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RESEARCH ARTICLE

Analysis of *Mycobacterium tuberculosis* Genotypic Lineage Distribution in Chile and Neighboring Countries

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Abstract

Tuberculosis (TB), caused by the pathogen *Mycobacterium tuberculosis* (MTB), remains a disease of high importance to global public health. Studies into the population structure of MTB have become vital to monitoring possible outbreaks and also to develop strategies regarding disease control. Although Chile has a low incidence of MTB, the current rates of migration have the potential to change this scenario. We collected and analyzed a total of 458 *M. tuberculosis* isolates (1 isolate per patient) originating from all 15 regions of Chile. The isolates were genotyped using the spoligotyping method and the data obtained were analyzed and compared with the SITVIT2 database. A total of 169 different patterns were identified, of which, 119 patterns (408 strains) corresponded to Spoligotype International Types (SITs) and 50 patterns corresponded to orphan strains. The most abundantly represented SITs/lineages were: SIT53/T1 (11.57%), SIT33/LAM3 (9.6%), SIT42/LAM9 (9.39%), SIT50/H3 (5.9%), SIT37/T3 (5%); analysis of the spoligotyping minimum spanning tree as well as spoligoforest were suggestive of a recent expansion of SIT42, SIT50 and SIT37; all of which potentially evolved from SIT53. The most abundantly represented lineages were LAM (40.6%), T (34.1%) and Haarlem (13.5%). LAM was more prevalent in the Santiago (43.6%) and Concepción (44.1%) isolates, rather than the Iquique (29.4%) strains. The proportion of X lineage was appreciably higher in Iquique and Concepción (11.7% in both) as compared to Santiago (1.6%). Global analysis of MTB lineage distribution in Chile versus neighboring countries showed that evolutionary recent lineages (LAM, T and Haarlem) accounted together for 88.2% of isolates in Chile, a pattern which mirrored MTB lineage distribution in neighboring countries (n = 7378 isolates recorded in SITVIT2 database for Peru, Brazil, Paraguay, and Argentina; and published studies), highlighting epidemiological advantage of Euro-American lineages in this region. Finally, we also observed exclusive emergence of patterns SIT4014/X1 and SIT4015 (unknown lineage signature) that have hitherto been found exclusively in Chile, indicating that conditions specific to Chile, along

with the unique genetic makeup of the Chilean population, might have allowed for a possible co-evolution leading to the success of these emerging genotypes.

Introduction

Mycobacterium tuberculosis (MTB), a Gram-positive bacterium, is the causative agent for tuberculosis (TB); a disease that presents millions of new cases and deaths every year and is considered as a major threat to public health [1]. Although a quick and assertive diagnosis is essential for early treatment and disease management, many people lack proper access to the facilities required for adequate or early diagnosis. In this context, the molecular typing of *MTB* has greatly improved our knowledge and control of tuberculosis by allowing for: (i) the detection of unsuspected transmission, (ii) the identification of false-positive cultures, (iii) discrimination between reinfection and relapse [2], and (iv) the study and analysis of global biodiversity and phylogeographical variations of the tubercle bacilli [3]. In the last 2 decades, the cumbersome "gold standard" IS*6110*-RFLP methodology necessitating Southern blotting [4,5] was progressively replaced by PCR-based methods, namely spoligotyping and Mycobacterial interspersed repetitive unit-variable number of tandem-repeat (MIRU-VNTR) typing [6–10]. These methods showed satisfactory discriminatory power and reproducibility [9], particularly when used concomitantly that further allows to identify MTB genetic lineages–a prerequisite to study TB population structure at local, regional, and global scale [11].

As far as TB in the Americas is concerned, it accounted for approximately 285,200 new cases of TB in 2013, which equals to 29 new cases per 100,000 inhabitants [12]. Despite two-thirds (69%) of all cases reported being from South American patients, wide epidemiological differences including varying incidence rates were found both country and region wise, highest incidence rates being from Brazil (46/100,000), Bolivia (123/100,000) and Peru (124/100,000) [12]. In Chile different rates of incidence ranging from 7.5/100,000 to 23.7/100,000, were observed, the highest rates being reported from the northern regions of the country [13]. According to the latest available data, the TB incidence in Chile for 2014 was 12.3 per 100,000, which remains significantly higher than the rate of elimination recommended for declassifying TB as a public health problem (<5 per 100,000).

Investigations conducted on MTB genotypic lineage distribution in Southern America have shown that although the Euro-American lineage is the most widely represented, regional differences in the distribution of lineages/sublineages are frequently observed both between as well as within countries [14–22]. According to the SITVIT2, the LAM, Haarlem and T families are the most commonly observed members of the Euro-American lineage in South and Central America and the Caribbean, a distribution profile shared with Europe and Middle Africa [23]. Nonetheless, some regional specificities such as cases involving a LAM family strain designated as RD^Rio associated with multiple drug resistance (MDR) in Brazil [18], and the almost exclusive "significant" presence of the Beijing family in Peru and Colombia associated both with MDR as well as XDR cases [20,21] may be cited. It is today possible to pinpoint such specificities as well underline the finer differences in MTB population structure at local, regional and macro regional levels, thanks to international genotyping databases and web tools for molecular epidemiology of tuberculosis [23, 24].

Limited MTB genotyping studies in Chile, conducted primarily in metropolitan regions, suggested that Chile is dominated by three major MTB lineages, LAM, T, and Haarlem [25–27]. To provide with a more comprehensive snapshot of MTB lineages circulating in Chile, we

collected and analyzed a total of 458 *M. tuberculosis* isolates (1 isolate per patient) originating from all 15 regions of Chile, including the Metropolitan Region and large cities in north (e.g., Iquique) as well as the south (e.g., Concepción). The data on MTB lineage distribution in Chile versus neighboring countries were compared using the SITVIT2 database [3, 28], so as to highlight exclusive emergence of certain genotypes as well as the potential associated risks in Chile.

Materials and Methods

Sample collection

A total of 458 isolates (1 isolate per patient) of *M. tuberculosis* were collected from 15 regions of Chile (S1 Fig). The isolates, obtained from treatment virgin patients (VT), were collected between 2011 (n = 338 or 73.80%) and 2012 (n = 120 or 26.20%), all the isolates were used in the study. Of them, 304 isolates were from male patients (66.38%) and 154 from female patients (33.62%). The isolates were extracted from body fluids (sputum: 95%, bronchoalveolar lavage fluid: 3.7%, tissue: 0.9%, blood 0.2% and pleural fluid: 0.2%). TB was diagnosed in the clinical centers of the respective cities and the diagnosis was confirmed at the Supranational Reference Mycobacteria Laboratory at the Institute of Public Health of Chile which also conducted first and second line drugs susceptibility tests using the Lowenstein–Jensen medium and the proportion method [29].

The strains used in this study were collected routinely during activities of the state TB control program. No patients were contacted to request additional information. The study was reviewed and approved by the review board of Biomedical Department of Public Health Institute who granted permission for use of the MTB isolates and clinical data for the purposes of the study and waived the need for written informed consent from participants. This study is part of the monitoring carried out by the Institute of Public Health of Chile for the diagnosis and characterization of infectious agents.

DNA extraction and genotyping

MTB isolates obtained from the Lowenstein Jensen medium cultures were resuspended in 500 µL TE (10 mM Tris pH 8.0, 1 mM EDTA pH 8.0). Suspensions were inactivated by heating at 95°C for 15 minutes. Bacterial DNA was isolated by treatment with cetyltrimethylammonium bromide (CTAB) in the presence of 0.7 M NaCl as described previously [30].

Spoligotyping was performed at the Molecular Genetics sub-department of Institute of Public Health of Chile by using the Spoligotyping kit (Ocimum Biosolutions) as described by Kamerbeek *et al.* [8]. Briefly, the 43 spacers between the direct repeats in the target region were amplified using biotinylated primers and the PCR products were then hybridized to a membrane and visualized by chemiluminescence. *M. tuberculosis* H37Rv and *M. bovis* BCG controls, included in the kit, were used as controls for each run. Spoligotyping results were converted into the octal code for comparison with the SITVIT2 proprietary database of Institut Pasteur de la Guadeloupe which is an updated version of the previously released SITVITWEB database (available at: http://www.pasteur-guadeloupe.fr:8081/SITVIT_ONLINE/) [23]. Within this database, a SIT is created when 2 or more isolates share an identical spoligotyping pattern.

Phylogenetic and statistical analysis

In order to study the phylogenetic relationships of given spoligotypes obtained in this study (n = 458 isolates), a minimum spanning tree (MST) was created using the BioNumerics version 6.6 software (Applied Maths, Sint-Martens-Latem, Belgium; available at: http://www.applied-

maths.com/bionumerics). Furthermore, a spoligoforest tree was constructed using the Fruch-
terman-Reingold algorithm in the SpolTools software (http://www.emi.unsw.edu.au/
spolTools) [31]; the tree was reshaped and colored using the GraphViz software (http://www.
graphviz.org) [32]. Unlike the MST, the spoligoforest is a directed graph which tentatively
highlights parent to descendant relationships between spoligotypes. Lastly, Fisher's Exact and
Pearson's Chi-squared tests were calculated using R software. A p-value<0.05 was considered
statistically significant.
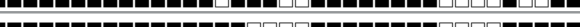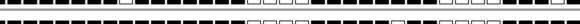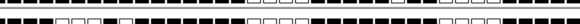
Results

The present study identified spoligotypes for clinical isolates of *M. tuberculosis* (n = 458) with a
global male/female sex ratio of 304/154 = 1.97. The isolates were collected from different cities
of Chile between the years 2011 and 2012. These cities were: Santiago (n = 181), Concepción
(n = 34), Iquique (n = 34), Valparaiso (n = 29), Rancagua (n = 20), Temuco (n = 18), Los Ange-
les (n = 16), Osorno (n = 15), Arica (n = 14), Puerto Montt (n = 12), Talca (n = 12), Talcahuano
(n = 12), Antofagasta (n = 11), Coquimbo (n = 11), Castro (n = 9), Punta Arenas (n = 7), Ovalle
(n = 6), Valdivia (n = 6), Copiapo (n = 5), Coihaique (n = 2), Viña del Mar (n = 2), Vallenar
(n = 1), and Calama (n = 1). Detailed demographic and genotyping information is listed in **S1
Table**. Analysis of drug resistance profiles showed that most isolates were pan-susceptible
(n = 402) while some were resistant to any drug (n = 44) or multidrug resistant (n = 6). For a
few cases, data regarding resistance was unavailable (n = 6). Three of the six MDR-TB strains
belonged to SIT53/T1 and two were from Santiago. Among strains that were resistant to any
antibiotic, our results showed that: (i) of the six belonging to SIT33, five were resistant to strep-
tomycin; (ii) the six strains of SIT42 presented with a heterogeneous resistance, one or a mix-
ture of antibiotics, and (iii) three out of a total of six strains of SIT4015 presented with some
form of resistance throughout the study.

Spoligotyping of the 458 isolates revealed a total of 169 different patterns: 119 patterns (408
strains, 89.08% of sample population) corresponded to the shared-types or SITs when com-
pared to the SITVIT2 database, and 50 patterns (50 strains, 10.92% of sample population) cor-
responded to orphan strains that have not yet been reported in literature. A total of 95/119
SITs (n = 357 isolates) matched a preexisting shared-type recorded in the database, whereas
24/119 SITs (n = 51 isolates) were newly created when they matched orphan strains recorded
in the database (SIT4014 –SIT4037). The 50 orphan remaining strains were also recorded in
the database. A detailed description of the 119 SITs (n = 408 isolates) and their corresponding
spoligotyping defined lineages/sublineages are shown in **Table 1**.

For the 458 isolates analyzed in this study, distribution of lineages was as follow: LAM
(n = 186 isolates, or 40.61%); T (n = 156 isolates, or 34.06%); Haarlem (n = 62 isolates, or
13.54%); X (n = 18 isolates, or 3.93%); Beijing (n = 2 isolates, or 0.44%); AFRI (n = 1 isolate, or
0.22%); Cameroon (n = 1 isolate, or 0.22%); and Unknown (n = 32 isolates, or 6.99%) (**S1
Table**). We observed significant differences in prevalence when the proportion of LAM, T,
Haarlem and X lineages were compared within three of Chile's most prominent cities, viz., San-
tiago, Concepción and Iquique (p-value = 0.0071). The observed proportion of Haarlem was
remarkably lower in Concepción city (2.94%) as compared to Santiago (16.57%) and Iquique
(11.76%). Regarding other lineages: (i) Beijing lineage was represented by about 3% of strains
in Iquique and Santiago city; (ii) LAM lineage represented around 44% of strains in Santiago
and Concepción, but only 29% in Iquique city; (iii) X lineage was more noticeable in Iquique
and Concepción, representing around 12% of isolates, but in Santiago its incidence was less
than 2%; (iv) the unknown strain was conspicuous in Iquique (11.8%) and Concepción
(14.7%) but comparatively less prevalent in Santiago (6%) (**Fig 1A**).

Table 1. Description of 119 shared-types (SITs; n = 408 isolates) and corresponding spoligotyping defined lineages/sublineages starting from a total of 458 *M. tuberculosis* strains isolated in various cities in Chile.

