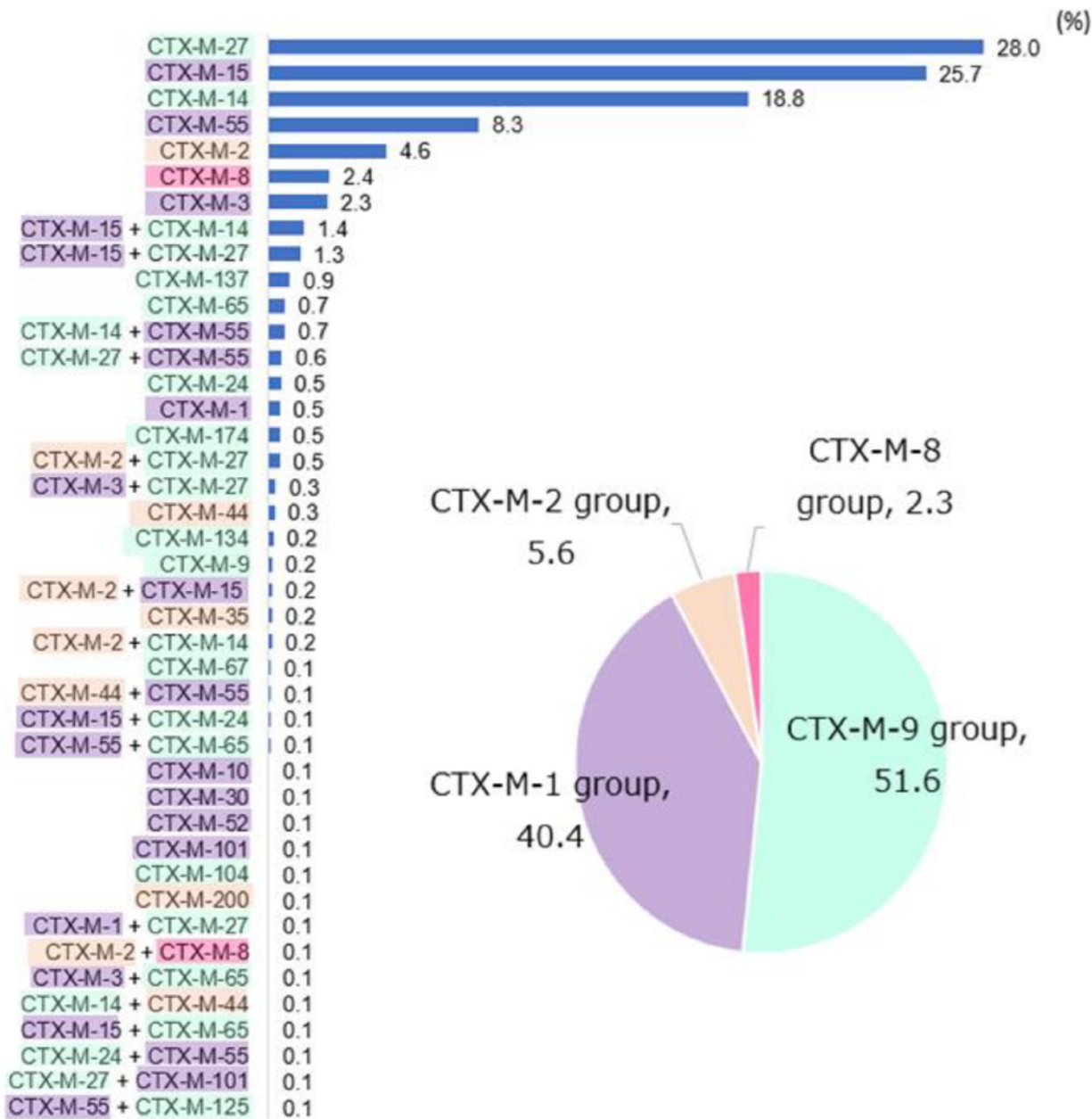
Types of plasmids harboring *bla*_{IMP}

| No. | Species | MLST | blaIMP-type | blaIMP location | MIC | |
|-----|--|------|-------------|--------------------|------|------|
| | | | | | IPM | MEPM |
| 1 | <i>Enterobacter hormaechei</i> subsp. <i>steigerwaltii</i> | 133 | IMP-1 | IncHI2 | 1 | 1 |
| 2 | <i>Enterobacter kobei</i> | 32 | IMP-1 | IncHI2 | 1 | 2 |
| 3 | <i>Escherichia coli</i> | 131 | IMP-1 | IncHI2 | 2 | 4 |
| 4 | <i>Klebsiella oxytoca</i> | 21 | IMP-1 | IncHI2 | 1 | 4 |
| 5 | <i>Mixta calida</i> | n.d. | IMP-1 | IncHI2 | >8 | >8 |
| 6 | <i>Citrobacter freundii</i> | 124 | IMP-1 | IncN | 2 | 2 |
| 7 | <i>Enterobacter asburiae</i> | 252 | IMP-1 | IncN | 4 | 4 |
| 8 | <i>Enterobacter kobei</i> | 99 | IMP-1 | IncN | 2 | 8 |
| 9 | <i>Enterobacter ludwigii</i> | 20 | IMP-1 | IncN | 2 | 8 |
| 10 | <i>Escherichia coli</i> | 70 | IMP-1 | IncN | 2 | 4 |
| 11 | <i>Klebsiella michiganensis</i> | 82 | IMP-1 | IncN | 2 | 2 |
| 12 | <i>Klebsiella pneumoniae</i> subsp. <i>pneumoniae</i> | 317 | IMP-1 | IncN | 4 | 4 |
| 13 | <i>Klebsiella variicola</i> | 415 | IMP-1 | IncN | 4 | >8 |
