FirmiData: a set of 40 genomes of Firmicutes with a curated annotation of ICEs and IMEs

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Abstract

Objectives: 'Integrative and Conjugative Elements' (ICEs) and 'Integrative and Mobilizable Elements' (IMEs) are two classes of mobile genetic elements that are complex to detect and delineate. Therefore, they are yet poorly annotated in bacterial genomes. FirmiData provides to the scientific community of microbiologists and bioinformaticians a reference resource of annotated ICEs and of IMEs from Firmicutes. It illustrates their prevalence and their diversity but also gives information on their organization.

FirmiData was designed to assist the scientific community in identifying and annotating these elements by using the sequences of these ICEs and IMEs for the identification of related elements in other genomes of Firmicutes. Therefore, Firmidata meets the needs of the scientific community.

Data description: Firmidata provides a manually curated annotation of 98 ICEs and 148 IMEs identified in 40 chromosomes of Firmicutes. The delineation at the nucleotide level of almost all of these elements allows for the characterization of the genes they carry.

Keywords: Integrative and conjugative element, Integrative and mobilizable element, Mobile element, Conjugation

Objective

Unlike conjugative or mobilizable plasmids, ICEs and IMEs are difficult to detect because of their integration into replicons. This is why they have been neglected and even completely ignored for a long time.

However, efforts were made in the last 10 years to develop semi-manual [1, 2] and automatic [3–5] methods to search for conjugative elements in bacterial genomes. These led to the identification of an increasing number of ICEs and IMEs and to the demonstration of their diversity. We currently know that these elements are highly widespread in bacteria and archaea [6–8].

Despite these recent efforts, ICE and IME annotation is very rarely performed and released in public genome databases. The poor annotation of ICEs and IMEs within bacterial genomes is multifactorial. It results both from the extreme variability of their gene content and from the low specificity of their signature proteins. It is also due to their complex organization since they often form composite elements, with ICEs/IMEs nested within each other and/or organized in tandems.

The objective of FirmiData is to offer to both the communities of microbiologists and bioinformaticians a semi-manual annotation of a large dataset of ICEs and IMEs from Firmicutes. In this work, an expert analysis was done to verify, to characterize and to delimit all ICEs and IMEs they carry. The chromosomes of diverse groups of Firmicutes were chosen to illustrate the diversity of the elements as well as of their various organization into composite elements. The sequences of these elements can be used as reference for the identification of related elements in other genomes of Firmicutes.
Data description
FirmiData is a set of 40 public annotated genomes of Firmicutes (information on strains are available in Table 1, 'Data file 41', [9]). These genomes were extracted from the Refseq database for which ICEs and IMEs annotation was added using the standard annotation features and qualifiers used in the Genbank format [9].

The search for ICEs and IMEs relies on data from the literature and on a semi-automated procedure that was described in [1] and [2]. All annotations were carefully

![Table 1 Data sets](image-url)
checked and corrected when necessary and almost all of these elements were delineated at the nucleotide level.

ICE expert annotation is based on the identification of genes carried by their conjugation module and encoding three proteins (relaxase, coupling protein and VirB4) needed for their transfer. ICE identification also relies on the search of three types of integrases (tyrosine integrases, serine integrases, and DDE transposases of the ISLre2 family). IME characterization was done in a similar fashion as for ICES except that we searched for genes carried by their mobilization modules encoding a relaxase and eventually a coupling protein.

The co-localization of the genes encoding the signature proteins attests for the presence of an ICE or an IME. Their boundaries were then searched. One relevant information for the ICE/IME delineation is the knowledge of the insertion site targeted by their integrase. To get this information, phylogenetic analyses were done to identify the closest integrase for which the integration site was already identified. ICE/IME boundaries were identified manually by the search for the Direct Repeats (DRs) flanking the elements. When the DRs were missing, too short or too degenerated to be detected, the region containing the element was compared with (i) target regions or genes lacking elements, or (ii) already known and well-delineated elements.

When an expected signature gene was not identified within an element, a thorough examination of all its genes and sequences was done to identify those encoding the missing signature proteins.

Results
A total of 98 ICES and 148 IMEs were annotated. We consider as ICES the elements that were delimited and that encode a relaxase, a coupling protein, a VirB4, and one to three integrases. IMEs are delimited elements that encode one or two relaxases and eventually a coupling protein, both distantly related or unrelated to those of ICES. We also annotated slightly decayed ICES and IMEs.

The name of the elements indicates (i) their type (ICE or IME), (ii) the strain of the host bacteria and (iii) the target gene. Elements marked with an asterisk are not integrated in their primary site but in a secondary one. Those marked with “unk” are integrated in a gene of unknown function. The site of insertion of those labeled with ND or NS is non-determined and non-specific, respectively.

In conclusion, the FirmiData dataset constitutes a valuable resource for (i) the microbiologist community interested in mobile genetic elements annotation (ii) the bioinformatics teams developing annotation tools and strategies to detect and annotate mobile genetic elements in bacterial genomes.

Limitations
- Isolate genes encoding a signature protein or too decayed ICES or IMEs were not taken into consideration.
- Elements encoding an integrase but devoid of relaxase were not annotated.

Abbreviations
ICE: Integrative and conjugative element; IME: Integrative and mobilizable element; DRs: Direct repeats.

Acknowledgements
Not applicable

Author contributions
GG: formal analysis, writing—review & editing; SP: formal analysis, writing—review & editing; JL: production of the new annotated Genbank files, writing—review & editing; TL: writing—review & editing; HC: funding acquisition, writing—review & editing; NLB: production of the new annotated Genbank files, funding acquisition, writing—original draft. All authors read and approved the final manuscript.

Funding
This work was supported by the Université de Lorraine, the Région Grand-Est and INRAE. This work was co-funded by the french PIA project “Lorraine Université d’Excellence” (ANR-15-IDEX-04-LUE), and by the European Union through the Regional Operational Program of the European Regional Development Fund (ERDF).

Availability of data and materials
The data described in this Data note can be freely and openly accessed on Data INRAE (https://doi.org/10.15454/VI7YRB). Please see Table 1 and reference [9] for details and links to the data.

Declarations
Ethics approval and consent to participate
Not applicable.

Consent for publication
The authors declare that they all consent for publication.

Competing interests
The authors declare that they have no competing interests.

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Received: 16 December 2021   Accepted: 11 April 2022
Published online: 10 May 2022

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