SIT*	Spoligotype Description	Octal Number	Nb in study (%)	% in study vs. database	Lineage**	Unique vs. Clustered SIT***
1		000000000003771	2 (0.44)	0.02	Beijing	Clustered
2		000000004020771	1 (0.22)	0.21	H2	Unique
4		000000007760771	1 (0.22)	0.26	Unknown	Unique
20		677777607760771	3 (0.66)	0.33	LAM1	Clustered
33		776177607760771	44 (9.61)	3.25	LAM3	Clustered
37		777737777760771	23 (5.02)	4.23	T3	Clustered
39		777777347760471	1 (0.22)	0.67	T4-CEU1	Unique
42		777777607760771	43 (9.39)	1.21	LAM9	Clustered
44		777777757760771	1 (0.22)	0.46	T5	Unique
47		777777774020771	5 (1.09)	0.3	H1	Clustered
50		777777777720771	27 (5.9)	0.68	H3	Clustered
51		777777777760700	3 (0.66)	0.95	T1	Clustered
52		777777777760731	2 (0.44)	0.21	T2	Clustered
53		777777777760771	53 (11.57)	0.8	T1	Clustered
58		777777557760771	4 (0.87)	2.05	T5-Madrid2	Clustered
60		777777607760731	5 (1.09)	1.12	LAM4	Clustered
61		777777743760771	1 (0.22)	0.1	Cameroon	Unique
62		777777774020731	1 (0.22)	0.17	H1	Unique
64		777777607560771	8 (1.75)	1.94	LAM6	Clustered
78		777777777760711	1 (0.22)	1.45	T	Unique
81		777377607760771	1 (0.22)	2.63	LAM9	Unique
91		700036777760771	5 (1.09)	1.36	X3	Clustered
93		777737607760771	1 (0.22)	0.22	LAM5	Unique
99		757777777720771	2 (0.44)	2.41	H3	Clustered
111		776167607760771	1 (0.22)	3.13	LAM3	Unique
118		777767777760771	1 (0.22)	0.6	T1	Unique
119		777776777760771	1 (0.22)	0.09	X1	Unique
124		777777777700771	1 (0.22)	1.47	Unknown	Unique
130		776177607760731	2 (0.44)	1.55	LAM3	Clustered
137		777776777760601	3 (0.66)	0.29	X2	Clustered
154		757777777760771	1 (0.22)	0.88	T1	Unique
162		777777607760671	1 (0.22)	2.86	LAM9	Unique
163		777777607760700	1 (0.22)	2.5	LAM4	Unique
180		677777777720771	2 (0.44)	3.23	H3	Clustered
194		677737607760731	2 (0.44)	6.06	LAM2	Clustered
195		677777607660771	1 (0.22)	6.25	LAM1	Unique
211		776137607760771	12 (2.62)	10.17	LAM3	Clustered
222		777774077560771	4 (0.87)	3.96	Unknown	Clustered
238		777777777700171	1 (0.22)	5.56	Unknown	Unique
239		777777777760031	1 (0.22)	1.64	T2	Unique
241		777777777760411	1 (0.22)	3.57	T1	Unique
244		777777777760601	1 (0.22)	0.84	T1	Unique
245		777777777760671	1 (0.22)	4.76	T1	Unique
283		777777704020771	6 (1.31)	8.11	H1	Clustered
393		777757777760771	1 (0.22)	2.44	T1	Unique
430		704003347760471	1 (0.22)	2.7	T4-CEU1	Unique
434		760777777740371	1 (0.22)	16.67	T1	Unique
435		763777607760771	1 (0.22)	16.67	LAM9	Unique
450		777776770000000	1 (0.22)	0.8	Unknown	Unique
504		777737737760771	1 (0.22)	4.35	T3	Unique
720		776177607760371	6 (1.31)	54.55	LAM3	Clustered
753		477777607760771	1 (0.22)	4.55	LAM1	Unique

(Continued)

Table 1. (*Continued*)

SIT*	Spoligotype Description	Octal Number	Nb in study (%)	% in study vs. database	Lineage**	Unique vs. Clustered SIT***
787		777777777760071	1 (0.22)	12.5	T1	Unique
798		437777777760771	2 (0.44)	33.33	T1	Clustered
880		777777000760771	1 (0.22)	10	T1	Unique
900		677777607740011	1 (0.22)	25	LAM	Unique
914		776377777720771	1 (0.22)	1.45	Unknown	Unique
948		777777760020611	2 (0.44)	14.29	H3	Clustered
1073		777637777760771	1 (0.22)	12.5	T1	Unique
1105		777773777760771	1 (0.22)	2.78	T1	Unique
1116		607777777720771	1 (0.22)	33.33	H3	Unique
1220		754377607760700	1 (0.22)	16.67	LAM	Unique
1232		777774077560731	1 (0.22)	10	T2	Unique
1259		777740000160771	1 (0.22)	25	T1	Unique
1277		777772207760771	6 (1.31)	16.67	LAM9	Clustered
1476		736177607700171	1 (0.22)	3.13	AFRI_2	Unique
1560		703777777760771	2 (0.44)	22.22	T1	Clustered
1626		777777776760771	1 (0.22)	7.69	T1	Unique
1685		776077607760771	3 (0.66)	37.5	LAM3	Clustered
1706		717777607760771	1 (0.22)	10	LAM9	Unique
1710		777737607760731	4 (0.87)	36.36	LAM	Clustered
1841		776177607740771	1 (0.22)	16.67	LAM3	Unique
1890		777777707760731	1 (0.22)	8.33	T2	Unique
2014		776177607360771	1 (0.22)	20	LAM3	Unique
2015		736177607760771	2 (0.44)	33.33	LAM3	Clustered
2028		777777604020771	1 (0.22)	10	Unknown	Unique
2045		776037607760771	1 (0.22)	6.25	LAM3	Unique
2054		677777607760371	1 (0.22)	8.33	LAM	Unique
2070		777777637760771	4 (0.87)	23.53	T1	Clustered
2353		776177600000000	2 (0.44)	18.18	Unknown	Clustered
2366		777777777760171	1 (0.22)	16.67	T1	Unique
2402		776177607760711	1 (0.22)	25	LAM3	Unique
2512		657757607760771	1 (0.22)	16.67	LAM1	Unique
2745		577777607760751	2 (0.44)	40	LAM9	Clustered
2885		777777477720771	1 (0.22)	6.25	H3	Unique
2911		777737777700771	1 (0.22)	33.33	Unknown	Unique
2941		074377607760700	1 (0.22)	25	LAM	Unique
3056		777777777560731	1 (0.22)	16.67	T2	Unique
3127		000000017760771	1 (0.22)	20	Unknown	Unique
3251		776177777720771	1 (0.22)	25	H3	Unique
3472		776177607760770	1 (0.22)	33.33	LAM3	Unique
3491		776177607760671	1 (0.22)	25	LAM3	Unique
3934		437777777760731	1 (0.22)	20	T2	Unique
3965		707774077560771	1 (0.22)	7.69	T1	Unique
3967		741774077560771	1 (0.22)	33.33	T1	Unique
4014*		703776777760771	7 (1.53)	100	X1	Clustered
4015*		776177703770371	7 (1.53)	100	Unknown	Clustered
4016*		777777774100771	2 (0.44)	100	Unknown	Clustered
4017*		777737637760771	3 (0.66)	75	T3	Clustered
4018*		777377636000771	2 (0.44)	100	Unknown	Clustered
4019*		776177607720771	1 (0.22)	50	H3	Unique
4020*		777347777760671	1 (0.22)	50	T1	Unique
4021*		777737777720671	1 (0.22)	50	H3	Unique
4022*		777777364020771	1 (0.22)	50	H1	Unique
4023*		777774077560711	1 (0.22)	50	T1	Unique

(*Continued*)

Table 1. (*Continued*)

SIT*	Spoligotype Description	Octal Number	Nb in study (%)	% in study vs. database	Lineage**	Unique vs. Clustered SIT***
4024*	(spoligotype pattern)	663777777720771	3 (0.66)	100	H3	Clustered
4025*	(spoligotype pattern)	777763347760471	4 (0.87)	100	T4-CEU1	Clustered
4026*	(spoligotype pattern)	763777607760700	2 (0.44)	100	LAM4	Clustered
4027*	(spoligotype pattern)	772177607760771	1 (0.22)	50	LAM3	Unique
4028*	(spoligotype pattern)	700036774360771	1 (0.22)	50	X3	Unique
4029*	(spoligotype pattern)	777777717560771	1 (0.22)	50	T1	Unique
4030*	(spoligotype pattern)	037777700000611	2 (0.44)	100	Unknown	Clustered
4031*	(spoligotype pattern)	777774037560771	2 (0.44)	100	T1	Clustered
4032*	(spoligotype pattern)	776077606160771	2 (0.44)	100	LAM3	Clustered
4033*	(spoligotype pattern)	776137607760371	1 (0.22)	50	LAM3	Unique
4034*	(spoligotype pattern)	776177417760771	2 (0.44)	100	T1	Clustered
4035*	(spoligotype pattern)	601777777760771	2 (0.44)	100	T1	Clustered
4036*	(spoligotype pattern)	777777607160731	1 (0.22)	50	LAM4	Unique
4037*	(spoligotype pattern)	777777734020771	1 (0.22)	50	H1	Unique

* A total of 95/119 SITs containing 357 isolates matched a preexisting shared-type in the database, whereas 24/119 SITs (n = 51 isolates) were newly created. A total of 46/119 SITs containing 335 isolates were clustered within this study (2 to 53 isolates per cluster) while 73/119 SITs containing 73 strains were unique (for total unique strains, one should add to this number the 50 orphan strains, which brings the number of unclustered isolates in this study to 123/458 or 26.86%, and clustered isolates to 335/458 or 73.14%). Note that SIT followed by an asterisk indicates "newly created" SIT due to 2 or more strains belonging to an identical new pattern within this study or after a match with an orphan in the database; SIT designations followed by number of strains: 4014* this study n = 7; 4015* this study n = 7; 4016* this study n = 2; 4017* this study n = 3, VEN n = 1; 4018* this study n = 2; 4019* this study n = 1, ESP n = 1; 4020* this study n = 1, ARG n = 1; 4021* this study n = 1, IDN n = 1; 4022* this study n = 1, TUN n = 1; 4023* this study n = 1, PER n = 1; 4024* this study n = 3; 4025* this study n = 4; 4026* this study n = 2; 4027* this study n = 1, ESP n = 1; 4028* this study n = 1, PER n = 1; 4029* this study n = 1, BRA n = 1; 4030* this study n = 2; 4031* this study n = 2; 4032* this study n = 2; 4033* this study n = 1, ITA n = 1; 4034* this study n = 2; 4035* this study n = 2; 4036* this study n = 1, BRA n = 1; 4037* this study n = 1, BRA n = 1. The 3 letter country codes are according to http://en.wikipedia.org/wiki/ISO_3166-1_alpha-3.

** Lineage designations according to SITVIT2 using revised SpolDB4 rules; "Unknown" designates patterns with signatures that do not belong to any of the major lineages described in the database.

*** Clustered strains correspond to a similar spoligotype pattern shared by 2 or more strains "within this study"; as opposed to unique strains harboring a spoligotype pattern that does not match with another strain from this study. Unique strains matching a preexisting pattern in the SITVIT2 database are classified as SITs, whereas in case of no match, they are designated as "orphan"

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A total of 257 isolates (56.11% of all 458) were clustered in fifteen of the most frequent spoligotypes (predominant SITs representing >1%, i.e., n = 5 or more isolates in our study): SIT53/T1 (n = 53; 11.57%), SIT33/LAM3 (n = 44; 9.61%), SIT42/LAM9 (n = 43; 9.39%), SIT50/H3 (n = 27; 5.90%), SIT37/T3 (n = 23; 5.02%), SIT211/LAM3 (n = 12; 2.62%), SIT64/LAM6 (n = 8; 1.75%), SIT4014/X1 (n = 7; 1.53%), SIT4015/Unknown (n = 7; 1.53%), SIT283/H1 (n = 6; 1.31%), SIT720/LAM3 (n = 6; 1.31%), SIT1277/LAM9 (n = 6; 1.31%), SIT47/H1 (n = 5; 1.09%), SIT60/LAM4 (n = 5; 1.09%) and SIT91/X3) (n = 5; 1.09%) (**Table 2**).

It is noteworthy that SIT33/LAM3 was particularly well represented in our study (n = 44; 9.61%). Also, SIT720/LAM3 was observed in the Chilean population with 6 isolates in our study representing around 54.55% of isolates recorded in SITVIT2 database; this SIT was reported exclusively in South America (see **Table 2**). The other two SITs that were well represented in this study as compared to the registered SITs in SITVIT2 databases, were SIT211 and SIT1277 (10.17% and 16.67% respectively). Interestingly, results obtained from our study suggest that the LAM3 sublineage is very well represented in the Chilean cohort. Interestingly two novel SITs, 4014 and 4015, have been reported at a relatively high proportion (n = 7 isolates each) for the first time in this study.
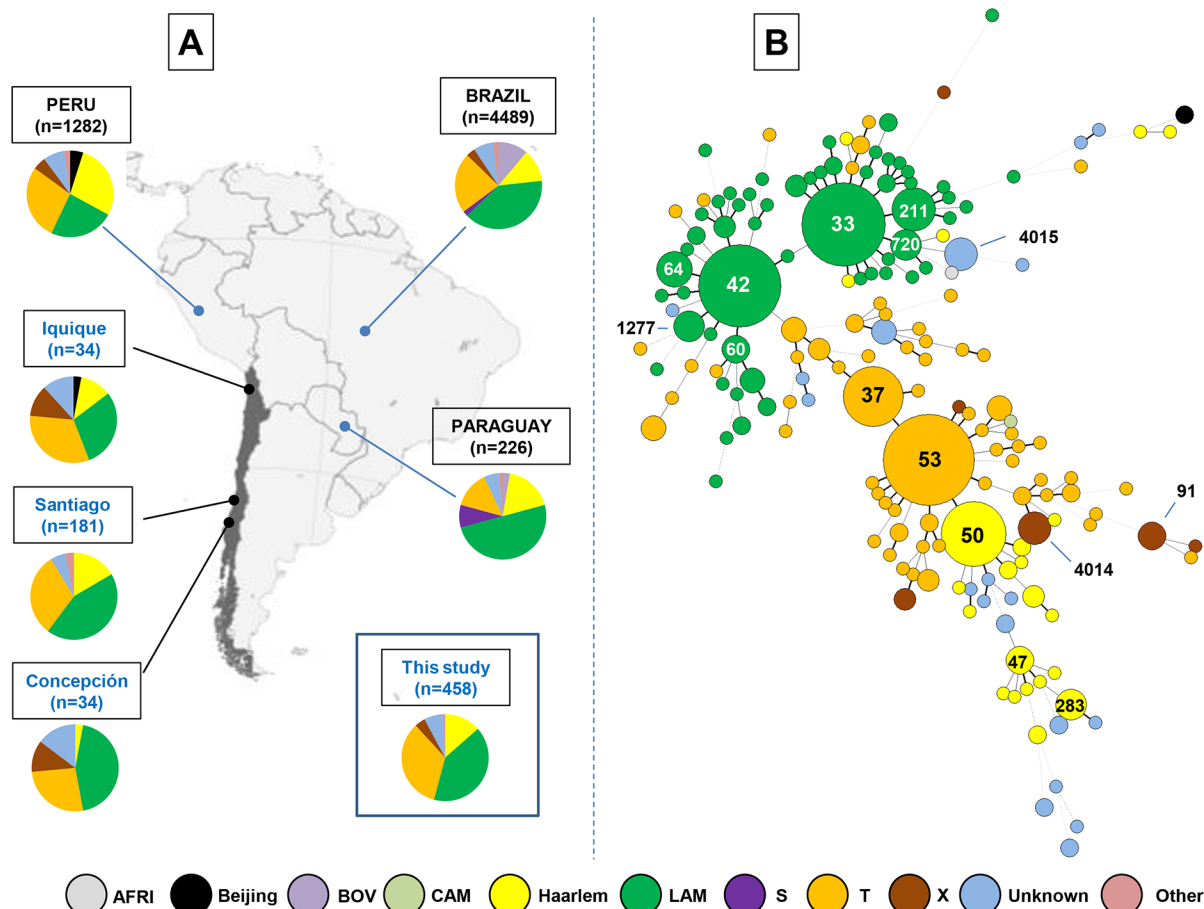
Fig 1. Phylogeographical distribution of *M. tuberculosis* lineages identified in our study and MST illustrating evolutionary relationships. (A) Phylogeographical distribution of major *M. tuberculosis* lineages in the 3 most important cities in our study (Santiago, Iquique, Concepción) as well as following neighboring countries: Peru, Brazil, and Paraguay (referring to the SITVIT2 database). (B) A minimum spanning tree (MST) illustrating evolutionary relationships between spoligotypes in various cities of Chile (n = 458 isolates). The phylogenetic tree connects each genotype based on degree of changes required to go from one allele to another. The structure of the tree is represented by branches (continuous vs. dashed and dotted lines) and circles representing each individual pattern. Note that the length of the branches represents the distance between patterns while the complexity of the lines (continuous, gray dashed and gray dotted) denotes the number of allele/spacer changes between two patterns: solid lines, 1 or 2 or 3 changes (thicker ones indicate a single change, while the thinner ones indicate 2 or 3 changes); gray dashed lines represent 4 changes; and gray dotted lines represent 5 or more changes. The size of the circle is proportional to the total number of isolates in our study, illustrating unique isolates (smaller nodes) versus clustered isolates (bigger nodes). The color of the circles indicates the phylogenetic lineage to which the specific pattern belongs. The labels of nodes indicate predominant SITs in study (containing at least 5 or more isolates).