| 14 | <i>Providencia rettgeri</i> | n.d. | IMP-1 | chromosome | 2 | 2 |
| 15 | <i>Serratia marcescens</i> | n.d. | IMP-1 | IncM2 | 8 | 4 |
| 16 | <i>Enterobacter hormaechei</i> subsp. <i>hoffmannii</i> | 78 | IMP-6 | IncN | 1 | 8 |
| 17 | <i>Enterobacter hormaechei</i> subsp. <i>steigerwaltii</i> | 113 | IMP-6 | IncN | ≤0.5 | 2 |
| 18 | <i>Escherichia coli</i> | 357 | IMP-6 | IncN | ≤0.5 | 8 |
| 19 | <i>Klebsiella pneumoniae</i> subsp. <i>pneumoniae</i> | 268 | IMP-6 | IncN | 2 | >8 |
| 20 | <i>Enterobacter hormaechei</i> subsp. <i>steigerwaltii</i> | 133 | IMP-6 | IncHI2 | 2 | >8 |
| 21 | <i>Pseudomonas aeruginosa</i> | 235 | IMP-7 | chromosome | >8 | >8 |
| 22 | <i>Pseudomonas aeruginosa</i> | 235 | IMP-10 | chromosome | >8 | >8 |
| 23 | <i>Klebsiella michiganensis</i> | n.d. | IMP-11 | untypeable plasmid | 2 | 8 |
| 24 | <i>Klebsiella pneumoniae</i> subsp. <i>ozaenae</i> | 399 | IMP-19 | untypeable plasmid | 1 | ≤0.5 |
| 25 | <i>Pseudomonas aeruginosa</i> | 235 | IMP-34 | ND | >8 | >8 |
| 26 | <i>Enterobacter asburiae</i> | 484 | IMP-60 | chromosome | 2 | 4 |
| 27 | <i>Escherichia coli</i> | 131 | IMP-66 | IncN | 4 | >8 |

