IS26-Mediated Genetic Rearrangements in Salmonella Genomic Island 1 of Proteus mirabilis

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Salmonella genomic island 1 (SGI1) is an integrative mobilizable element integrated into the chromosome of bacteria, which plays an important role in the dissemination of antimicrobial resistance genes. Lots of SGI1 variants are found mainly in Salmonella enterica and Proteus mirabilis. In this study, a total of 157 S. enterica and 132 P. mirabilis strains were collected from food-producing animals in Sichuan Province of China between December 2016 and November 2017. Detection of the SGI1 integrase gene showed that three S. enterica and five P. mirabilis strains were positive for SGI1, which displayed different multidrug resistance profiles. Five different SGI1 variants, including two novel variants (SGI1-PmBC1123 and SGI1-PmSC1111), were characterized by whole genome sequencing and PCR linkage. In two novel SGI1 variants, IS26-mediated rearrangements resulted in large sequence inversions of the MDR regions extending outside the SGI1 backbone. The sul3-type III class 1 integron (5′CS-sat-psp-aadA2-cmlA1-aadA1-qacH-IS440-sul3) and gene cassettes aac(6′)-lb-cr-blaOXA−1-catB3-arr-3 are found in SGI1-PmSC1111. Mobilization experiments indicated that three known variants were conjugally mobilized in trans to Escherichia coli with the help of a conjugative IncC plasmid. However, the two novel variants seemed to lose the mobilization, which might result from the sequence inversion of partial SGI1 backbone. The identification of the two novel SGI1 variants in this study suggested that IS26-mediated rearrangements promote the diversity of SGI1.

Keywords: Salmonella, Proteus, genomic island, SGI1, multidrug resistance, IS26

INTRODUCTION

Genomic islands (GIs), such as integrative and conjugative elements (ICEs) and integrative mobilizable elements (IMEs), are distinct regions integrated into the chromosome of bacteria and acquired via horizontal transfer (Bellanger et al., 2014; Partridge et al., 2018). GIs often contain various genes endowing their hosts with new traits, like antimicrobial resistance and virulence that enhance bacterial adaptation to environment (Bellanger et al., 2014). Salmonella genomic island 1 (SGI1) is an IME initially identified in the multidrug resistance (MDR) Salmonella Typhimurium DT104 clone (Boyd et al., 2001). SGI1 (42.4 kb) is comprised of a backbone containing 28 ORFs (S001-S027 and S044) and a 13 kb MDR region that consists of a complex In4-type class 1 integron named In104 (Boyd et al., 2001; Levings et al., 2005). It can form extrachromosomal circular form and is specifically mobilized in trans by conjugative IncA/C plasmids (Doubilet et al., 2005; Douard et al., 2010). In recent years, the mobilization mechanism of SGI1 with the help of IncA/C plasmids has been extensively studied. However, the mechanism of SGI1 mobilization is still not fully understood.
plasmids has been revealed in some studies and many aspects have been explored including the basic transfer elements (Carraro et al., 2014; Kiss et al., 2015, 2019; Siebor et al., 2016). SGI1 was reported in Proteus mirabilis in 2007 (Ahmed et al., 2007), and recently found in Morganella morgani, Providencia stuartii and Escherichia coli (Schultz et al., 2017a; Cummins et al., 2019; Soliman et al., 2019), indicating that SGI1 has a broad host bacterial range and has the potential to spread among enterobacteria.

Since the first report of SGI1 in S. Typhimurium DT104, many different SGI1 variants have been described (Hall, 2010; Bi et al., 2011; Siebor and Neuwirth, 2011, 2013; Lei et al., 2014; Lei et al., 2015; Qin et al., 2015; Schultz et al., 2015; Bie et al., 2018; de Curraize et al., 2018), most of which result from various insertion sequences, homologous recombinations, transpositions, and loss or exchange of gene cassettes within the MDR region (Hall, 2010).