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When the proportion of predominant SITs found in Chile (n = 458 isolates) as well as the distribution patterns for major cities (Santiago, Iquique and Concepción) were compared, it was observed that the strains belonging to SIT91/X3 were localized to Iquique, whereas the strains belonging to SIT37/T3, SIT60/LAM4, SIT64/LAM6, SIT283/H1 and SIT720/LAM3 were mostly isolated from the Santiago based population, and strains belonging to newly created SIT4014/X1 were predominantly found in Concepción city (p-value<0.008; **Table 3**). Significant differences were noted when the distribution patterns of predominant SITs in this study were compared with that of neighboring countries (Peru, Brazil, Paraguay, Argentina) as recorded in the SITVIT2 database (n = 7378 isolates; p-value<0.00001; **Table 3** and **Fig 1A**). In comparison to neighboring countries, SIT33 is well represented in Chile (9.61% of isolates)

Table 2. Description of clusters containing >1% (n = 5 or more isolates) in this study, and their worldwide distribution in the SITVIT2 database.

SIT (Lineage) Octal NumberSpoligotype Description	Number (%) in study	% in study vs. database	Distribution in Regions with ≥ 3%of a given SIT *	Distribution in countries with ≥ 3%of a given SIT **
33 (LAM3) 776177607760771	44 (9.61)	3.25	AMER-S 37.08, AFRI-S 24.0, AMER-N 11.74, EURO-S 10.49, EURO-W 6.06, AMER-C 3.99	ZAF 24.0, PER 16.4, USA 11.74, BRA 10.56, ESP 6.57, ARG 4.21, CHL 4.06, FXX 3.91, ITA 3.4, HND 3.18
37 (T3) 777737777760771	23 (5.02)	4.23	AFRI-E 18.38, AMER-S 13.05, EURO-N 11.4, EURO-W 11.03, ASIA-W 10.11, AMER-N 8.27, ASIA-E 5.88, EURO-S 5.52,EURO-E 4.23, ASIA-S 3.49, AFRI-S 3.13	ETH 15.99, USA 7.35, CHL 5.52, SWE 4.96, SAU 4.78, CHN 4.78, FXX 4.04, ITA 3.86, BRA 3.49, ZAF 3.13, DNK 3.13
42 (LAM9) 777777607760771	43 (9.39)	1.21	AMER-S 31.99, AMER-N 11.19, EURO-S 10.68, EURO-W 8.94, AFRI-N 8.09, EURO-N 4.62, CARI 4.0, AMER-C 3.35, AFRI-E 3.35	BRA 12.91, USA 11.19, COL 7.19, MAR 6.65, ITA 6.17,FXX 4.76, PER 3.5, ESP 3.16, VEN 3.13
47 (H1) 777777774020771	5 (1.09)	0.3	EURO-W 19.03, AMER-S 17.06, AMER-N 14.54, EURO-S 12.63, EURO-N 9.81, EURO-E 6.76, ASIA-W 3.77, AFRI-N 3.41	USA 14.24, ITA 7.72, PER 7.54, AUT 7.54, BRA 7.12, FXX 6.22, FIN 5.63, CZE 3.53, ESP 3.35, SWE 3.17
50 (H3) 777777777720771	27 (5.9)	0.68	AMER-S 26.58, EURO-W 14.88, AMER-N 14.88, EURO-S 9.78, CARI 4.93, EURO-E 4.68, EURO-N 4.63, AFRI-N 3.6,AFRI-S 3.43, AFRI-M 3.2	USA 14.85, PER 13.55, BRA 7.1, FXX 5.83, AUT 5.15,ITA 4.6, ESP 4.6, ZAF 3.43, CMR 3.15, CZE 3.1
53 (T1) 777777777760771	53 (11.57)	0.8	AMER-S 15.03, EURO-W 14.88, AMER-N 12.82, EURO-S 8.95, EURO-N 7.12, ASIA-W 6.95, AFRI-S 4.72, AFRI-E 4.42, ASIA-E 4.06, AFRI-N 3.35, EURO-E 3.1, CARI 3.07, AMER-C 3.07	USA 12.55, FXX 7.49, BRA 5.57, ITA 5.07, ZAF 4.62,PER 3.71, TUR 3.3, AUT 3.26
60 (LAM4) 777777607760731	5 (1.09)	1.12	AFRI-S 36.63, AMER-S 24.49, EURO-W 6.97, AFRI-N 6.74,AFRI-W 6.07, EURO-S 5.39, AMER-N 4.27	ZAF 36.63, BRA 14.16, FXX 4.94, USA 4.27, MAR 4.27, GMB 3.82, ITA 3.6, VEN 3.37, PER 3.15
64 (LAM6) 777777607560771	8 (1.75)	1.94	AMER-S 54.0, AMER-N 22.76, EURO-W 5.81, EURO-S 4.36	BRA 40.44, USA 22.76, GUF 5.81, PRT 3.39
91 (X3) 700036777760771	5 (1.09)	1.36	AMER-S 37.88, AMER-N 34.33, CARI 17.98, EURO-S 4.36, EURO-N 3.0	USA 32.15, PER 27.79, HTI 16.35, ESP 4.36, COL 3.27
211 (LAM3) 776137607760771	12 (2.62)	10.17	AMER-S 27.12, AMER-N 27.12, AMER-C 18.64,EURO-W 17.8, EURO-S 6.78	USA 27.12, MEX 18.64, FXX 16.95, CHL 12.71,BRA 10.17, ESP 4.24
283 (H1) 777777704020771	6 (1.31)	8.11	EURO-N 25.68, EURO-W 20.27, AMER-S 18.92, ASIA-S 10.81, AMER-N 8.11, EURO-S 5.41, EURO-E 4.05, AUST 4.05	LVA 18.92, IND 9.46, AUT 9.46, USA 8.11, CHL 8.11, PER 6.76, FXX 6.76, SWE 5.41, NLD 4.05, CZE 4.05, AUS 4.05
720 (LAM3) 776177607760371	6 (1.31)	54.55	AMER-S 100.0	CHL 54.55, ARG 36.36, PER 9.09
1277 (LAM9) 777777207760771	6 (1.31)	16.67	AMER-S 47.22, CARI 22.22, AMER-N 8.33,AMER-C 8.33, EURO-S 5.56	DOM 22.22, CHL 22.22, USA 8.33, MEX 8.33, BRA 8.33, PER 5.56, ESP 5.56, ARG 5.56
4014 (X1) 703776777760771	7 (1.53)	100	AMER-S 100.0	CHL 100.0
4015 (Unknown) 776177703770371	7 (1.53)	100	AMER-S 100.0	CHL 100.0

* Worldwide distribution is reported for regions with more than 3% of a given SITs as compared to their total number in the SITVIT2 database. The definition of macro-geographical regions and sub-regions (http://unstats.un.org/unsd/methods/m49/m49regin.htm) is according to the United Nations; Regions: AFRI (Africa), AMER (Americas), ASIA (Asia), EURO (Europe), and OCE (Oceania), subdivided in: E (Eastern), M (Middle), C (Central), N (Northern), S (Southern), SE (South-Eastern), and W (Western). Furthermore, CARIB (Caribbean) belongs to Americas, while Oceania is subdivided in 4 sub-regions, AUST (Australasia), MEL (Melanesia), MIC (Micronesia), and POLY (Polynesia). Note that in our classification scheme, Russia has been attributed a new sub-region by itself (Northern Asia) instead of including it among rest of the Eastern Europe. It reflects its geographical localization as well as due to the similarity of specific TB genotypes circulating in Russia (a majority of Beijing genotypes) with those prevalent in Central, Eastern and South-Eastern Asia.
** The 3 letter country codes are according to http://en.wikipedia.org/wiki/ISO_3166-1_alpha-3; countrywide distribution is only shown for SITs with ≥3% of a given SITs as compared to their total number in the SITVIT2 database. Note that FXX code designates Metropolitan France.

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Table 3. A comparison of the proportion of predominant SIT's found in Chile (n = 458 isolates in total, as well as distribution patterns for major cities, i.e., Santiago, Iquique, and Concepción), as compared to neighboring countries (Peru, Brazil, Paraguay, Argentina), recorded in the SITVIT2 database.

SIT (Lineage)	Major M. tuberculosis lineages in the 3 most important cities in our study (Santiago, Iquique, Concepción)						Comparison with neighboring countries available in SITVIT2 database (n = 7378 isolates)							
	Iquique (n = 34)	Santiago (n = 181)	Concepción (n = 34)	Other cities (n = 299)	This study (n = 458)	%	PERU (n = 1282)	%	BRAZIL (n = 4489)	%	PARAGUAY (n = 226)	%	ARGENTINA (n = 1381)	%
33 (LAM3)	2	23	3	16	44	9,61	56	4,37	132	2,94	2	0,88	57	4,13
37 (T3)	0	14	0	9	23	5,02	0	0,00	10	0,22	0	0,00	0	0,00
42 (LAM9)	2	11	1	29	43	9,39	73	5,69	401	8,93	40	17,70	63	4,56
47 (H1)	1	3	0	1	5	1,09	40	3,12	110	2,45	2	0,88	8	0,58
50 (H3)	1	13	0	13	27	5,90	146	11,39	239	5,32	9	3,98	29	2,10
53 (T1)	4	16	2	31	53	11,57	171	13,34	322	7,17	6	2,65	64	4,63
60 (LAM4)	0	3	1	1	5	1,09	2	0,16	58	1,29	2	0,88	2	0,14
64 (LAM6)	1	5	0	2	8	1,75	7	0,55	138	3,07	0	0,00	4	0,29
91 (X3)	3	0	0	2	5	1,09	25	1,95	4	0,09	0	0,00	3	0,22
211 (LAM3)	0	4	2	6	12	2,62	1	0,08	10	0,22	1	0,44	1	0,07
283 (H1)	0	4	0	2	6	1,31	1	0,08	1	0,02	0	0,00	2	0,14
720 (LAM3)	0	5	0	1	6	1,31	1	0,08	0	0,00	0	0,00	4	0,29
1277 (LAM9)	1	3	0	2	6	1,31	0	0,00	3	0,07	0	0,00	2	0,14
4014 (X1)	0	1	4	2	7	1,53	0	0,00	0	0,00	0	0,00	0	0,00
4015 (Unknown)	0	2	2	3	7	1,53	0	0,00	0	0,00	0	0,00	0	0,00

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as compared to others countries. Similar results have also been reported in case of SIT211 and other SITs such as SIT37, SIT64, SIT91, SIT283, SIT720, SIT1277, SIT4014 and SIT4015, which are yet to be reported or present in very low percentages. On the other hand, SIT53, SIT50 and SIT42, which are well represented in our study (11.57%, 5.90%, 9.39% respectively) have also been reported with a relative high percentage in the neighboring countries. In general, it can be concluded that last three SITs are widely distributed. All the analysis described is collated in a phylogeographical distribution map ([Fig 1A](#)) of major *M. tuberculosis* lineages in the three of the most important Chilean cities enrolled in this study (Santiago, Iquique and Concepción), as well as the neighboring countries (Brazil, Paraguay and Peru; data extracted from the SITVIT2 database).

The [Fig 1B](#) shows the spoligotyping-based MST; it is evident that LAM and T lineages compose two of the most predominant groups in our study and include most of the isolates with frequently observed patterns SIT33, SIT42, and SIT53, SIT37 respectively. Other isolates were classified as the Haarlem (SIT50 recorded as most frequent) and X (SIT4014 recorded as most frequent) lineages. More distance was observed amongst isolates that join in with the Haarlem than those integrating with LAM or T lineages.

The spoligotype analysis of common SITs (SIT42, SIT53, SIT33, SIT50 and SIT37) clearly demonstrated that they were composed of very closely related isolates and were distinguished from one another by changes in only few alleles/spacers. The spoligoforest tree generated by means of the Fruchterman-Reingold algorithm is illustrated in [Fig 2](#). It allows the visualization of all genetic associations and mutations in our strain sample. In this tree, each node represents a spoligotype colored according to the lineage involved, while any potential mutation event that might have occurred from the parental spoligotype is represented as an edge. Thus spoligoforest analysis not only allowed to identify genetic associations between different MTB strains but also helped to gain insight into their genetic diversity and evolution as follows. Briefly, it confirmed the dominance of SIT42, SIT33 (LAM) and SIT53 (T), and to a lesser extent that of SIT50 (H) and SIT37 (T). The SIT42/LAM9 cluster was the largest node evolved from SIT53/T1 and multiple spoligotypes were observed to be rising from it, e.g., SIT33/LAM3, while the second largest spoligotype pattern SIT50/H3 appeared to have derived originally from SIT53/T1. Lastly, the newly created SIT4014/X1 (found only in this study) was a relative precursor of SIT91/X3 (predominantly found in USA, Peru, and Haiti).

Discussion

In this study, we analyzed the genetic diversity of MTB isolates obtained from clinical samples encompassing 15 regions of Chile. To the best of our knowledge, this is the first study of its kind aimed at investigating the genetic diversity of MTB at the level of the entire country. Our results indicated that the LAM (40.61%), T (34.06%) and Haarlem (13.54%) genotypes were the most abundant spoligotypes of all of *M. tuberculosis* samples collected and analyzed. Together, these three lineage families accounted for 88.21% of all genotypes while all other families, namely Beijing, X, AFRI and Cameroon, accounted for only 4.81%. Interestingly, it was noted that the X lineage is poorly represented in the Santiago population (1.66%) whereas in Iquique and Concepción it accounts for nearly 11.76% each. This difference can potentially be explained as a result of: (i) immigration patterns, which have greatly increased in recent years from countries like Peru, Colombia or Ecuador, or (ii) a genetic predisposition that makes the population of these cities more susceptible to certain genotypes.