Various IMP types

Isolate panel creation based on our surveillance

CTX-M-type beta-lactamases in Japan



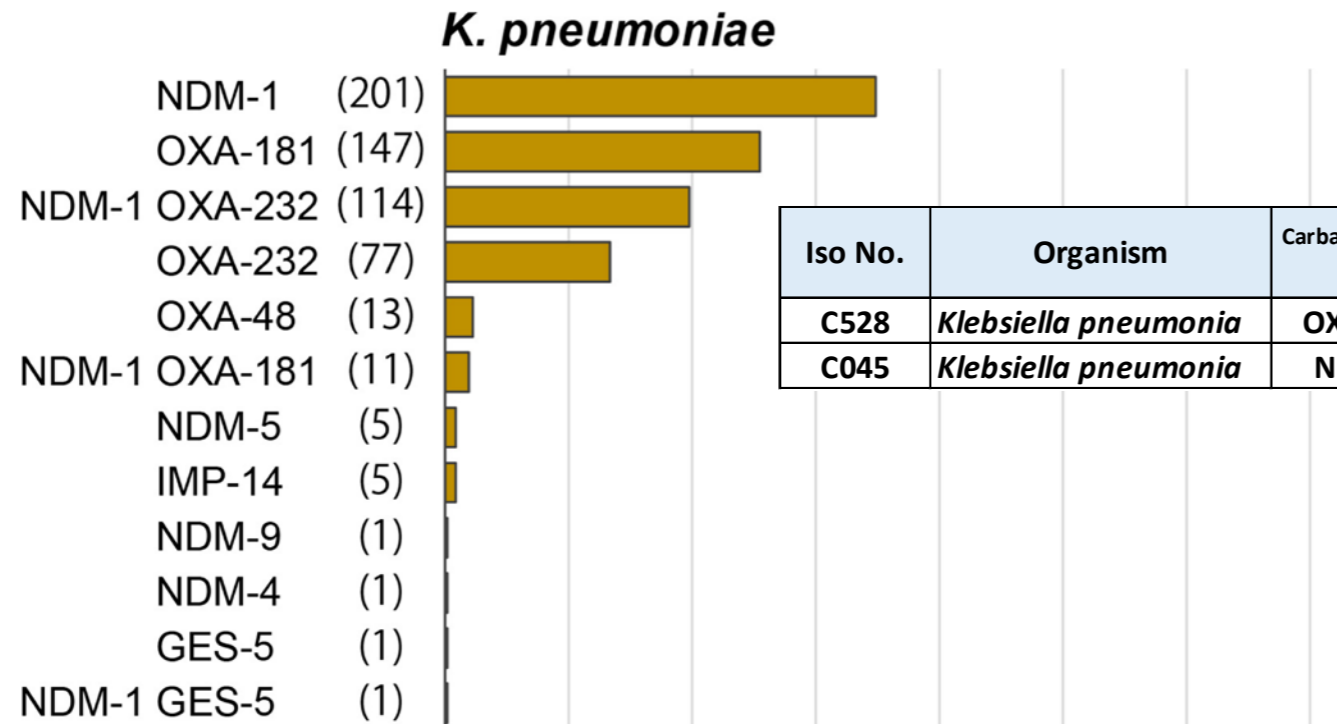
among *E. coli* carrying at least a $bla_{\text{CTX-M}}$ gene (N=1985)