A deletion of 2,780 bp in size from part of ORFs S005 to S009 that is replaced by ISVch4 is found in some variants like SGI1-K (Doublet et al., 2008). Besides, several SGI1 related islands (SGI1, PGI1, AGI1, PGI2 and GI/Pmi) have been reported (Levings et al., 2008; Siebor and Neuwirth, 2014; Girlich et al., 2015; Hamidian et al., 2015; Lei et al., 2018b; Siebor et al., 2018, 2019), all of which incorporate into chromosomes at a specific location (3′ end of the trmE gene) as SGI1. SGI1 and related islands often harbor various antimicrobial resistance genes including carbapenem resistance gene blaNDM–1 (Girlich et al., 2015), extended-spectrum β-lactamase (ESBL) genes blavca8–6 and blavcaT–M–15 (Siebor and Neuwirth, 2011; de Curraize et al., 2018), and fluoroquinolones resistance genes qnrA1 and qnrB2 (Siebor and Neuwirth, 2011; Lei et al., 2014), indicating SGI1 and related islands are important vehicles for clinically important resistance genes. Recently, many variants of SGI1 and SGI1-related islands have been characterized in P. mirabilis, which are summarized in Supplementary Table S1. These variants were found in P. mirabilis isolates from food, human, poultry, swine and other animals such as dog and horse.

In the present study, we characterized the SGI1/PGI genomic islands in Salmonella enterica and P. mirabilis of food-producing animal origin in Sichuan Province of China and described two novel SGI1 variants in P. mirabilis.

MATERIALS AND METHODS

Bacterial Strains and Detection of SGI1 and Related Islands

A total of 157 S. enterica strains (61 from swine and 96 from chicken) and 132 P. mirabilis strains (74 from swine and 58 from chicken) isolated from diseased tissues or anal swabs of animals among 30 poultry and 30 swine farms in Sichuan Province between December 2016 and November 2017. All isolates were identified using an automated system (BD Diagnostic Systems, Sparks, MD, United States). The presence of SGI1/PGI/AGI/GIPvmi1 was screened by PCR targeting the integrase gene (the primers used to detection are listed in Supplementary Table S2) (Schultz et al., 2017b). Positive PCR products were sent to Chengdu Qingke Biological Engineering Technology & Services Co., Ltd., and sequenced by ABI 3730xl DNA Sequencer (Applied Biosystems, United States).

Antimicrobial Susceptibility Testing

Antimicrobial susceptibility testing for strains positive for SGI1/PGI1 was determined by the disk diffusion method according to CLSI guidelines. Antimicrobial agents included ampicillin (AMP), amoxicillin-clavulanic acid (AMC), cefotixin (FOX), cefotaxime (CTX), ceftriaxone (CRO), chloramphenicol (CHL), florfenicol (FFC), nalidixic acid (NAL), ciprofloxacin (CIP), streptomycin (STR), spectinomycin (SPT), apramycin (APR), doxycycline (DOX), trimethoprim (TMP), sulfisoxazole (SUL), trimethoprim-sulfamethoxazole (SXT) and polymyxin B (PB). E. coli ATCC25922 was used as a quality control strain.

Whole Genome Sequencing and Analysis

All SGI1/PGI-positive strains were sequenced using Illumina HiSeq platform (400-bp paired-end reads with about 200-fold average coverage). The draft genomes were assembled using software SPAdes_3.12.0. The gaps among contigs that carried SGI1 fragments were filled in by PCR linkage. Because the complete genetic structures of SGI1 in strains PmBC1123 and PmSC1111 could not be assembled by PCR linkage, whole genomes of those two strains were further sequenced using PacBio RS II sequencing instrument (100-fold average read depth). The chromosomes were assembled into one scaffold using software SMRT portal v.3.2.0. The MDR regions were confirmed by PCR linkage between regions belonging to non-repeated genetic elements. Multi-locus sequence type of S. enterica and acquired antimicrobial resistance genes were identified by MLST software SMRT portal v.3.2.0, respectively. The complete nucleotide sequences of SGI1 variants were analyzed using the BLAST programs. SNPs from genomes of the strains positive for SGI1/PG1 were called and a phylogeny based on the concatenated alignment of the high quality SNPs was inferred using CSI Phylogeny with parameters as defaults.

Mobilization Assays of SGI1

Many SGI1 variants can form the circular extrachromosomal forms that are conjugally mobilized in trans to other bacteria with the help of the conjugative IncA/C plasmid (Hall, 2010). The circular extrachromosomal forms of SGI1 variants were detected through two rounds of PCR amplification using primers listed in Supplementary Table S2. Mobilization assays were carried out as previously described (Siebor et al., 2016), using E. coli C600 harboring an IncC plasmid pR55 as recipient strain. Transconjugants were selected on Shigella and Salmonella agar plates containing 300 mg/L rifampicin and trimethoprim (30 mg/L)/streptomycin (30 mg/L). The transfer frequency of SGI1 was determined by dividing the number of E. coli SGI1 transconjugants by the number of P. mirabilis or S. enterica donor cells (Doudard et al., 2010). The transconjugants were further