This is consistent with data available from most South American countries which claim that the most represented lineages are LAM, T and Haarlem in proportions that are similar to those reported by us; in some cases the proportions may be subject to change but invariably it is
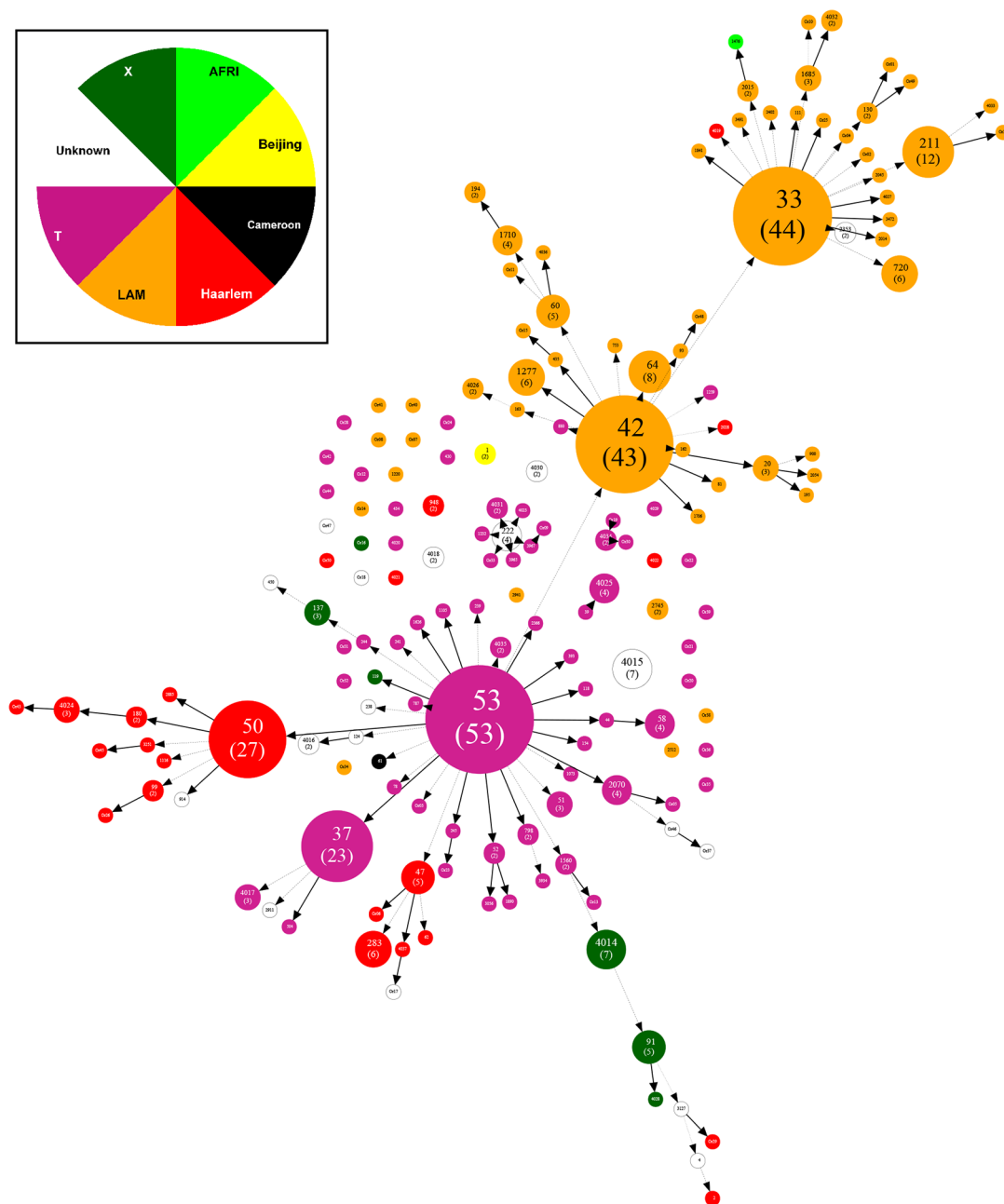
Fig 2. Spoligoforest tree based on all spoligotypes (n = 458 isolates). Spoligoforest was drawn using the Fruchterman-Reingold algorithm from the SpolTools software (http://www.emi.unsw.edu.au/spolTools)[29], and reshaped and colored using the GraphViz software (http://www.graphviz.org)[30]. Each spoligotype pattern from the study is represented by a node with area size being proportional to the total number of isolates with that specific pattern. Changes (loss of spacers) are represented by directed edges between nodes, with the arrowheads pointing to descendant spoligotypes. The heuristic used selects a single inbound edge with a maximum weight using a Zipf model. Solid black lines link patterns that are very similar, i.e., loss of one spacer only (maximum weigh being 1.0), while dashed lines represent links of weight comprised between 0.5 and 1, and dotted lines a weight less than 0.5.

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these three families that dominate epidemiologically. In **Fig 1A**, a representation of data available from three of our neighboring countries (Peru, Brazil and Paraguay) and three of the major Chilean cities included in this study are plotted. Several published reports on population

structure of MTB in South America have emphatically proven that each family is adequately represented from an epidemiological perspective [14–22]. In Brazil, Vasconcellos and collaborators demonstrated via spoligotyping that LAM is represented in 43.6%, T in 34.9% and Haarlem 18.3% of case studies. Similar results were also found in a study where isolates from patients belonging to 11 states of Brazil were analyzed. The mentioned study demonstrated that the predominant MTB lineage was LAM (46%) followed by T (18.6%), Haarlem (12.2%), X (4.7%), S (1.9%) and, lastly, the East African Indian (EAI) (0.85%) families [14]. However, in Peru and Bolivia it is reported that the most represented family is Haarlem, followed by the LAM and T families [20,33,34]. For Argentina there is comparatively less information in literature but available data clearly show that Haarlem is predominant except for MDR cases where the LAM family dominates [35,36]. In a recent work that was conducted in the border areas of Brazil, Argentina and Paraguay, a higher presence of the LAM family was reported [37]. All of the above mentioned variance can be potentially accounted for by: i) number of isolates analyzed, ii) region of sampling (restricted to a small region or spanning all country) iii) year of sampling, etc.

Fifteen SITs were noted to be the most represented (n = 5 or more isolates) in this study (**Table 2**). SIT53/T1 was the most prevalent suggesting that this particular lineage is actively circulating in Chile. This finding is corroborated by findings regarding the worldwide scene which also states that this particular SIT is widely distributed (**Table 2**) [22]. SIT33/LAM3 (9.61%) and SIT42/LAM9 (9.39%) are present in Brazil in proportions similar to reported by us but in Peru and Paraguay the presence of these two SITs is only about 3% (**Table 3**). **Fig 1B** represents the main SITs obtained in this study (labeled circle) as well as the genetic evolution based on distance and allele/spacer change between patterns. In case of the MST, it is possible to ascertain major evolutionary pathways followed by the MTB lineages by observing the similarity between each strain. Further analysis leads us to observe that the Beijing family group is very far from the Euro American lineage present in the central nodes. We also concluded that the strains belonging to the LAM lineage have a high genetic diversity and that the T and Haarlem lineages are genetically closer.

Three additional published studies have analyzed the genetic diversity of MTB in Chile [25–27]. Although all three studies were limited by the fact that they were restricted to a single region of the country; they unanimously concluded that the LAM family was the most predominant lineage in Chile. A recently published work [27] showed that almost two-thirds of the circulating strains in Santiago city could be accounted for by the prevalence of LAM and T genotypes. The most frequent SITs that were seen to cluster spoligotypes were SIT33/LAM3 (10.7%), SIT53/T1 (8.7%), SIT50/H3 (7.8%) and SIT37/T3 (6.8%). The distribution pattern in the above mentioned study goes in parallel with data obtained in our study. Last but not least, our study further corroborated the high presence of SIT37/T3 (n = 23) in the Chilean population, a pattern that was usually found in Eastern Africa in the international database.

Currently, the National Control Program of Human Tuberculosis in Chile [13] has managed to position our country among nations that have managed to control this disease. The incidence of TB in Chile, when compared to other South American countries, is low at only 12.5 per 100,000. During the 2009–2013 period, the incidence value for Brazil was of 46, 44 in Paraguay and 124 in Peru (per 100,000). The situation in Peru, a neighboring country with which we share the border, attracts our attention because the differences in incidence rates are so overwhelming. This could be a possible effect of immigration and public health policies. As with other airborne diseases, the spread of MTB is facilitated by high population densities and crowded indoor environments that optimize the transmission of the pathogen. Other host-related factors that are implicated in increasing the chances of infection are: (i) immune suppression, (ii) smoking, (iii) poor nutrition, (iv) diabetes, and (v) respiratory comorbidities. All

these factors can also result in an increase in the risk of transitioning from latent to active MTB [38]. This is a very important issue in the developing world where overcrowding, malnutrition and HIV infection contribute to a high burden of the disease.

Drug resistant tests conducted as part of our study revealed that 87.7% (n = 402) of the isolates were pan-susceptible, 27.8% (n = 44) were resistant to any drugs, and 1.31% (n = 6) were MDR; for 1.31% (n = 6 isolates) the data could not be obtained. Three of the six strains that presented with multi drug resistance belonged to SIT53/T1. Conversely, LAM (which is the most prevalent lineage in our study), was apparently overrepresented among MDR cases in French departments of the Americas–based on data collection over an extended period of time [39], as well as in Peru [40]. Lastly, half of the SIT4015 isolates (of a lineage with unknown signature) showed drug resistance. This pattern should be carefully surveyed in coming years to see if its emergence is not linked to specific host factors since different ethnic groups may have varying susceptibilities to various MTB strains [41]. Indeed, both SIT4014/X1 (n = 7 isolates) and SIT4015 (Unknown signature; n = 7 isolates) have only been found in Chile so far. Considering that most of the samples belonging to these SITs were collected in the city of Concepcion and its vicinity, one should take into account associated factors such as susceptibility genetics of the host when studying emerging MTB clones. A similar case can be made for SIT720/LAM3, which is so far restricted to South America. In summary, our results underline the importance of tracking circulating and emerging MTB clones in conjunction with development of phylogenetical databases in order to maintain proper vigilance. These measures are a powerful way to safeguard against possible future outbreaks.

Although Spoligotyping can contribute to identifying outbreaks and tracking the spread of disease, it has been known to overestimate clustering of isolates. Therefore, it is our belief that a more polymorphic technique such as MIRU-VNTR technique would be able to impart greater in-depth information that will help improve our knowledge of current epidemiological data in Chile.

To conclude, in this study, spanning 15 regions of Chile, we have shown that the LAM, T, and Haarlem lineages together represent 88.2% of the isolates. This corroborates that the data obtained from the neighboring countries also show that the Euro-American lineages have a clear epidemiological superiority. The exclusive emergence of SIT4014 and SIT4015 indicates that conditions specific to Chile, along with the unique genetic makeup of the Chilean population, might have allowed for a possible co-evolution of certain genotypes leading to their relative success to cause disease.

Supporting Information

S1 Fig. Geographic distribution of isolates collected within of 15 regions of Chile (n = 458 strains).
(TIF)

S1 Table. Detailed demographic and genotyping information on *M. tuberculosis* isolates from Chile (n = 458 strains).
(PDF)

Author Contributions

Conceived and designed the experiments: JL FA JF.

Performed the experiments: JF TL JT FA JCH CA.

Analyzed the data: JL LA JF DC NR.

Contributed reagents/materials/analysis tools: JL JCH JF FA TL DC NR CA.

**Wrote the paper:** JT LA JF DC NR.

References

1. "Global Tuberculosis Report 2013". WHO report 2013: Available: http://www.who.int/tb/publications/global_report/en/. Accessed 10 March 2015.

2. Barnes PF, Cave MD. Molecular epidemiology of tuberculosis. N Engl J Med. 2003 Sep 18; 349 (12):1149–56. Review. PMID: 13679530.

3. Couvin D, Rastogi N. The establishment of databases on circulating genotypes of Mycobacterium tuberculosis complex and web tools for an effective response to better monitor, understand and control the tuberculosis epidemic worldwide. EuroReference-Journal of Reference, 2014. 12: p. 36–48. Available: https://pro.anses.fr/euroreference/Documents/ER12-RESEAUX-MycobacteriumEN.pdf

4. Alland D, Kalkut GE, Moss AR, McAdam RA, Hahn JA, Bosworth W, et al. Transmission of tuberculosis in New York City. An analysis by DNA fingerprinting and conventional epidemiologic methods. N Engl J Med. 1994 Jun 16; 330(24):1710–6. PMID: 7993412.

5. van Embden JD, Cave MD, Crawford JT, Dale JW, Eisenach KD, Gicquel B et al. Strain identification of Mycobacterium tuberculosis by DNA fingerprinting: recommendations for a standardized methodology. J Clin Microbiol. 1993 Feb; 31(2):406–9. PMID: 8381814

6. Cronin WA, Golub JE, Magder LS, Baruch NG, Lathan MJ, Mukasa LN, et al. Epidemiologic usefulness of spoligotyping for secondary typing of Mycobacterium tuberculosis isolates with low copy numbers of IS6110. J Clin Microbiol. 2001 Oct; 39(10):3709–11. PMID: 11574598

7. Supply P, Lesjean S, Savine E, Kremer K, van Soolingen D, Locht C. Automated high-throughput genotyping for study of global epidemiology of Mycobacterium tuberculosis based on mycobacterial interspersed repetitive units. J Clin Microbiol. 2001 Oct; 39(10):3563–71. PMID: 11574573

8. Kamerbeek J, Schouls L, Kolk A, van Agterveld M, van Soolingen D, Kuijper S, et al. Simultaneous detection and strain differentiation of Mycobacterium tuberculosis for diagnosis and epidemiology. J Clin Microbiol. 1997 Apr; 35(4):907–14. PMID: 9157152

9. Kremer K, Arnold C, Cataldi A, Gutiérrez MC, Haas WH, Panaiotov S, et al. Discriminatory power and reproducibility of novel DNA typing methods for Mycobacterium tuberculosis complex strains. J Clin Microbiol. 2005 Nov; 43(11):5628–38. PMID: 16272496

10. Supply P, Allix C, Lesjean S, Cardoso-Oelemann M, Rüsch-Gerdes S, Willery E, et al. Proposal for standardization of optimized mycobacterial interspersed repetitive unit-variable-number tandem repeat typing of Mycobacterium tuberculosis. J Clin Microbiol. 2006 Dec; 44(12):4498–510. Epub 2006 Sep 27. PMID: 17005759

11. García de Viedma D, Mokrousov I, Rastogi N. Innovations in the molecular epidemiology of tuberculosis. Enferm Infecc Microbiol Clin. 2011 Mar; 29 Suppl 1:8–13 doi: 10.1016/S0213-005X(11)70012-X PMID: 21420561

12. Tuberculosis in the Americas Regional Report 2014: Epidemiology, Control, and Financing. Available: http://www.paho.org/hq/index.php?option=com_topics&view=readall&cid=5504&Itemid=40242&lang=es. Accessed 14 September 2015.

13. "Tuberculosis Informe de Situación Chile: 2013". September 2014, Ministerio de Salud de Chile: Available: http://web.minsal.cl/sites/default/files/files/TUBERCULOSIS-INFORME%202013.pdf. Accessed 10 September 2015.