Kayama S. et al., in revision

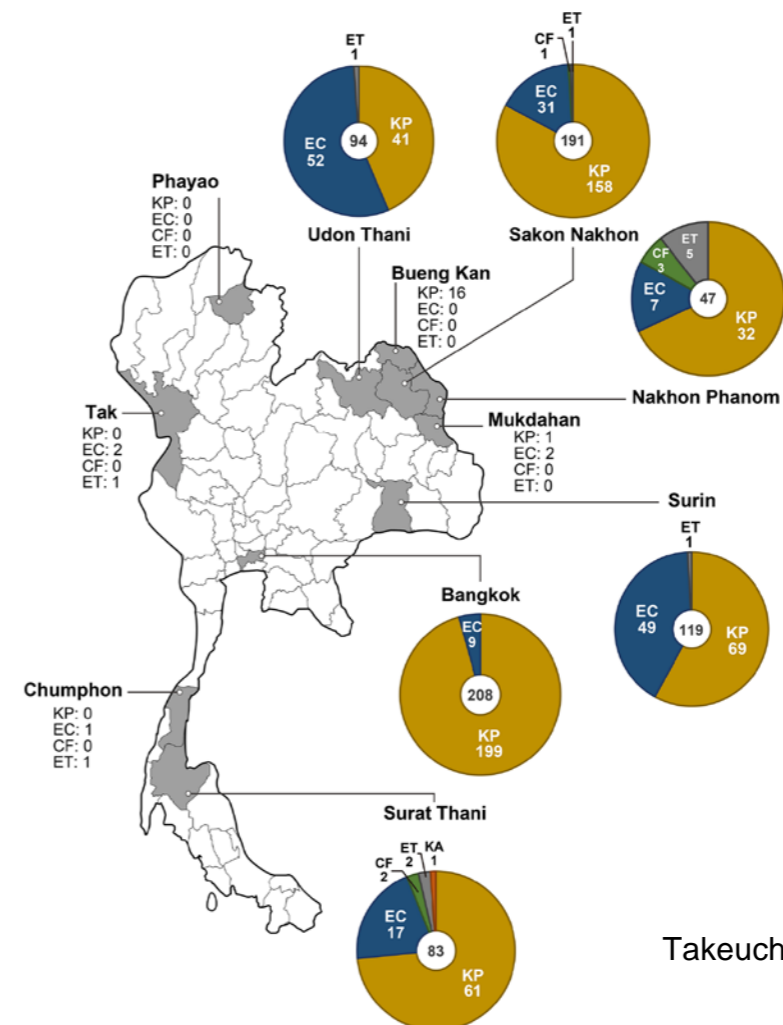
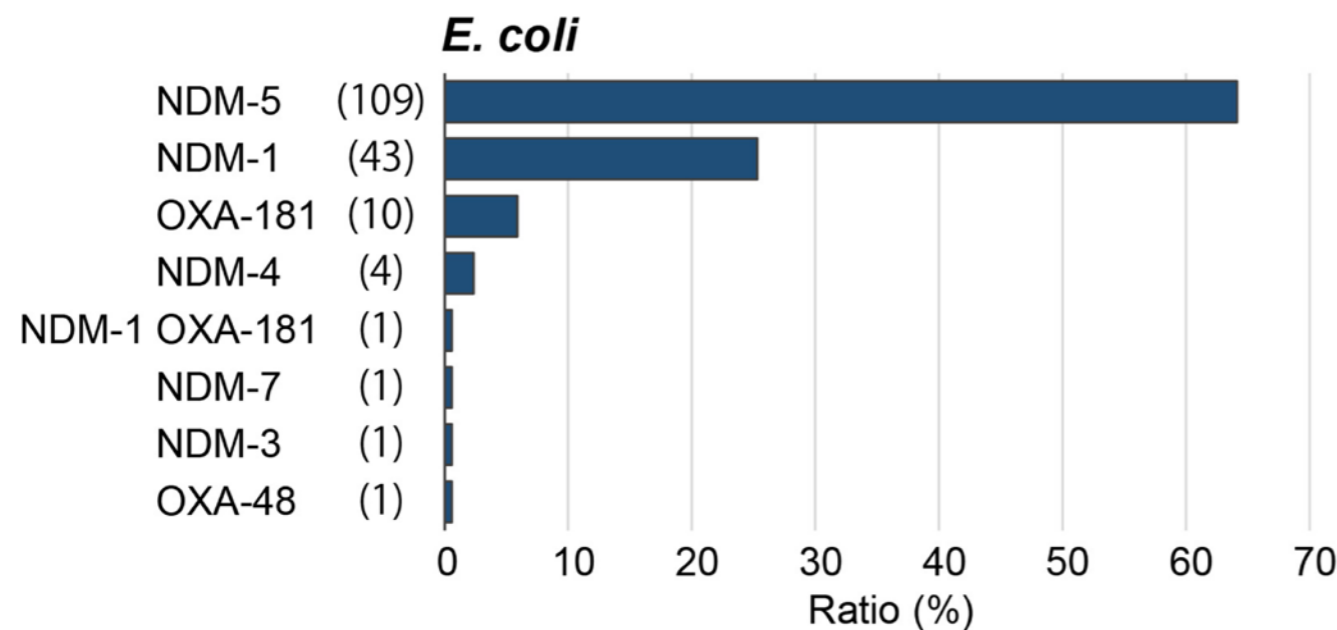
- **ESBL/AmpC producing Enterobacterales panel**
(*in preparation*)
Various CTX-M types, DHA-1, CMY-2, etc.
- **VRE panel**
(*in preparation*)
vanA, *vanB*, *vanC1*, *vanC2*, and *vanD1* strains.
- ***Acinetobacter baumannii* panel**
- **Multidrug-resistant *Pseudomonas aeruginosa* panel**

Isolates from other Asian countries

Carbapenemase-producing Enterobacterales clinical isolates from Thailand was donated from Kasetsart Univ. (Thailand) /Osaka Univ. and will be available from JARBB.



| Iso No. | Organism | Carbapenemase type | MLST | AST | | | | | | | | | |
|---------|------------------------------|--------------------|------|-----|----|------|----|-----|------|-----|----|------|---|
| | | | | CP | CL | MEPM | GM | AMK | MINO | FOM | ST | LVFX | |
| C528 | <i>Klebsiella pneumoniae</i> | OXA-232 | 231 | R | R | R | R | R | R | R | R | S | R |
| C045 | <i>Klebsiella pneumoniae</i> | NDM-1 | 231 | R | R | R | R | R | R | R | R | R | R |