1 https://cge.cbs.dtu.dk/services/MLST/
2 https://cge.cbs.dtu.dk/services/ResFinder/
3 http://blast.ncbi.nlm.nih.gov/Blast.cgi
4 https://cge.cbs.dtu.dk/services/CSIPhylogeny/
TABLE 1 | SGI1-containing S. enterica and P. mirabilis isolates characterized in this study.

| Strain     | Species        | Source    | Antimicrobial resistance profilea | Sequence type | SGI1   |
|------------|----------------|-----------|----------------------------------|---------------|--------|
| SCMYP1     | S. Albany      | Swine     | AMP, CTX, CRO, CHL, FFC, NAL, STR, SPT, DOX, TMP, SUL, SXT, PB | ST292         | SGI1-F 42,647 |
| SC10       | S. Infantis    | Chicken   | AMP, CHL, FFC, DOX, TMP, SUL, SXT | ST32          | SGI1-F 42,647 |
| SC968      | S. Derby       | Chicken   | CHL, FFC, STR, SPT, DOX, TMP, SUL, SXT | ST40          | SGI1-I 42,777 |
| PmBC55     | P. mirabilis   | Swine     | AMP, CHL, FFC, STR, SPT, APR, TMP, SUL, SXT | –             | SGI1-W 33,909 |
| PmBC1123   | P. mirabilis   | Swine     | AMP, CHL, FFC, NAL, CIP, STR, SPT, APR, TMP, SUL, SXT | –             | SGI1-PmBC1123 58,069 |
| PmSC1111   | P. mirabilis   | Swine     | AMP, CHL, FFC, NAL, CIP, STR, SPT, APR, TMP, SUL, SXT | –             | SGI1-PmSC1111 82,352 |
| PmSN55     | P. mirabilis   | Swine     | AMP, AMC, FOX, CTX, CRO, CHL, FFC, NAL, APR, SPT, SUL, SXT | –             | SGI1-W 33,909 |
| PmDJ107    | P. mirabilis   | Chicken   | AMP, AMC, FOX, CTX, CRO, CHL, FFC, NAL, STR, SPT, APR, SUL, SXT | –             | SGI1-W 33,909 |

aProteus mirabilis is intrinsically resistant to doxycycline and polymyxin B.

FIGURE 1 | Genetic structures of SGI1-PmBC1123 (A) and SGI1-PmSC1111 (B). Structures are drawn to scale from GenBank accession numbers MH998664 (SGI1-PmBC1123), MH998665 (SGI1-PmSC1111), AM942759 (P. mirabilis H4320), KP662516 (SGI1-Pm58), MF805806 (Tn6450), KJ186151 (SGI1-W), KJ186150 (SGI1-O) and KU341381 (pHNSHP45-2). Genes and ORFs are shown as arrows, and their orientations of transcription are indicated by the arrowheads. Shared regions with above 99% identity are indicated by shading. Resistance genes are in red and transposase or integrase genes are in blue. DR-L and DR-R represent the 18-bp direct repeats at the ends of SGI1. IRi and IRT represent the inverted repeats defining the left and right ends of class 1 integron, respectively.
examined for the presence of SGI1 integrase gene and the location of SGI1 in E. coli with primers listed in Supplementary Table S2.

Nucleotide Sequence Accession Numbers

The complete nucleotide sequences of two novel SGI1 variants and the genomes of P. mirabilis strains PmSC1111 and PmBC1123 were submitted to GenBank and assigned accession numbers MH998664 (SGI1-PmBC1123), MH998665 (SGI1-PmSC1111), CP034091 (PmBC1123) and CP034090 (PmSC1111), respectively. The Whole Genome Shotgun projects have been deposited at DDBJ/ENA/GenBank under the accession RQSE00000000 (SCMY1), RQJQ00000000 (SC10), RQSD00000000 (SC968), RQSF00000000 (PmBC55), RQSG00000000 (PmSN55) and RQSH00000000 (PmD107).

RESULTS AND DISCUSSION

Prevalence of SGI/PGI in S. enterica and P. mirabilis

Detection and sequence analysis of SGI/PGI/AGI/GIPm1 integrase gene showed that 3 S. enterica and 5 P. mirabilis strains were positive for SGI1. Antimicrobial susceptibility testing indicated those 8 strains displayed different MDR profiles (Table 1) (P. mirabilis is intrinsically resistant to doxycycline and polymixin B). S. Albany strain SCMY1 of swine origin exhibited resistance to the third generation cephalosporins and polymyxin B. Two P. mirabilis strains (PmSN55 and PmD107) of chicken origin were resistance to amoxicillin-clavulanic acid, cefoxitin and the third generation cephalosporins. Three SGI1-containing S. enterica strains belonged to different STs (Table 1). A total of 28,848 SNPs were called and phylogenetic analysis showed the five P. mirabilis strains were not clonally related.