14. Gomes HM, Elias AR, Oelemann MA, Pereira MA, Montes FF, Marsico AG, et al. Spoligotypes of Mycobacterium tuberculosis complex isolates from patients residents of 11 states of Brazil. Infect Genet Evol. 2012 Jun; 12(4):649–56. doi: 10.1016/j.meegid.2011.08.027 PMID: 21907830.

15. Abadía E, Sequera M, Ortega D, Méndez MV, Escalona A, Da Mata O, et al. Mycobacterium tuberculosis ecology in Venezuela: epidemiologic correlates of common spoligotypes and a large clonal cluster defined by MIRU-VNTR-24. BMC Infect Dis. 2009 Aug 6; 9:122. doi: 10.1186/1471-2334-9-122 PMID: 19660112

16. Candia N, Lopez B, Zozio T, Carrivale M, Diaz C, Russomando G, et al. First insight into Mycobacterium tuberculosis genetic diversity in Paraguay. BMC Microbiol. 2007 Aug 8; 7:75. PMID: 17686181

17. Cerezo I, Jiménez Y, Hernandez J, Zozio T, Murcia MI, Rastogi N. A first insight on the population structure of Mycobacterium tuberculosis complex as studied by spoligotyping and MIRU-VNTRs in Bogotá, Colombia. Infect Genet Evol. 2012 Jun; 12(4):657–63. doi: 10.1016/j.meegid.2011.07.006 PMID: 21784173.

18. Dalla Costa ER, Lazzarini LC, Perizzolo PF, Díaz CA, Spies FS, Costa LL, et al. Mycobacterium tuberculosis of the RDRio genotype is the predominant cause of tuberculosis and associated with multidrug

resistance in Porto Alegre City, South Brazil. J Clin Microbiol. 2013 Apr; 51(4):1071–7. doi: 10.1128/JCM.01511-12 PMID: 23325819

19. Realpe T, Correa N, Rozo JC, Ferro BE, Gomez V, Zapata E, et al. Population structure among myco-bacterium tuberculosis isolates from pulmonary tuberculosis patients in Colombia. PLoS One. 2014 Apr 18; 9(4):e93848. doi: 10.1371/journal.pone.0093848. Erratum in: PLoS One. 2014;9(9):e109456. PMID: 24747767

20. Taype CA, Agapito JC, Accinelli RA, Espinoza JR, Godreuil S, Goodman SJ, et al. Genetic diversity, population structure and drug resistance of Mycobacterium tuberculosis in Peru. Infect Genet Evol. 2012 Apr; 12(3):577–85. doi: 10.1016/j.meegid.2012.02.002 PMID: 22342744

21. Alvarez N, Haft D, Hurtado UA, Robledo J, Rouzaud F. Whole-Genome Sequence of a Beijing Exten-sively Drug-Resistant Mycobacterium tuberculosis Clinical Isolate from Buenaventura, Colombia. Genome Announc. 2016 Jan 14; 4(1). pii: e01549-15. doi: 10.1128/genomeA.01549-15 PMID: 26769935; PubMed Central PMCID:PMC4714117.

22. Vasconcellos SE, Acosta CC, Gomes LL, Conceição EC, Lima KV, de Araujo MI, et al. Strain classifica-tion of Mycobacterium tuberculosis isolates in Brazil based on genotypes obtained by spoligotyping, mycobacterial interspersed repetitive unit typing and the presence of large sequence and single nucleo-tide polymorphism. PLoS One. 2014 Oct 14; 9(10):e107747. doi: 10.1371/journal.pone.0107747 PMID: 25314118

23. Demay C, Liens B, Burguière T, Hill V, Couvin D, Millet J, et al. SITVITWEB—a publicly available inter-national multimarker database for studying Mycobacterium tuberculosis genetic diversity and molecular epidemiology. Infect Genet Evol. 2012 Jun; 12(4):755–66. doi: 10.1016/j.meegid.2012.02.004 PMID: 22365971.

24. Shabbeer A, Ozcaglar C, Yener B, Bennett KP (2012) Web tools for molecular epidemiology of tubercu-losis. Infect Genet Evol; 12(4): 767–81. doi: 10.1016/j.meegid.2011.08.019 PMID: 21903179

25. Mancilla EM, Martínez HA, Palavecino BC, Rehren SG, Lucero LP, León RG, Zárraga O AM. [Genetic variants of Mycobacterium tuberculosis isolated from patients of the Xth Region of Chile]. Rev Chilena Infectol. 2006 Sep; 23(3):220–5. Spanish. PMID: 16896494.

26. Meza P, Balcells ME, Miranda C, Cifuentes M, Wozniak A, García P. [Presence of Bejing genotype among Mycobacterium tuberculosis strains in two centres of the Region Metropolitana of Chile]. Rev Chilena Infectol. 2014 Feb; 31(1):21–7. doi: 10.4067/S0716-10182014000100003 Spanish. PMID: 24740770.

27. Balcells ME, García P, Meza P, Peña C, Cifuentes M, Couvin D, et al. A first insight on the population structure of Mycobacterium tuberculosis complex as studied by spoligotyping and MIRU-VNTRs in Santiago, Chile. PLoS One. 2015 Feb 11; 10(2):e0118007. doi: 10.1371/journal.pone.0118007 PMID: 25671320

28. Couvin D, Rastogi N. Tuberculosis—A global emergency: Tools and methods to monitor, understand, and control the epidemic with specific example of the Beijing lineage. Tuberculosis (Edinb). 2015 Jun; 95 Suppl 1:S177–89. doi: 10.1016/j.tube.2015.02.023 Epub 2015 Feb 13.

29. Laszlo A, Rahman M, Raviglione M, Bustreo F. Quality assurance programme for drug susceptibility testing of Mycobacterium tuberculosis in the WHO/IUATLD Supranational Laboratory Network: first round of proficiency testing. Int J Tuberc Lung Dis. 1997 Jun; 1(3):231–8. PMID: 9432369.

30. Araya P, Velasco M, Tognarelli J, Arias F, Leiva T, Sccapatticio A, et al. [Detection of genes associated with drug resistance in Mycobacterium tuberculosis strains isolated in Chile]. Rev Med Chil. 2011 Apr; 139(4):467–73. /S0034-98872011000400008. Epub 2011 Aug 25. Spanish. PMID: 21879185.

31. Reyes JF, Francis AR, Tanaka MM. Models of deletion for visualizing bacterial variation: an application to tuberculosis spoligotypes. BMC Bioinformatics. 2008 Nov 27; 9:496. doi: 10.1186/1471-2105-9-496 PMID: 19036166

32. Ellson J., et al., Graphviz and dynagraph–static and dynamic graph drawing tools. In: Graph Drawing Software. 2004. Jünger M. Mutzel P. Editors. Springer-Verlag. p. 127–148 doi: 10.1007/978-3-642-18638-7

33. Sheen P, Couvin D, Grandjean L, Zimic M, Dominguez M, Luna G, et al. Genetic diversity of Mycobac-terium tuberculosis in Peru and exploration of phylogenetic associations with drug resistance. PLoS One. 2013 Jun 24; 8(6):e65873. doi: 10.1371/journal.pone.0065873 PMID: 23826083

34. Monteserin J, Camacho M, Barrera L, Palomino JC, Ritacco V, Martin A. Genotypes of Mycobacterium tuberculosis in patients at risk of drug resistance in Bolivia. Infect Genet Evol. 2013 Jul; 17:195–201. doi: 10.1016/j.meegid.2013.04.010 PMID: 23603419.

35. Gonzalo X, Ambroggi M, Cordova E, Brown T, Poggi S, Drobniewski F. Molecular Epidemiology of *Mycobacterium tuberculosis*, Buenos Aires, Argentina. Emerging Infectious Diseases. 2011; 17 (3):528–531. doi: 10.3201/eid1703100394 PMID: 21392451

36. Ritacco V, López B, Ambroggi M, Palmero D, Salvadores B, Gravina E, et al. HIV infection and geographically bound transmission of drug-resistant tuberculosis, Argentina. Emerg Infect Dis. 2012 Nov; 18(11):1802–10. doi: 10.3201/eid1811.120126 PMID: 23092584

37. Machado LN, Marcondes NR, Leite CQ, Santos AC, Pavan FR, Baldin VP, et al. First baseline of circulating genotypic lineages of Mycobacterium tuberculosis in patients from the Brazilian borders with Argentina and Paraguay. PLoS One. 2014 Sep 9; 9(9):e107106. doi: 10.1371/journal.pone.0107106 PMID: 25202909

38. Zumla A, Nahid P, Cole ST. Advances in the development of new tuberculosis drugs and treatment regimens. Nat Rev Drug Discov. 2013 May; 12(5):388–404. doi: 10.1038/nrd4001 Review. PMID: 23629506

39. Millet J, Streit E, Berchel M, Bomer AG, Schuster F, Paasch D, et al. A systematic follow-up of Mycobacterium tuberculosis drug-resistance and associated genotypic lineages in the French Departments of the Americas over a seventeen-year period. Biomed Res Int. 2014; 2014:689852. doi: 10.1155/2014/689852 Epub 2014 Mar 13. PMID: 24738068

40. Grandjean L, Iwamoto T, Lithgow A, Gilman RH, Arikawa K, Nakanishi N, et al. The Association between Mycobacterium Tuberculosis Genotype and Drug Resistance in Peru. PLoS One. 2015; 10 (5):e0126271. doi: 10.1371/journal.pone.0126271 PMID: 25984723

41. Gagneux S, Small PM. Global phylogeography of *Mycobacterium tuberculosis* and implications for tuberculosis product development. Lancet Infect Dis 2007; 7(5):328–337. PMID: 17448936

	Regions of Chile	City	N° Samples
	XV	Arica	14
	I	Iquique	34
	II	Antofagasta	11
	II	Calama	1
	III	Vallenar	1
	III	Copiapo	5
	IV	Ovalle	6
	V	Coquimbo	11
	V	Valparaíso	29
	V	Viña del Mar	2
	XIII	Santiago	181
	VI	Rancagua	20
	VII	Talca	12
	VIII	Concepción	34
	VIII	Los Angeles	16
	VIII	Talcahuano	12
	IX	Osorno	15
	IX	Temuco	18
	XIV	Valdivia	6
	X	Castro	9
	X	Pto. Montt	12
	XI	Coyhaique	2
	XII	Pta. Arenas	7
		TOTAL	458

Supplemental Table S1: Detailed demographic and genotyping information on *M. tuberculosis* isolates from Chile (n=458 strains).