Quality Control Panel (*in preparation*)

Selection of carbapenemase-producing isolates meeting the following requirements is underway (a collaborative study with Prof. Yoshikazu Ishii, Toho Univ.):

- The resistant phenotype is stable under the long-term cultivation without any antibiotics.
 - >Screen the isolates maintaining stable resistant phenotypes among 43 CPE isolates with MEPM MIC 0.5-4 mg/L after 7days daily passaging cultures without antibiotics.
- The viability and resistant phenotype are not affected by lyophilization.
 - >Test the conditions for lyophilization that will not change the phenotype of the strain. Verify that the MIC values do not differ among vials in the same lot.

Preliminary candidate strain: *Enterobacter hormaechei*
(MEPM MIC: 2 mg/L)



US CDC-FDA AR Isolate Panel

| |
|----------------------|
| AR Isolate Bank Home |
| About the Bank + |
| All Isolate Panels |
| Isolate Search |
| Contact Us |



All Isolate Panels

Order pre-assembled resistance panels from CDC's isolate collection below.

Isolates are gathered through CDC's outbreak response and surveillance programs, validated, and used to increase lab efficiencies and public health innovations. The isolates represent samples from various sources associated with infections.

Dear Customer.

Details of the isolates (resistance mechanism, sequence data, MIC value...) are available at the AR Isolate Bank website.

The panels are distributed by JARBB on behalf of CDC to those who wish to get them in Japan.

CDC & FDA AR Isolate Panel

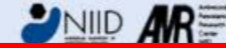
- ***Acinetobacter baumannii* Panel**
- **Aminoglycoside/tetracycline Resistance Panel**
- **Cefepime/zidebactam Panel**
- **Ceftazidime/avibactam**
- **Ceftolozane/tazobactam**
- **Clostridioides difficile EIP 2016**
- **Delafloxacin Panel**
- **Difficult-to-Detect *Staphylococcus aureus* Panel**
- **Enteric Pathogen Diversity Panel**
- **Enterobacterales Carbapenem Breakpoint Panel**
- **Enterobacterales Carbapenemase Diversity**
- **Gram Negative Carbapenemase Detection**
- **Imipenem/relebactam**
- **Isolates with New or Novel Antibiotic Resistance**
- **Meropenem/vaborbactam Verification Panel**
- ***Neisseria gonorrhoeae* Ciprofloxacin Panel**
- ***Neisseria gonorrhoeae* Panel**
- ***Neisseria* species MALDI-TOF Verification Panel**
- **Plazomicin Panel**
- ***Pseudomonas aeruginosa* Panel**
- ***Salmonella enterica* serovar Infantis Panel**
- **Staphylococcus with Borderline Oxacillin Susceptibility Panel**
- **Tedizolid/Linezolid (Oxazolidinones) Resistant Staphylococci**
- **Vancomycin Intermediate *Staphylococcus aureus* Panel**
- **Vancomycin-Resistant Enterococci Panel**
- **WHO *Neisseria gonorrhoeae* Reference Panel**

How to get the panels

国立感染症研究所・薬剤耐性研究センター
薬剤耐性菌バンク



> ENGLISH



Please visit

<https://jarbb.jp/obtain/>

or

<https://jarbb.jp/en/obtain/>

National Institute of Infectious Diseases, Antimicrobi
Japan Antimicrobial Res

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お知らせ

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パネルを入手する

Order Panels

How to order

Please sign up and place your order through the "Message" section.