Characterization of SGI1 Variants

Five different SGI1 variants were identified in the eight strains through whole genome sequencing and PCR linkage. S. Albany strain SCMY1 (ST292) and S. Infantis strain SC10 (ST32) harbors SGI1 variant SGI1-F that carries dfrA1-orfC and blaCARB-2 (ampicillin) gene cassettes, as well as resistance genes sul1 (sulphonamides), tetA(G) (tetracycline) and floR (chloramphenicol and florfenicol). S. Derby strain SC968 (ST40) harbors SGI1 variant SGI1-I that carries gene cassettes adaA2 (streptomycin and spectinomycin) and dfrA1-orfC. Three P. mirabilis strains harbor SGI1 variant SGI1-W carrying adaA2-lnuF gene cassettes. SGI1-W was firstly detected in P. mirabilis of poultry origin in China (Lei et al., 2014), and then found in P. mirabilis and P. stuartii in Egypt (Soliman et al., 2017, 2019), suggesting this variant of SGI1 had the potential to spread among enterobacterial strains worldwide. It is interesting that two novel SGI1 variants, SGI1-PmBC1123 and SGI1-PmSC1111 (Figure 1), are characterized in this study for the first time.

SGI1-PmBC1123 is 58,069 bp in size (corresponding to bases 1,348-32,501 and 37,667-64,581 in accession no. MH998664) that carries gene cassettes dfrA12-orfF-adaA2 and adaA2-lnuF found in SGI1-Z (Qin et al., 2015) and SGI1-W (Lei et al., 2014), respectively. The MDR region of SGI1-PmBC1123 is divided into two parts separated by a chromosomal DNA fragment of 5,148 bp (truncated PMI3120 and PMI3121-PMI3124). We hypothesize that an initial single IS26 transposition event occurred in the chromosome in locus PMI3120 and has subsequently generated an inversion between two IS26 elements in opposite orientation, resulting in the right end of SGI1-PmBC1123 and this 5,148 bp chromosomal DNA fragment being in inverse orientation. The similar phenomenon is also found in PGI1 (Siebro and Neuwirth, 2014). The 20.74 kb region in SGI1-PmBC1123 (corresponding to bases 43,839-64,581 in accession no. MH998664) that carries floR, sul2 (sulphonamides), hph (hygromycin) and aacC4 (apramycin) shows 99.9% nucleotide identity to the corresponding region of Tn6450 (Chen et al., 2018), indicating they might have a common origin.

SGI1-PmSC1111 is 82,352 bp in size (corresponding to bases 1,348-83,699 in accession no. MH998665). A 1,258 bp insertion sequence, encoding transposable OrfAB subunits A and B, was inserted into the backbone gene S007 and flanked by 3-bp target site duplication (AAG). This IS element shows 98.6% nucleotide identity to ISalg firstly described in Vibrio cholerae serogroup O103 (Sozhamannan et al., 1999), and 86% nucleotide identity to ISVch4 of some SGI1 variants like SGI1-K (Doubelt et al., 2008). An IS26-mediated recombination event occurred in S010, which caused the middle region of SGI1-PmSC1111 (corresponding to bases 10,880-75,577 in accession no. MH998665) being in inverse orientation and flanked by 8-bp inverted repeats (AAATGTGT) (Figure 1B). The downstream region of the 3’-partial of S010 (corresponding to bases 10,880-54,663 in accession no. MH998665) shows 99.9% nucleotide identity to the corresponding region of plasmid PHSHP45-2 (accession no. KU341381) with the addition of two regions, aphA1-1S26 and floR-ISC2R-1S26. It harbors an atypical class 1 integron (5’S-attP-spaaadA2-clmaA1-adaA1-qacH-1IS440-sul3) belonging to sul3-type III (Antunes et al., 2007). The class 1 integron adjacent to the res gene (S027) carries gene cassettes dfrA1-orfC. This region contains five copies of IS26 in the same orientation. However, the 8-bp target site duplications could not be observed around these IS26, suggesting this complicated MDR region might be formed via the incorporation of several IS26-mediated translocatable units successively (Harmer and Hall, 2015, 2016). The right end of SGI1-PmSC1111 harbors four gene cassettes, aac(6’)-Ib-cr (fluoroquinolones and aminoglycosides), blaOXA-1 (ampicillin),