Strain Number	Year	Sex	Isolation city	Spoligotype Description	Octal code	SIT*	Lineage	Drug resistance**
2035-2011-S-1414	2011	Male	Iquique		000000000003771	1	Beijing	Pansusceptible
406-2012-S-288	2012	Male	Santiago		000000000003771	1	Beijing	Pansusceptible
283-2012-S-215	2012	Male	Valparaiso		000000004020771	2	H2	Pansusceptible
2060-2011-S-1435	2011	Male	Coquimbo		000000007760771	4	Unknown	Pansusceptible
1758-2011-S-1173	2011	Female	Rancagua		677777607760771	20	LAM1	Pansusceptible
1831-2011-S-1267	2011	Male	Santiago		677777607760771	20	LAM1	R (SM)
829-2011-S-505	2011	Female	Puerto Montt		677777607760771	20	LAM1	Pansusceptible
1000-2012-S-632	2012	Male	Los Angeles		776177607760771	33	LAM3	Pansusceptible
1013-2011-S-629	2011	Female	Santiago		776177607760771	33	LAM3	Pansusceptible
1035-2012-S-655	2012	Male	Santiago		776177607760771	33	LAM3	Pansusceptible
1097-2011-S-687	2011	Female	Talcahuano		776177607760771	33	LAM3	Pansusceptible
1101-2011-S-690	2011	Male	Santiago		776177607760771	33	LAM3	R (SM)
1139-2011-S-718	2011	Female	Santiago		776177607760771	33	LAM3	Pansusceptible
1187-2011-S-751	2011	Male	Santiago		776177607760771	33	LAM3	Pansusceptible
1208-2011-S-763	2011	Female	Santiago		776177607760771	33	LAM3	Pansusceptible
1231-2011-S-781	2011	Male	Santiago		776177607760771	33	LAM3	Pansusceptible
1263-2011-S-796	2011	Female	Iquique		776177607760771	33	LAM3	R (SM)
1307-2011-S-830	2011	Male	Santiago		776177607760771	33	LAM3	Pansusceptible
1319-2011-S-833	2011	Female	Los Angeles		776177607760771	33	LAM3	Pansusceptible
1354-2011-S-857	2011	Male	Vallenar		776177607760771	33	LAM3	Pansusceptible
1370-2011-S-870	2011	Male	Santiago		776177607760771	33	LAM3	Pansusceptible
1413-2011-S-903	2011	Female	Santiago		776177607760771	33	LAM3	Pansusceptible
1460-2011-S-942	2011	Male	Antofagasta		776177607760771	33	LAM3	Pansusceptible
1474-2011-S-951	2011	Male	Santiago		776177607760771	33	LAM3	Pansusceptible
1475-2011-S-952	2011	Male	Santiago		776177607760771	33	LAM3	R (SM)
1744-2011-S-1159	2011	Male	Rancagua		776177607760771	33	LAM3	Pansusceptible
1767-2011-S-1181	2011	Male	Santiago		776177607760771	33	LAM3	Pansusceptible
1779-2011-S-1189	2011	Female	Santiago		776177607760771	33	LAM3	Pansusceptible
1783-2011-S-1192	2011	Male	Los Angeles		776177607760771	33	LAM3	Pansusceptible
1828-2011-S-1264	2011	Male	Santiago		776177607760771	33	LAM3	Pansusceptible
1840-2011-S-1275	2011	Male	Castro		776177607760771	33	LAM3	Pansusceptible
1857-2011-S-1285	2011	Male	Santiago		776177607760771	33	LAM3	R (PZA)
1961-2011-S-1365	2011	Female	Osorno		776177607760771	33	LAM3	Pansusceptible
2020-2011-S-1404	2011	Male	Concepcion		776177607760771	33	LAM3	Pansusceptible
259-2012-S-201	2012	Male	Santiago		776177607760771	33	LAM3	Pansusceptible
304-2012-S-231	2012	Male	Concepcion		776177607760771	33	LAM3	Pansusceptible
319-2012-S-238	2012	Male	Coihaique		776177607760771	33	LAM3	Pansusceptible
419-2012-S-294	2012	Male	Los Angeles		776177607760771	33	LAM3	Pansusceptible
714-2012-S-478	2012	Female	Ovalle		776177607760771	33	LAM3	Pansusceptible
736-2012-S-489	2012	Female	Los Angeles		776177607760771	33	LAM3	Pansusceptible
743-2012-S-492	2012	Female	Santiago		776177607760771	33	LAM3	R (SM)
762-2012-S-505	2012	Male	Punta Arenas		776177607760771	33	LAM3	Pansusceptible
820-2012-S-535	2012	Male	Talca		776177607760771	33	LAM3	Pansusceptible
822-2012-S-537	2012	Male	Santiago		776177607760771	33	LAM3	Pansusceptible
830-2011-S-506	2011	Male	Puerto Montt		776177607760771	33	LAM3	Pansusceptible
832-2011-S-507	2011	Male	Santiago		776177607760771	33	LAM3	Pansusceptible
875-2011-S-532	2011	Male	Santiago		776177607760771	33	LAM3	Pansusceptible
886-2012-S-569	2012	Male	Santiago		776177607760771	33	LAM3	Pansusceptible
948-2011-S-581	2011	Male	Concepcion		776177607760771	33	LAM3	Pansusceptible
955-2011-S-588	2011	Male	Santiago		776177607760771	33	LAM3	Pansusceptible
975-2011-S-599	2011	Male	Iquique		776177607760771	33	LAM3	R (SM)
1082-2011-S-676	2011	Male	Temuco		777737777760771	37	T3	Pansusceptible
1183-2012-S-745	2012	Female	Santiago		777737777760771	37	T3	Pansusceptible
1190-2012-S-751	2012	Male	Santiago		777737777760771	37	T3	Pansusceptible
1280-2011-S-807	2011	Male	Santiago		777737777760771	37	T3	Pansusceptible
1367-2011-S-867	2011	Male	Temuco		777737777760771	37	T3	Pansusceptible
1827-2011-S-1263	2011	Male	Santiago		777737777760771	37	T3	Pansusceptible
1844-2011-S-1279	2011	Male	Santiago		777737777760771	37	T3	Pansusceptible
1924-2011-S-1337	2011	Male	Santiago		777737777760771	37	T3	Pansusceptible
1926-2011-S-1338	2011	Male	Santiago		777737777760771	37	T3	Pansusceptible
1985-2011-S-1381	2011	Male	Antofagasta		777737777760771	37	T3	Pansusceptible
2008-2011-S-1397	2011	Female	Valparaiso		777737777760771	37	T3	Pansusceptible
272-2012-S-211	2012	Female	Puerto Montt		777737777760771	37	T3	Pansusceptible
458-2012-S-319	2012	Male	Santiago		777737777760771	37	T3	Pansusceptible
513-2012-S-352	2012	Female	Santiago		777737777760771	37	T3	Pansusceptible
602-2012-S-410	2012	Male	Valparaiso		777737777760771	37	T3	Pansusceptible
677-2012-S-450	2012	Male	Santiago		777737777760771	37	T3	Pansusceptible
916-2011-S-559	2011	Male	Santiago		777737777760771	37	T3	Pansusceptible
939-2011-S-575	2011	Female	Arica		777737777760771	37	T3	Pansusceptible
942-2011-S-577	2011	Female	Arica		777737777760771	37	T3	Pansusceptible
952-2011-S-585	2011	Male	Santiago		777737777760771	37	T3	Pansusceptible
953-2011-S-586	2011	Male	Santiago		777737777760771	37	T3	Pansusceptible
972-2011-S-597	2011	Male	Santiago		777737777760771	37	T3	Pansusceptible
993-2012-S-629	2012	Male	Rancagua		777737777760771	37	T3	Pansusceptible
1233-2011-S-783	2011	Male	Santiago		777777347760471	39	T4-CEU1	Pansusceptible
101-2012-S-89	2012	Male	Rancagua		777777607760771	42	LAM9	Pansusceptible
1078-2011-S-672	2011	Female	Temuco		777777607760771	42	LAM9	Pansusceptible
1112-2011-S-699	2011	Female	Puerto Montt		777777607760771	42	LAM9	Pansusceptible
1141-2011-S-719	2011	Female	Santiago		777777607760771	42	LAM9	Pansusceptible
1201-2011-S-760	2011	Male	Puerto Montt		777777607760771	42	LAM9	Pansusceptible
1240-2011-S-786	2011	Male	Valparaiso		777777607760771	42	LAM9	Pansusceptible
1264-2011-S-797	2011	Male	Iquique		777777607760771	42	LAM9	Pansusceptible
1283-2011-S-810	2011	Male	Concepcion		777777607760771	42	LAM9	Pansusceptible
1309-2011-S-831	2011	Female	Santiago		777777607760771	42	LAM9	Pansusceptible
1321-2011-S-835	2011	Female	Viña del Mar		777777607760771	42	LAM9	R (PZA)
1346-2011-S-855	2011	Female	Iquique		777777607760771	42	LAM9	Pansusceptible
136-2012-S-118	2012	Female	Santiago		777777607760771	42	LAM9	Pansusceptible
1365-2011-S-865	2011	Male	Valdivia		777777607760771	42	LAM9	Pansusceptible
1366-2011-S-866	2011	Female	Temuco		777777607760771	42	LAM9	Pansusceptible
1372-2011-S-872	2011	Male	Santiago		777777607760771	42	LAM9	Pansusceptible
1420-2011-S-910	2011	Male	Santiago		777777607760771	42	LAM9	R (PZA)
1461-2011-S-943	2011	Male	Temuco		777777607760771	42	LAM9	Pansusceptible
1496-2011-S-970	2011	Male	Valparaiso		777777607760771	42	LAM9	Pansusceptible
1497-2011-S-971	2011	Male	Valparaiso		777777607760771	42	LAM9	Pansusceptible
156-2012-S-128	2012	Male	Talcahuano		777777607760771	42	LAM9	R (SM)
1642-2011-S-1085	2011	Male	Antofagasta		777777607760771	42	LAM9	Pansusceptible
1733-2011-S-1152	2011	Male	Punta Arenas		777777607760771	42	LAM9	Pansusceptible
1750-2011-S-1164	2011	Male	Rancagua		777777607760771	42	LAM9	R (PZA)
1853-2011-S-1282	2011	Male	Arica		777777607760771	42	LAM9	Pansusceptible
1865-2011-S-1290	2011	Female	Rancagua		777777607760771	42	LAM9	Pansusceptible

ID	Year	Sex	City	Spoligotype	Octal	SIT	Family	Resistance
1866-2011-S-1291	2011	Female	Rancagua	[pattern]	777777607760771	42	LAM9	Pansusceptible
1887-2011-S-1307	2011	Male	Valparaiso	[pattern]	777777607760771	42	LAM9	Pansusceptible
2028-2011-S-1410	2011	Male	Santiago	[pattern]	777777607760771	42	LAM9	Pansusceptible
418-2012-S-293	2012	Male	Los Angeles	[pattern]	777777607760771	42	LAM9	Pansusceptible
544-2012-S-366	2012	Male	Puerto Montt	[pattern]	777777607760771	42	LAM9	Pansusceptible
563-2012-S-382	2012	Male	Santiago	[pattern]	777777607760771	42	LAM9	Pansusceptible
547-2012-S-372	2012	Male	Ovalle	[pattern]	777777607760771	42	LAM9	Pansusceptible
700-2012-S-464	2012	Male	Antofagasta	[pattern]	777777607760771	42	LAM9	Pansusceptible
760-2012-S-503	2012	Male	Talca	[pattern]	777777607760771	42	LAM9	R (INH)
761-2012-S-504	2012	Female	Talca	[pattern]	777777607760771	42	LAM9	Pansusceptible
789-2011-S-489	2012	Female	Santiago	[pattern]	777777607760771	42	LAM9	Pansusceptible
827-2011-S-504	2011	Male	Temuco	[pattern]	777777607760771	42	LAM9	Pansusceptible
885-2011-S-538	2011	Male	Valdivia	[pattern]	777777607760771	42	LAM9	Pansusceptible
910-2011-S-553	2011	Female	Santiago	[pattern]	777777607760771	42	LAM9	Pansusceptible
912-2011-S-555	2011	Male	Santiago	[pattern]	777777607760771	42	LAM9	Pansusceptible
921-2011-S-565	2011	Female	Castro	[pattern]	777777607760771	42	LAM9	R (INH+SM)
954-2011-S-587	2011	Male	Santiago	[pattern]	777777607760771	42	LAM9	Pansusceptible
99-2012-S-88	2012	Male	Talca	[pattern]	777777607760771	42	LAM9	Pansusceptible
1405-2011-S-897	2011	Female	Coquimbo	[pattern]	777777757760771	44	T5	NA
1060-2011-S-661	2011	Female	Santiago	[pattern]	777777774020771	47	H1	Pansusceptible
1123-2011-S-708	2011	Male	Valparaiso	[pattern]	777777774020771	47	H1	Pansusceptible
1728-2011-S-1151	2011	Male	Santiago	[pattern]	777777774020771	47	H1	R (INH)
246-2012-S-193	2012	Male	Santiago	[pattern]	777777774020771	47	H1	Pansusceptible
980-2011-S-604	2011	Male	Iquique	[pattern]	777777774020771	47	H1	R (PZA)
1051-2011-S-657	2011	Male	Arica	[pattern]	777777777720771	50	H3	R (INH+SM)
1176-2011-S-744	2011	Female	Temuco	[pattern]	777777777720771	50	H3	Pansusceptible
1221-2011-S-774	2011	Male	Coquimbo	[pattern]	777777777720771	50	H3	Pansusceptible
1260-2011-S-793	2011	Female	Santiago	[pattern]	777777777720771	50	H3	Pansusceptible
1261-2011-S-794	2011	Female	Santiago	[pattern]	777777777720771	50	H3	Pansusceptible
1265-2011-S-798	2011	Male	Iquique	[pattern]	777777777720771	50	H3	Pansusceptible
1281-2011-S-808	2011	Male	Santiago	[pattern]	777777777720771	50	H3	Pansusceptible
1326-2011-S-838	2011	Male	Santiago	[pattern]	777777777720771	50	H3	MDR (INH+RF)
1359-2011-S-861	2011	Male	Santiago	[pattern]	777777777720771	50	H3	Pansusceptible
139-2012-S-121	2012	Male	Santiago	[pattern]	777777777720771	50	H3	R (INH)
1397-2011-S-889	2011	Male	Santiago	[pattern]	777777777720771	50	H3	Pansusceptible
1399-2011-S-891	2011	Male	Coquimbo	[pattern]	777777777720771	50	H3	Pansusceptible
1438-2011-S-923	2011	Male	Santiago	[pattern]	777777777720771	50	H3	Pansusceptible
1457-2011-S-939	2011	Male	Arica	[pattern]	777777777720771	50	H3	Pansusceptible
1746-2011-S-1161	2011	Male	Rancagua	[pattern]	777777777720771	50	H3	Pansusceptible
1942-2011-S-1351	2011	Female	Santiago	[pattern]	777777777720771	50	H3	Pansusceptible
1948-2011-S-1353	2011	Female	Copiapo	[pattern]	777777777720771	50	H3	Pansusceptible
496-2012-S-341	2012	Male	Santiago	[pattern]	777777777720771	50	H3	Pansusceptible
702-2012-S-466	2012	Male	Antofagasta	[pattern]	777777777720771	50	H3	Pansusceptible
708-2012-S-472	2012	Female	Rancagua	[pattern]	777777777720771	50	H3	Pansusceptible
745-2012-S-494	2012	Male	Santiago	[pattern]	777777777720771	50	H3	Pansusceptible
836-2011-S-510	2011	Male	Arica	[pattern]	777777777720771	50	H3	Pansusceptible
845-2011-S-514	2011	Male	Valparaiso	[pattern]	777777777720771	50	H3	Pansusceptible
860-2011-S-526	2011	Male	Santiago	[pattern]	777777777720771	50	H3	Pansusceptible
878-2012-S-567	2012	Female	Rancagua	[pattern]	777777777720771	50	H3	R (SM)
968-2011-S-593	2011	Male	Santiago	[pattern]	777777777720771	50	H3	R (INH)
98-2012-S-87	2012	Female	Viña del Mar	[pattern]	777777777720771	50	H3	Pansusceptible
1009-2011-S-625	2011	Male	Talcahuano	[pattern]	777777777760700	51	T1	Pansusceptible
135-2012-S-117	2012	Male	Santiago	[pattern]	777777777760700	51	T1	Pansusceptible
1863-2011-S-1288	2011	Female	Santiago	[pattern]	777777777760700	51	T1	Pansusceptible
1378-2011-S-878	2011	Male	Concepcion	[pattern]	777777777760731	52	T2	Pansusceptible
263-2012-S-204	2012	Female	Santiago	[pattern]	777777777760731	52	T2	Pansusceptible
1041-2012-S-660	2012	Male	Los Angeles	[pattern]	777777777760771	53	T1	Pansusceptible
1048-2011-S-654	2011	Male	Punta Arenas	[pattern]	777777777760771	53	T1	Pansusceptible
1130-2011-S-713	2011	Male	Santiago	[pattern]	777777777760771	53	T1	Pansusceptible
1149-2011-S-725	2011	Female	Osorno	[pattern]	777777777760771	53	T1	Pansusceptible
1170-2011-S-739	2011	Female	Santiago	[pattern]	777777777760771	53	T1	MDR (INH+RIF), SM
1173-2011-S-742	2011	Male	Valdivia	[pattern]	777777777760771	53	T1	Pansusceptible
1200-2011-S-759	2011	Female	Puerto Montt	[pattern]	777777777760771	53	T1	Pansusceptible
1228-2011-S-780	2011	Male	Santiago	[pattern]	777777777760771	53	T1	Pansusceptible
1299-2011-S-827	2011	Male	Temuco	[pattern]	777777777760771	53	T1	Pansusceptible
1325-2011-S-837	2011	Male	Talcahuano	[pattern]	777777777760771	53	T1	Pansusceptible
1328-2011-S-839	2011	Male	Antofagasta	[pattern]	777777777760771	53	T1	Pansusceptible
1358-2011-S-860	2011	Male	Los Angeles	[pattern]	777777777760771	53	T1	Pansusceptible
1361-2011-S-863	2011	Male	Valdivia	[pattern]	777777777760771	53	T1	Pansusceptible
1374-2011-S-874	2011	Female	Santiago	[pattern]	777777777760771	53	T1	Pansusceptible
1442-2011-S-927	2011	Female	Valparaiso	[pattern]	777777777760771	53	T1	Pansusceptible
1453-2011-S-936	2011	Female	Iquique	[pattern]	777777777760771	53	T1	Pansusceptible
1484-2011-S-962	2011	Female	Arica	[pattern]	777777777760771	53	T1	Pansusceptible
1588-2011-S-1041	2011	Female	Puerto Montt	[pattern]	777777777760771	53	T1	R (PZA)
1615-2011-S-1066	2011	Female	Santiago	[pattern]	777777777760771	53	T1	Pansusceptible
1628-2011-S-1078	2011	Female	Santiago	[pattern]	777777777760771	53	T1	Pansusceptible
1639-2011-S-1083	2011	Female	Osorno	[pattern]	777777777760771	53	T1	R (PZA)
1737-2011-S-1154	2011	Male	Rancagua	[pattern]	777777777760771	53	T1	Pansusceptible
1742-2011-S-1157	2011	Male	Rancagua	[pattern]	777777777760771	53	T1	Pansusceptible
1762-2011-S-1176	2011	Male	Rancagua	[pattern]	777777777760771	53	T1	Pansusceptible
189-2012-S-154	2012	Female	Ovalle	[pattern]	777777777760771	53	T1	MDR (INH+RF)
1905-2011-S-1322	2011	Male	Iquique	[pattern]	777777777760771	53	T1	Pansusceptible
1907-2011-S-1324	2011	Female	Iquique	[pattern]	777777777760771	53	T1	Pansusceptible
1917-2011-S-1332	2011	Female	Santiago	[pattern]	777777777760771	53	T1	Pansusceptible
1929-2011-S-1341	2011	Male	Rancagua	[pattern]	777777777760771	53	T1	Pansusceptible
1952-2011-S-1356	2011	Male	Osorno	[pattern]	777777777760771	53	T1	Pansusceptible
1955-2011-S-1359	2011	Female	Concepcion	[pattern]	777777777760771	53	T1	Pansusceptible
1987-2011-S-1382	2011	Female	Punta Arenas	[pattern]	777777777760771	53	T1	NA
247-2012-S-194	2012	Female	Santiago	[pattern]	777777777760771	53	T1	MDR (INH+RIF), SM
248-2012-S-195	2012	Male	Santiago	[pattern]	777777777760771	53	T1	Pansusceptible
270-2012-S-209	2012	Female	Castro	[pattern]	777777777760771	53	T1	Pansusceptible
271-2012-S-210	2012	Female	Castro	[pattern]	777777777760771	53	T1	Pansusceptible
289-2012-S-219	2012	Male	Santiago	[pattern]	777777777760771	53	T1	Pansusceptible
428-2012-S-302	2012	Male	Rancagua	[pattern]	777777777760771	53	T1	Pansusceptible
459-2012-S-320	2012	Male	Santiago	[pattern]	777777777760771	53	T1	R (SM)
479-2012-S-333	2012	Male	Santiago	[pattern]	777777777760771	53	T1	Pansusceptible
505-2012-S-347	2012	Female	Santiago	[pattern]	777777777760771	53	T1	Pansusceptible
596-2012-S-406	2012	Male	Los Angeles	[pattern]	777777777760771	53	T1	Pansusceptible
696-2012-S-462	2012	Female	Santiago	[pattern]	777777777760771	53	T1	R (INH+SM)
701-2012-S-465	2012	Male	Antofagasta	[pattern]	777777777760771	53	T1	Pansusceptible
841-2012-S-548	2012	Male	Los Angeles	[pattern]	777777777760771	53	T1	Pansusceptible
880-2011-S-534	2011	Male	Arica	[pattern]	777777777760771	53	T1	Pansusceptible
887-2011-S-540	2011	Male	Temuco	[pattern]	777777777760771	53	T1	Pansusceptible
913-2011-S-556	2011	Female	Santiago	[pattern]	777777777760771	53	T1	Pansusceptible
918-2012-S-587	2012	Male	Santiago	[pattern]	777777777760771	53	T1	Pansusceptible
919-2011-S-562	2011	Male	Coquimbo	[pattern]	777777777760771	53	T1	Pansusceptible
949-2011-S-582	2011	Male	Concepcion	[pattern]	777777777760771	53	T1	Pansusceptible
981-2011-S-605	2011	Male	Iquique	[pattern]	777777777760771	53	T1	Pansusceptible

