

S1 Fig. Phylogenetic tree of isolates used in this study. Clinical isolates of *Pseudomonas aeruginosa* obtained from a person with cystic fibrosis shown in red. Reference strains of *Pseudomonas aeruginosa* are shown in black and were chosen to represent the common genetic diversity within *P. aeruginosa* species from (De Soyza et al., 2013. *MicrobiologyOpen*, 2(6) 1010-1023). Zoomed in area shows the positioning of the closely related patient isolates excluding the distant E-S2239-15 isolate.



	Date of Collection	Patient	FEV1 % predicted ^a	Antibiotic treatment at							
Sample	(MM/DD/YY)	age	at sputum sampling	time of sampling							
	Early Isolates										
E-S2239-16											
E-MSB2494	12/91	26	53 p	Cotrimoxizole,							
E-MSB3405	12/51	20	55	Ciprofloxacin, Gentamycin							
E-S2239-15											
			_								
		Late	Isolates								
L-001-1A	45 100 140	10	10								
L-001-1B	15/08/12	46	18	Azithromycin							
L-001-1C											
L-001-2A	17/10/12	47	21	Azithromycin, Tobramycin,							
L-001-2B	17/10/12	17	<u> </u>	Cefepime							
L-001-3A	21/11/12	17	21	No Data							
L-001-3B	21/11/12	47	21	No Data							
L-001-4	21/01/13	47	17	Tobramycin, Meropenem							
L-001-5A	10/04/12	47	17	No Data							
L-001-5B	18/04/13	47	1/	NO Data							
L-001-6	06/05/13	47	17	Tobramycin, Ceftazidime,							
				Azithromycin							

S1 Table. Summary of isolates taken for study, patient details and antibiotic treatment at time of sampling.

^a Sinclair SW, Avery SF, Brady DM, Smith DA, Holst PE, O'Donnell TV. Prediction formulae for normal pulmonary function values in New Zealand European subjects. N Z Med J. 1980;91(651):1-5.

FEV1% predicted is defined as the Forced Expiratory Volume of the patient divided by the average FEV1% within the population for any person of similar age, sex, and body composition. This is used as a measure of reduced lung function, compared to what would be expected of a person with 'normal' lung function.

^b Precise FEV1 is not available at time of sampling, number presented is average FEV1 % for the 2nd half of 1991

S2 Table. Summary of antibiotics administered to the patient at time of, or between sampling of early and late isolates of *P. aeruginosa*.

Known antibiotic treatments given (1991-2013) ^{a, b}
Augmentin
Azithromycin
Cefepime
Ceftazidime
Ciprofloxacin
Clarithromycin
Colomycin/Colistin
Cotrimoxazole
Fucidin
Gentamycin
Meropenem
Moxifloxacin
Piperacillin
Tobramycin

^a This is not an exhaustive list of all antibiotics the patient received, but covers those administered at time of sampling or between samples.

^b Antibiotics listed are ones the patient received, this is not a list of antibiotics administered solely to combat P. aeruginosa infection.

isolate	total_length	n_contigs	circular	N_count	gaps	ont_N50	ont_qscore	ont_bases	ont_cov	miseq_qscore	miseq_bases	miseq_cov	pred_CDS	Biosample
E-S2239-15	6,407,559	1	yes	0	0	19,875	13.3	1,394,937,072	217.7	35.3	103,038,935	16.1	5802	SAMN13234651
E-S2239-16	6,315,896	1	yes	0	0	23,364	13.3	1,146,375,768	181.5	35.3	114,392,328	18.1	5717	SAMN13234648
E-MSB2494	6,330,120	1	yes	0	0	7,556	13.1	1,001,416,848	158.2	35.3	154,738,111	24.4	5737	SAMN13234649
E-MSB3405	6,315,897	1	yes	0	0	22,478	13.3	1,196,529,488	189.4	35.3	96,322,838	15.3	5718	SAMN13234650
L-001-1A	6,269,726	1	yes	0	0	20,311	13.3	824,514,262	131.5	35.3	71,982,494	11.5	5691	SAMN13234657
L-001-1B	6,270,234	1	yes	0	0	26,365	13.3	658,327,564	105.0	35.3	118,980,668	19.0	5705	SAMN13234652
L-001-1C	6,268,635	1	yes	0	0	17,303	13.3	1,290,121,361	205.8	35.2	96,909,163	15.5	5688	SAMN13234659
L-001-2A	6,268,813	1	yes	0	0	19,144	13.3	1,139,680,807	181.8	35.3	84,017,737	13.4	5691	SAMN13234660
L-001-2B	6,270,419	1	yes	0	0	19,382	13.2	1,173,114,665	187.1	35.3	97,922,867	15.6	5695	SAMN13234658
L-001-3A	6,267,105	1	yes	0	0	19,255	13.3	1,084,955,690	173.1	35.2	97,672,750	15.6	5692	SAMN13234661
L-001-3B	6,269,926	1	yes	0	0	17,568	13.3	719,291,575	114.7	35.3	117,042,558	18.7	5699	SAMN13234655
L-001-4	6,269,046	1	yes	0	0	20,001	13.2	697,520,061	111.3	35.3	113,721,808	18.1	5692	SAMN13234654
L-001-5A	6,270,090	1	yes	0	0	22,496	13.3	626,823,565	100.0	35.1	112,667,053	18.0	5696	SAMN13234662
L-001-5B	6,270,238	1	yes	0	0	20,014	13.2	993,479,333	158.4	35.3	100,880,789	16.1	5709	SAMN13234653
L-001-6	6,255,746	1	yes	0	0	17,642	13.3	815,860,744	130.4	35.3	113,412,261	18.1	5681	SAMN13234656

S3 Table. Summary assembly and gene prediction statistics for isolates whole-genome sequenced.