How to sign up

Please sign up

Sign up

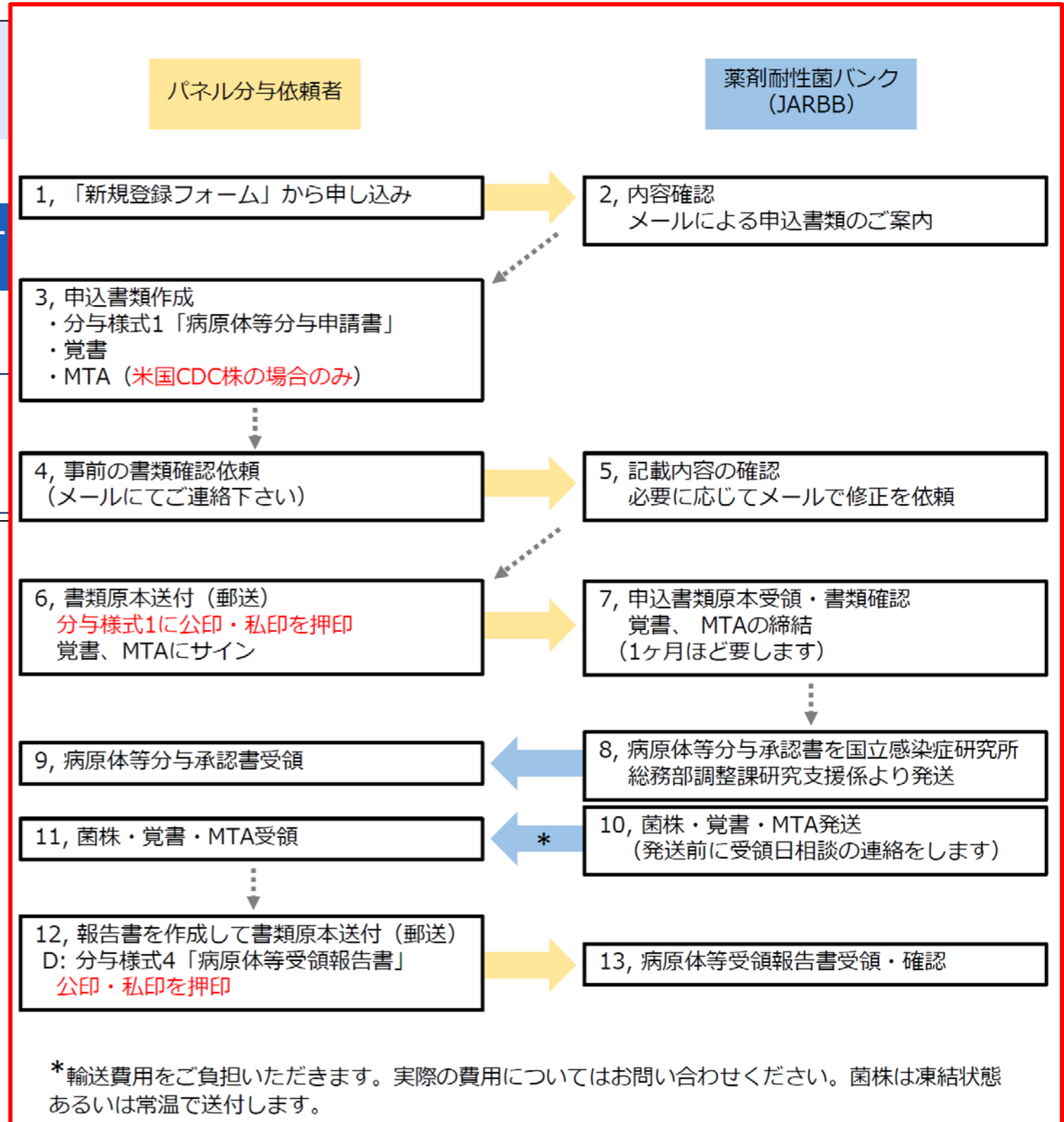
The panels have been available
since Feb 2023

How to get the panels



Details of the documentation procedures are available on the website (Japanese version only).

Shipping charges are the responsibility of the recipient.



Your comments help us accelerate our output

Strain collection at JARBB

~220,000 strains (As of July 2023)

Surveillances
conducted by
AMR-RC,NIID



JARBS National surveillance
30,862 strains



WHO Tricycle surveillance
19,418 strains

Ministry of Health Labour Welfare
Food Surveillance
971 strains

Donations
from external
organizations



Daiichi Sankyo strains (YK strains)
106,918 strains

Hiroshima Univ/Juntendo Univ/Osaka Univ
strains
19,372 strains



Animal hospital strains (VDT strains)
32,295 strains



Three Academic Societies Joint
Antimicrobial Susceptibility Surveillance
Program strains
5,680 strains

⋮

**We welcome your
requests and
suggestions.**

**Distribution of AMR
bacterial panels via
JARBB website**



<https://jarbb.jp/en/>