ID	Year	Sex	City	Octal	No.	Lineage	Resistance
998-2012-S-631	2012	Male	Los Angeles	777777777760771	53	T1	Pansusceptible
1275-2011-S-805	2011	Female	Iquique	777777557760771	58	T5-Madrid2	Pansusceptible
1401-2011-S-893	2011	Male	Coquimbo	777777557760771	58	T5-Madrid2	Pansusceptible
1403-2011-S-895	2011	Male	Coquimbo	777777557760771	58	T5-Madrid2	Pansusceptible
1755-2011-S-1168	2011	Male	Rancagua	777777557760771	58	T5-Madrid2	Pansusceptible
1213-2011-S-767	2011	Male	Santiago	777777607760731	60	LAM4	Pansusceptible
1232-2011-S-782	2011	Male	Santiago	777777607760731	60	LAM4	Pansusceptible
1416-2011-S-906	2011	Male	Santiago	777777607760731	60	LAM4	Pansusceptible
1494-2011-S-968	2011	Female	Valparaiso	777777607760731	60	LAM4	Pansusceptible
306-2012-S-233	2012	Male	Concepcion	777777607760731	60	LAM4	Pansusceptible
791-2012-S-519	2012	Female	Santiago	777777743760771	61	Cameroon	Pansusceptible
925-2011-S-569	2011	Male	Santiago	777777774760771	62	H1	Pansusceptible
1472-2011-S-949	2011	Female	Santiago	777777607560771	64	LAM6	Pansusceptible
1485-2011-S-963	2011	Male	Arica	777777607560771	64	LAM6	Pansusceptible
181-2012-S-146	2012	Male	Santiago	777777607560771	64	LAM6	Pansusceptible
182-2012-S-147	2012	Male	Santiago	777777607560771	64	LAM6	Pansusceptible
1903-2011-S-1320	2011	Male	Iquique	777777607560771	64	LAM6	Pansusceptible
224-2012-S-178	2012	Male	Santiago	777777607560771	64	LAM6	Pansusceptible
511-2012-S-350	2012	Male	Santiago	777777607560771	64	LAM6	R (SM)
971-2011-S-596	2011	Male	Castro	777777607560771	64	LAM6	Pansusceptible
1049-2011-S-655	2011	Male	Punta Arenas	777777777760711	78	T	R (SM)
1379-2011-S-879	2011	Male	Arica	777377607760771	81	LAM9	Pansusceptible
1269-2011-S-801	2011	Male	Iquique	700036777760771	91	X3	Pansusceptible
1273-2011-S-803	2011	Male	Iquique	700036777760771	91	X3	Pansusceptible
526-2012-S-358	2012	Female	Ovalle	700036777760771	91	X3	NA
737-2012-S-490	2012	Male	Los Angeles	700036777760771	91	X3	R (INH+SM)
976-2011-S-600	2011	Male	Iquique	700036777760771	91	X3	Pansusceptible
1223-2011-S-776	2011	Female	Antofagasta	777737607760771	93	LAM5	Pansusceptible
1036-2012-S-656	2012	Male	Santiago	757777777720771	99	H3	Pansusceptible
1393-2011-S-887	2011	Female	Osorno	757777777720771	99	H3	Pansusceptible
881-2011-S-535	2011	Male	Arica	776167607760771	111	LAM3	Pansusceptible
936-2011-S-572	2011	Female	Puerto Montt	777767777760771	118	T1	Pansusceptible
1928-2011-S-1339	2011	Female	Rancagua	777776777760771	119	X1	Pansusceptible
937-2011-S-573	2011	Male	Los Angeles	777777777700771	124	Unknown	Pansusceptible
1287-2011-S-814	2011	Male	Valparaiso	776177607760731	130	LAM3	Pansusceptible
1381-2011-S-881	2011	Male	Concepcion	776177607760731	130	LAM3	Pansusceptible
1003-2011-S-621	2011	Male	Talca	777776777760601	137	X2	R (INH)
1274-2011-S-804	2011	Female	Iquique	777776777760601	137	X2	Pansusceptible
1980-2011-S-1376	2011	Male	Valparaiso	777776777760601	137	X2	Pansusceptible
205-2012-S-167	2012	Male	Rancagua	757777777760771	154	T1	Pansusceptible
1032-2011-S-638	2011	Male	Concepcion	777777607760671	162	LAM9	R (PZA)
694-2012-S-460	2012	Male	Santiago	777777607760700	163	LAM4	Pansusceptible
245-2012-S-192	2012	Female	Santiago	677777777720771	180	H3	R (INH+SM)
269-2012-S-208	2012	Male	Santiago	677777777720771	180	H3	Pansusceptible
1402-2011-S-894	2011	Female	Coquimbo	677737607760731	194	LAM2	Pansusceptible
1898-2011-S-1316	2011	Female	Iquique	677737607760731	194	LAM2	Pansusceptible
1410-2011-S-901	2011	Male	Santiago	677777607660771	195	LAM1	Pansusceptible
1163-2011-S-734	2011	Male	Santiago	776137607760771	211	LAM3	Pansusceptible
1177-2011-S-745	2011	Male	Temuco	776137607760771	211	LAM3	Pansusceptible
1193-2011-S-755	2011	Female	Concepcion	776137607760771	211	LAM3	Pansusceptible
1297-2011-S-825	2011	Male	Temuco	776137607760771	211	LAM3	Pansusceptible
1368-2011-S-868	2011	Male	Temuco	776137607760771	211	LAM3	Pansusceptible
187-2012-S-152	2012	Male	Ovalle	776137607760771	211	LAM3	Pansusceptible
1959-2011-S-1363	2011	Male	Concepcion	776137607760771	211	LAM3	Pansusceptible
704-2012-S-468	2012	Male	Rancagua	776137607760771	211	LAM3	Pansusceptible
922-2011-S-566	2011	Male	Santiago	776137607760771	211	LAM3	Pansusceptible
927-2011-S-570	2011	Female	Santiago	776137607760771	211	LAM3	Pansusceptible
930-2012-S-598	2012	Male	Santiago	776137607760771	211	LAM3	Pansusceptible
938-2011-S-574	2011	Male	Valdivia	776137607760771	211	LAM3	Pansusceptible
1897-2011-S-1315	2011	Male	Iquique	777774077560771	222	Unknown	Pansusceptible
2015-2011-S-1402	2011	Male	Rancagua	777774077560771	222	Unknown	Pansusceptible
510-2012-S-349	2012	Male	Santiago	777774077560771	222	Unknown	R (SM)
947-2011-S-580	2011	Male	Concepcion	777774077560771	222	Unknown	Pansusceptible
839-2012-S-546	2011	Male	Los Angeles	777777777700171	238	Unknown	R (SM)
1640-2011-S-1084	2011	Female	Osorno	777777777760031	239	T2	Pansusceptible
1134-2011-S-715	2011	Male	Copiapo	777777777760471	241	T1	Pansusceptible
985-2011-S-608	2011	Female	Temuco	777777777760601	244	T1	Pansusceptible
967-2011-S-592	2011	Male	Valparaiso	777777777760671	245	T1	Pansusceptible
1131-2011-S-714	2011	Male	Santiago	777777704020771	283	H1	Pansusceptible
1353-2011-S-856	2011	Male	Santiago	777777704020771	283	H1	Pansusceptible
1443-2011-S-928	2011	Male	Valparaiso	777777704020771	283	H1	MDR (INH+RF)
254-2012-S-198	2012	Female	Santiago	777777704020771	283	H1	Pansusceptible
290-2012-S-220	2012	Male	Santiago	777777704020771	283	H1	Pansusceptible
998-2011-S-618	2011	Male	Valparaiso	777777704020771	283	H1	Pansusceptible
180-2012-S-145	2012	Male	Santiago	777757777760771	393	T1	Pansusceptible
1337-2011-S-843	2011	Female	Santiago	704003347760471	430	T4-CEU1	Pansusceptible
288-2012-S-218	2012	Male	Santiago	760777777740371	434	T1	Pansusceptible
1341-2011-S-846	2011	Male	Antofagasta	763777607760771	435	LAM9	Pansusceptible
886-2011-S-539	2011	Female	Temuco	777776770000000	450	Unknown	Pansusceptible
1089-2011-S-682	2011	Male	Osorno	777737737760771	504	T3	Pansusceptible
1180-2011-S-748	2011	Male	Santiago	776177607760371	720	LAM3	Pansusceptible
1234-2011-S-784	2011	Male	Santiago	776177607760371	720	LAM3	Pansusceptible
1235-2011-S-785	2011	Female	Santiago	776177607760371	720	LAM3	Pansusceptible
1437-2011-S-922	2011	Male	Santiago	776177607760371	720	LAM3	Pansusceptible
344-2012-S-255	2012	Male	Punta Arenas	776177607760371	720	LAM3	Pansusceptible
562-2012-S-381	2012	Male	Santiago	776177607760371	720	LAM3	Pansusceptible
1320-2011-S-834	2011	Female	Copiapo	477777607760771	753	LAM1	Pansusceptible
1404-2011-S-896	2011	Male	Osorno	777777777760071	787	T1	Pansusceptible
2058-2011-S-1434	2011	Female	Santiago	437777777760771	798	T1	Pansusceptible
2082-2011-S-1450	2011	Female	Concepcion	437777777760771	798	T1	Pansusceptible
1960-2011-S-1364	2011	Male	Concepcion	777777000760771	880	T1	Pansusceptible
1895-2011-S-1313	2011	Male	Iquique	677777607740011	900	LAM	Pansusceptible
287-2012-S-217	2012	Male	Santiago	776377777720771	914	Unknown	Pansusceptible
1382-2011-S-882	2011	Male	Concepcion	777777760020611	948	H3	Pansusceptible
262-2012-S-203	2012	Male	Santiago	777777760020611	948	H3	R (SM)
1736-2011-S-1153	2011	Female	Talca	776637777760771	1073	T1	Pansusceptible
1020-2011-S-631	2011	Male	Temuco	777737777760771	1105	T1	Pansusceptible
695-2012-S-461	2012	Male	Santiago	607777777720771	1116	H3	Pansusceptible
664-2012-S-442	2012	Female	Santiago	754377607760700	1220	LAM	Pansusceptible
2016-2011-S-1403	2011	Male	Talcahuano	777774077560731	1232	T2	Pansusceptible
1081-2011-S-675	2011	Male	Temuco	777740000160771	1259	T1	Pansusceptible
1727-2011-S-1150	2011	Male	Santiago	777777207760771	1277	LAM9	Pansusceptible
1768-2011-S-1182	2011	Male	Santiago	777777207760771	1277	LAM9	Pansusceptible
2036-2011-S-1415	2011	Female	Iquique	777777207760771	1277	LAM9	R (SM)
2064-2011-S-1438	2011	Male	Valparaiso	777777207760771	1277	LAM9	Pansusceptible
824-2012-S-538	2012	Male	Punta Arenas	777777207760771	1277	LAM9	R (SM+PZA)
861-2011-S-527	2011	Male	Santiago	777777207760771	1277	LAM9	Pansusceptible
1152-2011-S-727	2011	Female	Santiago	736177607700171	1476	AFRI_2	Pansusceptible