	LEGEND
isolate	Strain IDs
total_length	Total length (bp) of contigs in the assembly
n_contigs	Number of contigs (if 1, then one chromosome w/ plasmid)
circular	Is contig 1 (chromosome) complete and circular (yes/no)
N_count	Number of uncalled nucleotides (N's) in final sequence)
gaps	Amount of gaps (stretches of N's) in the assembly
ont_N50	Read length that delimits 50% of sequenced bases (Nanopore)
ont_qscore	Mean Phred quality score of Nanopore (long) reads
ont_bases	Total amount of bases sequenced per nanopore library
ont_cov	Amount of nanopore bases divided by genome size
miseq_qscore	Mean Phred quality score of Illumina MiSeq (short) reads
miseq_bases	Total amount of bases sequenced per MiSeq library
miseq_cov	Amount of MiSeq bases divided by genome size
pred_CDS	Number of predicted protein coding genes (from Prokka)

	Number of	Sequence	Number of	
Sample	paired reads	length range	bootstraps	Mapping (%)
E-S2239-16				
01	3446702	20-125	1000	80.4
02	4903036	20-125	1000	86.6
03	4142012	20-125	1000	83.9
L-001-1C				
01	5021309	20-125	1000	80.6
02	4928204	20-125	1000	85.7
03	4994328	20-125	1000	83.5

S4 Table. Summary mapping statistics for RNAseq of early isolate E-S2239-16 and late isolate L-001-1C

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S2 Fig. Heatmap showing significantly differentially expressed genes from RNAseq of L-001-1C and E-S2239-16. Expression quantified as log of the counts per gene. Triplicates of L-001-1C RNAseq are shown in the left columns, triplicates of E-S2239-16 RNAseq are shown in the right columns.



a clear inversion of 0.9Mb (highlighted) in 4 of the 11 late isolates, occuring between rRNA operons which are the inversion endpoints.

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S3 Fig. Rearrangements within isolates. Mauve alignment of complete genomes isolated from patient 20 years apart (excluding S2239-15). Showing

	E-S2239-16	MSB2494	MSB3464	L-001-1A	L-001-1B	L-001-1C	L-001-2A	L-001-2B	L-001-3A	L-001-3B	L-001-4	L-001-5A	L-001-5B	L-001-6
E-S2239-16	0	12	4	179	246	211	209	197	214	245	206	216	266	239
E-MSB2494	I	0	12	185	252	219	215	205	220	251	212	222	272	245
E-MSB3464	I	ı	0	179	246	213	209	199	214	245	206	216	266	239
L-001-1A	I	I	ı	0	167	46	44	30	49	94	51	49	185	86
L-001-1B	ı	ı		ı	0	195	191	183	198	229	190	198	40	221
L-001-1C	I	ļ	·	ı	·	0	16	64	23	124	81	77	213	114
L-001-2A	I	ļ	·	ı	·	·	0	62	13	122	79	75	211	112
L-001-2B	I	ļ	ı	ı	ı	ı	ı	0	69	112	71	65	203	106
L-001-3A	I	I	ı	ı	ı	ı	ı	ı	0	127	86	82	218	119
L-001-3B	I	ı		ı						0	81	127	247	52
L-001-4	I	ļ	ı	ı	ı	ı	ı	ı	ı	·	0	84	208	71
L-001-5A	I	ļ	·	ı	·	·	·		·	·	·	0	216	117
L-001-5B	I	I	ı	ı	ı	ı	ı	ı	ı	I	ı	ı	0	239
L-001-6	I	ı	I	I	ı	ı	ı	ı	ı	I	ı	ı	I	0

S6 Table. Pairwise matrix of non-synonymous changes between isolates of P. aeruginosa from patient with CF

Number of non-synonymous changes **S8 Table.** Prevalence of specific nucleotide changes across all single nucleotide in all *P. aeruginosa* isolates analysed in this study

			Μ	lutant allel	e (freq)				
	Single nucleotide mutation (n=935)	Α	т	G		с			
e	A		0	2	22	1			
alle	т		4	0	6	19	fre	q	(%)
rting	G		49	298	0	4		0	
Stai	с		326	54	3	0		10	
								50	
			r	Mutant alle	ele (%)			100	
	Single nucleotide mutation (n=935)	Α	т	G		с		200	
ele	Α		0.0	0.3	2.8	0.1		400	
g alle	т		0.5	0.0	0.8	2.4			
artin	G		6.2	37.8	0.0	0.5			
Sti	c		41.4	6.9	0.4	0.0			