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**TABLE 2** | Conjugative transfer frequency of S. enterica or P. mirabilis SGI1s.

| Donor strain | SGI1 variant | Conjugative plasmid | SGI1 transfer frequency |
|--------------|--------------|---------------------|------------------------|
| SCMY1        | SGI1-F       | IncC plasmid pR55   | 1.7 x 10^-6            |
| SC10         | SGI1-F       | IncC plasmid pR55   | 1.9 x 10^-6            |
| SC968        | SGI1-I       | IncC plasmid pR55   | 2.3 x 10^-7            |
| PmBC55       | SGI1-W       | IncC plasmid pR55   | 4.3 x 10^-6            |
| PmSN55       | SGI1-W       | IncC plasmid pR55   | 3.7 x 10^-6            |
| PmD107       | SGI1-W       | IncC plasmid pR55   | 3.4 x 10^-6            |
### TABLE 3 | Acquired antimicrobial resistance genes in SGI1-containing *S. enterica* and *P. mirabilis* isolates.

| Strain | Aminoglycoside | β-lactam | Colistin | Fluoroquinolone | MLS – Macrolide, Lincosamide and Streptogramin B | Phenicol | Rifampicin | Sulfonamide | Tetracycline | Trimethoprim |
|--------|----------------|----------|----------|-----------------|-----------------------------------------------|----------|------------|-------------|--------------|--------------|
| SCMYP1 |                |          |          |                 | **bla**<sub>CARB-2</sub> **mcr-1</sub> |            |            |            |              |              |
| SC10   | **aadA2**      |          |          |                 | **floR** |            |            |            |              |              |
| SC968  | **strB**       |          |          |                 | **floR** |            |            |            |              |              |
| PmBC55 | **strA**       |          |          |                 | **Inu(F)** |            |            |            |              |              |
|        | **aadA2**      |          |          |                 | **floR** |            |            |            |              |              |
|        |                | **catB2**|          |                 |            |            |            |            |              |              |
| PmBC1123| **aphA1**     |          |          |                 | **bla**<sub>OXA-1</sub> **Inu(F)** |            |            |            |              |              |
|        | **strB**       |          |          |                 |            |            |            |            |              |              |
|        | **aacC4**      |          |          |                 | **ere(A)** |            |            |            |              |              |
|        | **hph**        |          |          |                 | **Inu(F)** |            |            |            |              |              |
|        | **aadA2**      |          |          |                 | **catB4** |            |            |            |              |              |
| PmSC1111| **hph**       |          |          |                 | **fluR** |            |            |            |              |              |
|        | **aacC4**      |          |          |                 | **ere(A)** |            |            |            |              |              |
|        | **aphA1**      |          |          |                 | **cfr** |            |            |            |              |              |
|        | **strB**       |          |          |                 | **mcr(E)** |            |            |            |              |              |
|        | **aadA1**      |          |          |                 | **msr(E)** |            |            |            |              |              |
|        | **aadA2**      |          |          |                 |            |            |            |            |              |              |
| PmSN55 | **hph**        |          |          |                 | **fluR** |            |            |            |              |              |
|        | **aacC4**      |          |          |                 | **ere(A)** |            |            |            |              |              |
|        | **aphA1**      |          |          |                 | **cfr** |            |            |            |              |              |
|        | **aadA2**      |          |          |                 | **mcr(E)** |            |            |            |              |              |
|        | **aadA14**     |          |          |                 | **msr(E)** |            |            |            |              |              |
| PmDJ107| **hph**        |          |          |                 | **fluR** |            |            |            |              |              |
|        | **aacC4**      |          |          |                 | **ere(A)** |            |            |            |              |              |
|        | **aphA1**      |          |          |                 | **cfr** |            |            |            |              |              |
|        | **aadA2**      |          |          |                 | **mcr(E)** |            |            |            |              |              |

*Antimicrobial resistance genes carried by SGI1 are indicated in bold. tetA(J) is inherent in the chromosome. *Acquired antimicrobial resistance genes were identified by ResFinder 3.1 (https://cge.cbs.dtu.dk/services/ResFinder/).*
catB3 (chloramphenicol) and arr-3 (rifampicin) never reported to date in SG1.