ID	Year	Sex	City	Spoligotype	SIT	Lineage	Resistance
109-2012-S-97	2012	Male	Talcahuano		703777777760771	1560	T1	Pansusceptible
1377-2011-S-877	2011	Female	Concepcion		703777777760771	1560	T1	Pansusceptible
457-2012-S-318	2012	Female	Santiago		777777776760771	1626	T1	Pansusceptible
1074-2011-S-668	2011	Male	Santiago		776077607760771	1685	LAM3	Pansusceptible
1094-2011-S-685	2011	Female	Los Angeles		776077607760771	1685	LAM3	Pansusceptible
1716-2011-S-1143	2011	Male	Concepcion		776077607760771	1685	LAM3	Pansusceptible
191-2012-S-156	2012	Male	Antofagasta		717777607760771	1706	LAM9	Pansusceptible
1967-2011-S-1367	2011	Female	Santiago		777737607760731	1710	LAM	R (RIF)
1968-2011-S-1368	2011	Female	Santiago		777737607760731	1710	LAM	Pansusceptible
421-2012-S-296	2012	Male	Los Angeles		777737607760731	1710	LAM	Pansusceptible
826-2011-S-503	2011	Male	Temuco		777737607760731	1710	LAM	Pansusceptible
908-2011-S-551	2011	Male	Concepcion		776177607740771	1841	LAM3	Pansusceptible
1447-2011-S-932	2011	Male	Valparaiso		777777707760731	1890	T2	Pansusceptible
1227-2011-S-779	2011	Female	Talca		776177607360771	2014	LAM3	Pansusceptible
1956-2011-S-1360	2011	Male	Concepcion		736177607760771	2015	LAM3	Pansusceptible
850-2011-S-519	2011	Male	Santiago		736177607760771	2015	LAM3	Pansusceptible
2094-2011-S-1460	2011	Male	Concepcion		777777604020771	2028	Unknown	Pansusceptible
2093-2011-S-1459	2011	Male	Valparaiso		776037607760771	2045	LAM3	Pansusceptible
997-2011-S-617	2011	Male	Valparaiso		677777607760371	2054	LAM	Pansusceptible
1063-2011-S-664	2011	Male	Santiago		777777637760771	2070	T1	Pansusceptible
1070-2011-S-666	2011	Male	Santiago		777777637760771	2070	T1	Pansusceptible
1118-2011-S-703	2011	Male	Copiapo		777777637760771	2070	T1	Pansusceptible
1165-2011-S-735	2011	Female	Puerto Montt		777777637760771	2070	T1	Pansusceptible
1062-2011-S-663	2011	Male	Santiago		776177600000000	2353	Unknown	Pansusceptible
30-2012-S-26	2012	Male	Santiago		776177600000000	2353	Unknown	Pansusceptible
1278-2011-S-806	2011	Male	Iquique		777777777760171	2366	T1	Pansusceptible
1398-2011-S-890	2011	Male	Santiago		776177607760711	2402	LAM3	Pansusceptible
1182-2011-S-750	2011	Female	Santiago		657757607760771	2512	LAM1	Pansusceptible
1891-2011-S-1310	2011	Female	Concepcion		577777607760751	2745	LAM9	Pansusceptible
911-2011-S-554	2011	Male	Santiago		577777607760751	2745	LAM9	Pansusceptible
1452-2011-S-935	2011	Male	Iquique		777777477720771	2885	H3	Pansusceptible
777-2012-S-510	2012	Male	Castro		777737777700771	2911	Unknown	Pansusceptible
1209-2011-S-764	2011	Male	Santiago		074377607760700	2941	LAM	Pansusceptible
1459-2011-S-941	2011	Male	Arica		777777777560731	3056	T2	Pansusceptible
1949-2011-S-1354	2011	Male	Osorno		000000017760771	3127	Unknown	Pansusceptible
982-2011-S-606	2011	Male	Iquique		776177777720771	3251	H3	Pansusceptible
137-2012-S-119	2012	Female	Santiago		776177607760770	3472	LAM3	Pansusceptible
666-2012-S-444	2012	Female	Santiago		776177607760671	3491	LAM3	Pansusceptible
1384-2011-S-884	2011	Female	Copiapo		437777777760771	3934	T2	Pansusceptible
1288-2011-S-815	2011	Female	Iquique		707774077560771	3965	T1	MDR (INH+RF), PZA
1282-2011-S-809	2011	Male	Concepcion		741774077560771	3967	T1	Pansusceptible
1002-2011-S-620	2011	Male	Santiago		703776777760771	4014*	X1	Pansusceptible
1008-2011-S-624	2011	Female	Talcahuano		703776777760771	4014*	X1	Pansusceptible
1893-2011-S-1311	2011	Male	Concepcion		703776777760771	4014*	X1	Pansusceptible
1957-2011-S-1361	2011	Male	Concepcion		703776777760771	4014*	X1	Pansusceptible
1958-2011-S-1362	2011	Female	Concepcion		703776777760771	4014*	X1	Pansusceptible
2021-2011-S-1405	2011	Male	Concepcion		703776777760771	4014*	X1	Pansusceptible
964-2012-S-617	2012	Male	Coihaique		703776777760771	4014*	X1	Pansusceptible
1006-2011-S-623	2011	Male	Talca		776177703770371	4015*	Unknown	Pansusceptible
1010-2011-S-626	2011	Male	Talcahuano		776177703770371	4015*	Unknown	R (PZA)
1012-2011-S-628	2011	Male	Santiago		776177703770371	4015*	Unknown	Pansusceptible
1029-2011-S-635	2011	Male	Concepcion		776177703770371	4015*	Unknown	R (INH+SM)
1030-2011-S-636	2011	Male	Concepcion		776177734000771	4015*	Unknown	Pansusceptible
1077-2011-S-671	2011	Male	Temuco		776177703770371	4015*	Unknown	Pansusceptible
1150-2011-S-726	2011	Male	Santiago		776177703770371	4015*	Unknown	NA
1059-2011-S-660	2011	Female	Santiago		777777774100771	4016*	Unknown	R (PZA)
1067-2011-S-665	2011	Male	Talcahuano		777777774100771	4016*	Unknown	Pansusceptible
1181-2011-S-749	2011	Male	Santiago		777737637760771	4017*	T3	Pansusceptible
1191-2011-S-753	2011	Female	Osorno		777737637760771	4017*	T3	Pansusceptible
1463-2011-S-944	2011	Female	Santiago		777737637760771	4017*	T3	R (INH)
1194-2011-S-756	2011	Male	Concepcion		777377636000771	4018*	Unknown	Pansusceptible
1143-2011-S-720	2011	Male	Talcahuano		777737636000771	4018*	Unknown	Pansusceptible
1211-2011-S-766	2011	Male	Talca		776177607720771	4019*	H3	Pansusceptible
1245-2011-S-787	2011	Female	Osorno		773347777760671	4020*	T1	Pansusceptible
1262-2011-S-795	2011	Male	Arica		777737777720671	4021*	H3	Pansusceptible
1285-2011-S-812	2011	Female	Valparaiso		777777364020771	4022*	H1	Pansusceptible
1303-2011-S-828	2011	Female	Santiago		777774077560711	4023*	T1	Pansusceptible
1329-2011-S-840	2011	Male	Valdivia		663777777720771	4024*	H3	Pansusceptible
1988-2011-S-1383	2011	Female	Ovalle		663777777720771	4024*	H3	Pansusceptible
444-2012-S-310	2012	Female	Santiago		663777777720771	4024*	H3	R (SM)
133-2012-S-116	2012	Male	Santiago		777763347760471	4025*	T4-CEU1	Pansusceptible
183-2012-S-148	2012	Male	Santiago		777763347760471	4025*	T4-CEU1	Pansusceptible
675-2012-S-448	2012	Male	Santiago		777763347760471	4025*	T4-CEU1	NA
923-2011-S-567	2011	Male	Santiago		777763347760471	4025*	T4-CEU1	Pansusceptible
1340-2011-S-845	2011	Female	Santiago		763777607760700	4026*	LAM4	Pansusceptible
727-2012-S-483	2012	Female	Santiago		763777607760700	4026*	LAM4	Pansusceptible
1418-2011-S-908	2011	Male	Santiago		772177607760771	4027*	LAM3	Pansusceptible
1421-2011-S-911	2011	Female	Santiago		700036774360771	4028*	X3	R (PZA)
1444-2011-S-929	2011	Male	Valparaiso		777777717560771	4029*	T1	Pansusceptible
1450-2011-S-933	2011	Female	Iquique		037777700000611	4030*	Unknown	Pansusceptible
979-2011-S-603	2011	Female	Iquique		037777700000611	4030*	Unknown	Pansusceptible
1489-2011-S-964	2011	Male	Santiago		777774037560771	4031*	T1	Pansusceptible
1491-2011-S-965	2011	Male	Santiago		777774037560771	4031*	T1	Pansusceptible
1653-2011-S-1095	2011	Male	Valparaiso		776077606160771	4032*	LAM3	Pansusceptible
1726-2011-S-1149	2011	Male	Santiago		776077606160771	4032*	LAM3	Pansusceptible
186-2012-S-151	2012	Male	Santiago		776137607760371	4033*	LAM3	Pansusceptible
1906-2011-S-1323	2011	Female	Iquique		776177417760771	4034*	T1	Pansusceptible
1908-2011-S-1325	2011	Female	Iquique		776177417760771	4034*	T1	Pansusceptible
2037-2011-S-1416	2011	Male	Iquique		601777777760771	4035*	T1	Pansusceptible
2070-2011-S-1443	2011	Male	Talca		601777777760771	4035*	T1	Pansusceptible
642-2012-S-429	2012	Male	Santiago		777777607160731	4036*	LAM4	Pansusceptible
966-2011-S-591	2011	Male	Talcahuano		777777734020771	4037*	H1	Pansusceptible
1005-2011-S-622	2011	Female	Talca		776177605760731	Or01	LAM3	NA
1045-2011-S-651	2011	Male	Santiago		776177607160771	Or02	LAM3	Pansusceptible
1083-2011-S-677	2011	Male	Castro		701777777760771	Or03	T1	Pansusceptible
1110-2011-S-697	2011	Male	Puerto Montt		740003607760771	Or04	LAM3	Pansusceptible
1122-2011-S-707	2011	Male	Santiago		777777637740771	Or05	T1	Pansusceptible
1161-2011-S-732	2011	Female	Santiago		777777774020771	Or06	H1	Pansusceptible
1153-2011-S-728	2011	Female	Santiago		271004606760720	Or07	LAM2	R (PZA)
1192-2011-S-754	2011	Female	Osorno		737177607760771	Or08	LAM9	Pansusceptible
1214-2011-S-768	2011	Male	Santiago		741774037560771	Or09	T1	Pansusceptible
1216-2011-S-770	2011	Female	Castro		776077607760731	Or10	LAM3	Pansusceptible
1220-2011-S-773	2011	Male	Coquimbo		763777607760731	Or11	LAM4	Pansusceptible
1335-2011-S-842	2011	Male	Santiago		763760677660771	Or12	T1	Pansusceptible
1375-2011-S-875	2011	Female	Castro		703775777760771	Or13	T1	Pansusceptible
1376-2011-S-876	2011	Female	Concepcion		771177607760771	Or14	LAM9	Pansusceptible
138-2012-S-120	2012	Male	Santiago		763760607760771	Or15	LAM9	Pansusceptible
1419-2011-S-909	2011	Female	Santiago		773046637760701	Or16	X1	Pansusceptible

ID	Year	Sex	City	Spoligotype	Octal	Orphan	Lineage	Drug resistance
1439-2011-S-924	2011	Female	Santiago		777777720000001	Or17	Unknown	Pansusceptible
1451-2011-S-934	2011	Male	Iquique		757777607700771	Or18	Unknown	Pansusceptible
1468-2011-S-946	2011	Female	Valparaiso		776177617760771	Or19	T1	Pansusceptible
1469-2011-S-947	2011	Male	Calama		777767707760471	Or20	T1	Pansusceptible
149-2012-S-123	2012	Female	Santiago		700017377760771	Or21	T4	Pansusceptible
1492-2011-S-966	2011	Male	Santiago		711077737760771	Or22	T1	Pansusceptible
1495-2011-S-969	2011	Male	Valparaiso		700777777760671	Or23	T1	Pansusceptible
1829-2011-S-1265	2011	Male	Santiago		777734077460771	Or24	T3	Pansusceptible
1830-2011-S-1266	2011	Male	Santiago		776176207760771	Or25	LAM3	Pansusceptible
1837-2011-S-1272	2011	Female	Santiago		757777774120771	Or26	H3	Pansusceptible
185-2012-S-150	2012	Female	Santiago		676137607760771	Or27	LAM3	Pansusceptible
1944-2011-S-1352	2011	Male	Talcahuano		677777417760771	Or28	T1	Pansusceptible
1951-2011-S-1355	2011	Female	Osorno		000000010020771	Or29	H3	Pansusceptible
1953-2011-S-1357	2011	Female	Osorno		776177417760731	Or30	T2	Pansusceptible
1954-2011-S-1358	2011	Male	Osorno		577777417760751	Or31	T1	Pansusceptible
1981-2011-S-1377	2011	Male	Valparaiso		777777767460770	Or32	T1	Pansusceptible
305-2012-S-232	2012	Male	Concepcion		777770017560771	Or33	T1	Pansusceptible
372-2012-S-273	2012	Male	Coquimbo		723777207760771	Or34	LAM9	R (SM)
38-2012-S-32	2012	Female	Coquimbo		557727637740771	Or35	T3	Pansusceptible
39-2012-S-33	2012	Female	Concepcion		401767637740771	Or36	T1	Pansusceptible
50-2012-S-43	2012	Male	Santiago		777767637700771	Or37	Unknown	Pansusceptible
61-2012-S-53	2012	Female	Concepcion		576127607740771	Or38	LAM3	Pansusceptible
63-2012-S-55	2012	Male	Iquique		777767637740611	Or39	T1	Pansusceptible
64-2012-S-56	2012	Male	Puerto Montt		557767207740771	Or40	LAM9	Pansusceptible
66-2012-S-58	2012	Female	Valparaiso		676167607740771	Or41	LAM3	Pansusceptible
67-2012-S-59	2012	Male	Valparaiso		577767637740601	Or42	T1	Pansusceptible
676-2012-S-449	2012	Male	Santiago		663777777320771	Or43	H3	Pansusceptible
68-2012-S-60	2012	Male	Valparaiso		777764037540771	Or44	T1	Pansusceptible
883-2011-S-536	2011	Male	Arica		776177637720771	Or45	H3	Pansusceptible
894-2011-S-547	2011	Male	Antofagasta		777777637700771	Or46	Unknown	Pansusceptible
924-2011-S-568	2011	Male	Santiago		416077703770371	Or47	Unknown	Pansusceptible
977-2011-S-601	2011	Female	Iquique		777737605760771	Or48	LAM5	Pansusceptible
978-2011-S-602	2011	Male	Iquique		576177607760731	Or49	LAM3	R (PZA)
984-2011-S-607	2011	Male	Talca		776077607720371	Or50	H3	Pansusceptible

* NEW SITs are followed by an asterisk (*) and highlighted in yellow; Orphan spoligotypes are highlighted in blue.
** Drug resistance: pansusceptible n=402; NA, not available n=6; MDR, multidrug resistant n=6; R, any resistance, n=44. Abbreviations for first line drugs: INH, Isoniazid; RIF, Rifampin; SM, Streptomycin; PZA, pyrazinamide.