Mobilization of SG1
A free circle can be formed after excision of SG1 from the chromosome (Doublet et al., 2005). SG1 appeared to be non-self-transmissible, but it could potentially be integrated into the chromosome of another bacterial species by the help of IncA/C plasmid (Douard et al., 2010; Sieb et al., 2016). In the recipient strain, the circular form of SG1 integrates in a specific site at the 3’ end of the chromosomal trmE gene (Doublet et al., 2005).

The circular forms of SG1 in all strains except for PmBC1123 and PmSC1111 were detected by two rounds of PCR amplification. We did not detect the circular form of SG1 in PmBC1123 because of the inversion of the right direct repeat in SG1-PmBC1123. The circular form of SG1-PmSC1111 could not be detected through three independent experiments. Mobilization assays showed that the three known SG1 variants (SGI-I, SGI-I and SGI-W) in S. enterica or P. mirabilis could be conjugally mobilized to E. coli and was incorporated into the 3’-end of trmE. The conjugative transfer of them were detected at frequencies between 10^{-6} and 10^{-7}, suggesting that these SG1s can be transferred between bacterial species (Table 2). However, the mobilization of SGI-PmBC1123 and SGI-PmSC1111 failed despite three independent attempts. The results indicate that the sequence inversion of partial SG1 backbone may result in the loss of mobility of SG1. We supposed that the inversion of the right direct repeat in SG1-PmBC1123 may lead to losing the capability to form a circular form and then mobility. Nevertheless, in SG1-PmSC1111, IS26-mediated rearrangements resulted in the loss of mobility of SGI1-M65 because of the inversion of the right direct repeat in SGI1-PmBC1123 and SGI1-PmSC1111. The wild strains might be carried by ICE Pmi and described two novel SGI1 variants, SGI1-PmBC1123 and SGI1-PmSC1111. The sul3-type III class 1 integron (5’CS-sat-psp-aadA2-cmlA1-aadA1-gacH-IS440-sul3) and gene cassettes aac(6’)-Ib-cr-blaOXA-1-catB3-arr-3 are reported in SG1 for the first time. Our study highlights that IS26-mediated rearrangements promote the diversity of SG1.

Other Resistance Genes That Were Not Associated With SG1
The acquired antimicrobial resistance genes in SG1-containing S. enterica and P. mirabilis isolates are listed in Table 3. S. Albany strain SCMYP1 harbors blaCTX-M-55 and mcr-1, explaining the resistance to third generation cephalosporins and polymyxin B, respectively. P. mirabilis strains PmSN55 and PmD107 harbors AmpC cephalosporinase gene blaCMY-2 carried by an 11.7-kb contig that is identical to the corresponding region of SXT/R391 ICE ICEPm1lp1 (Harada et al., 2010; Lei et al., 2016), indicating the blaCMY-2 gene in those two strains might be carried by ICEPm1lp1. It is notable that strain PmSC1111 harbors the multiresistance gene cfr that is also carried by SXT/R391 ICE (accession no. CP034090). Very recently we reported a novel SXT/R391 ICE that carried cfr, blaCTX-M-65, fosA3, and aac(6’)-Ib-cr in P. mirabilis and could be transferred to E. coli (Lei et al., 2018a). Taken together, SXT/R391 ICE could mediate the dissemination of clinically important resistance genes in P. mirabilis, which needs to draw more attention.

CONCLUSION
In this study, we characterized SG1 in S. enterica and P. mirabilis of food-producing animal origin in Sichuan Province and described two novel SG1 variants, SGI1-PmBC1123 and SGI1-PmSC1111. The sul3-type III class 1 integron (5’CS-sat-psp-aadA2-cmlA1-aadA1-gacH-IS440-sul3) and gene cassettes aac(6’)-Ib-cr-blaOXA-1-catB3-arr-3 are reported in SG1 for the first time. Our study highlights that IS26-mediated rearrangements promote the diversity of SG1.

DATA AVAILABILITY STATEMENT
The datasets generated for this study can be found in the GeneBank, MH998664, MH998665, CP034091 and CP034090.

ETHICS STATEMENT
This study was carried out in accordance with the recommendation of ethical guidelines of Sichuan University. The protocol was approved by the Sichuan University Animal Ethics Committee. Individual informed consent for the use of samples was obtained from all the animal owners.

AUTHOR CONTRIBUTIONS
X-CW, C-WL, Z-ZK, and YZ performed the experiments. C-WL and Z-ZK wrote the manuscript. All authors contributed to manuscript revision and approved the final manuscript.

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SUPPLEMENTARY MATERIAL
The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmicb.2019.02245/full#supplementary-material
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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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