



THE UNIVERSITY of EDINBURGH
The Royal (Dick) School
of Veterinary Studies



Multi-drug resistant *E. coli* associated with urinary tract infections in dogs

A story of diversity, vulnerability, antibiotics and lots of plasmids !!

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Canine UTI: Background



- Canine bacterial UTI is common
- Role of asymptomatic bacteriuria?
- 75% of cases a single pathogen is present. *E. coli* accounts for up to half of all positive urine cultures in dogs



Antimicrobials used in UTI

- Amoxicillin clavulanate
- Cefalexin
- Cefovecin
- Fluoroquinolone
- TMPS



10 year old male Dachshund

Amoxiclav	R	Amikacin	S
Cefalexin	R	Amoxiclav	R
Ciprofloxacin	R	Cefotaxime	R
Co-trimoxazole	S	Cefalexin	R
Gentamicin	S	Ciprofloxacin	R
Tetracycline	R	Co-trimoxazole	R
		Enrofloxacin	R
		Gentamicin	R
		Tetracycline	R
		Ticarcillin	R

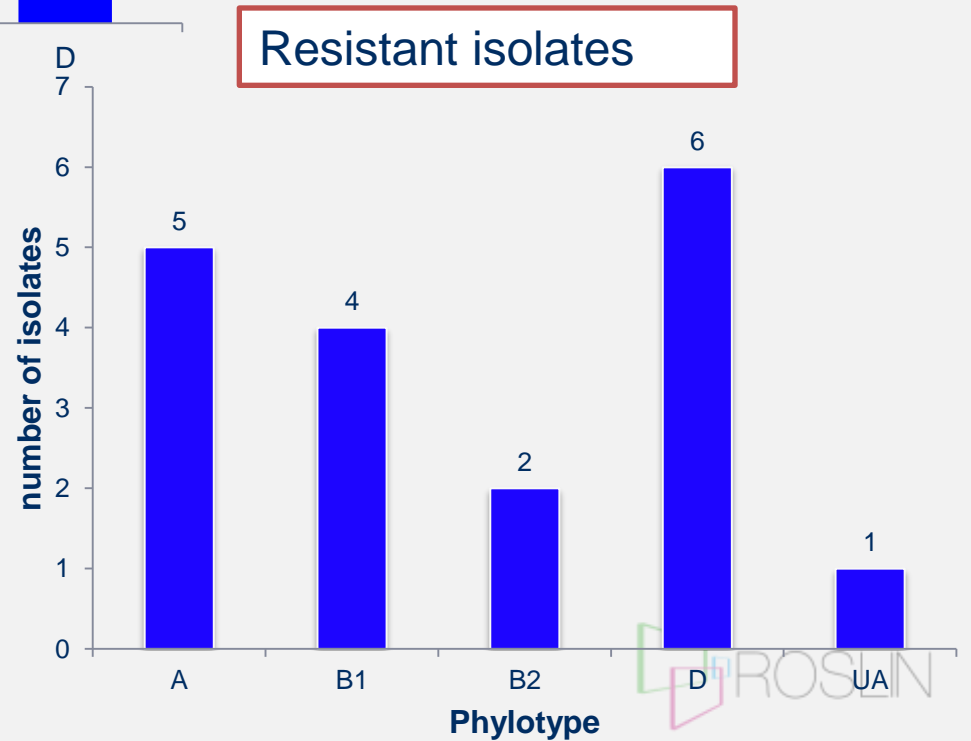
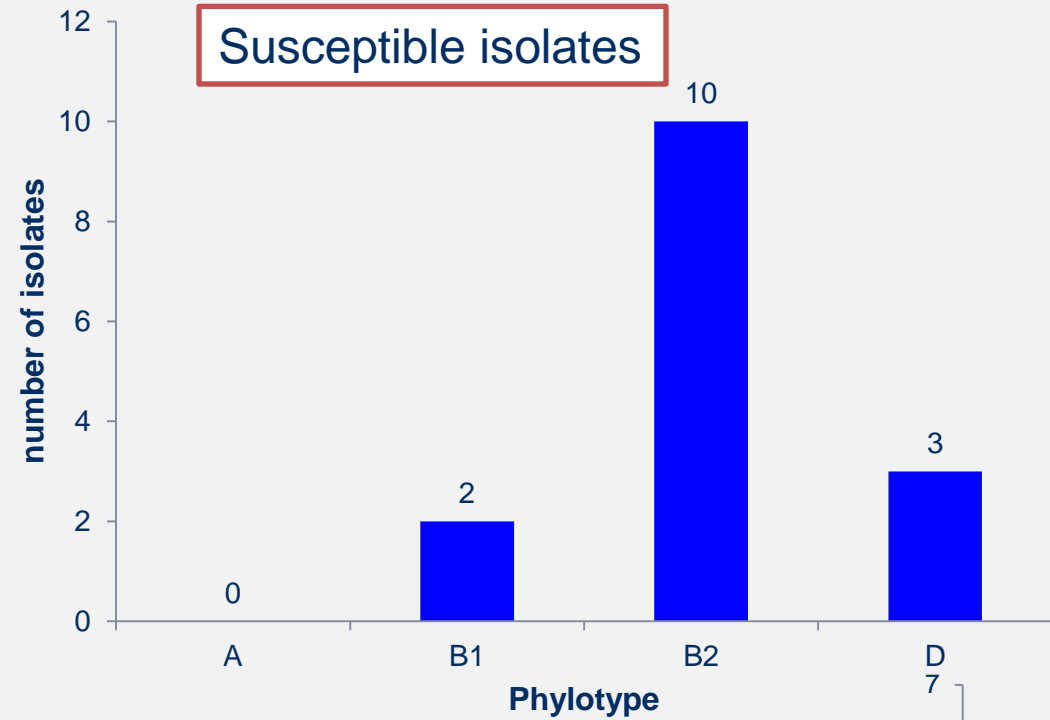


Isolate	Breed	Age	Summary of clinical details
R1	Dachshund	10 yr	Intervertebral disc prolapse. Surgical intervention with prophylactic antibiotics
R2	Weimeraner	9 yr	Prostatic abscess
R4	Cocker Spaniel	4 yr	Immune mediated haemolytic anaemia
R5	Cross breed	11 yr	Hyperadrenocorticism
R6	Boxer	9 yr	Multiple mast cell tumours
R7	Schnauzer	6 yr	Mast cell tumour
R8	Labrador	10 yr	Surgery to resect intestinal adenocarcinoma
R9	Collie	10 yr	Diabetes mellitus
R10	German Shepherd	8 yr	Paraprostatic cysts and a perineal hernia accompanied by recurrent cystitis
R11	Bouvier de Flandres	6 yr	Had a PEG tube for feeding
R12	Bearded Collie	1 yr	Diagnosed as a pyelonephritis
R13	Cocker Spaniel	7 yr	Diagnosed with a complex pancreatitis
R14	Golden Retriever	5 yr	Ectopic ureters
R15	Yorkshire Terrier	11 yr	Concurrent urolithiasis
R16	Boxer cross (F)	7 yr	Detrusor muscle atony



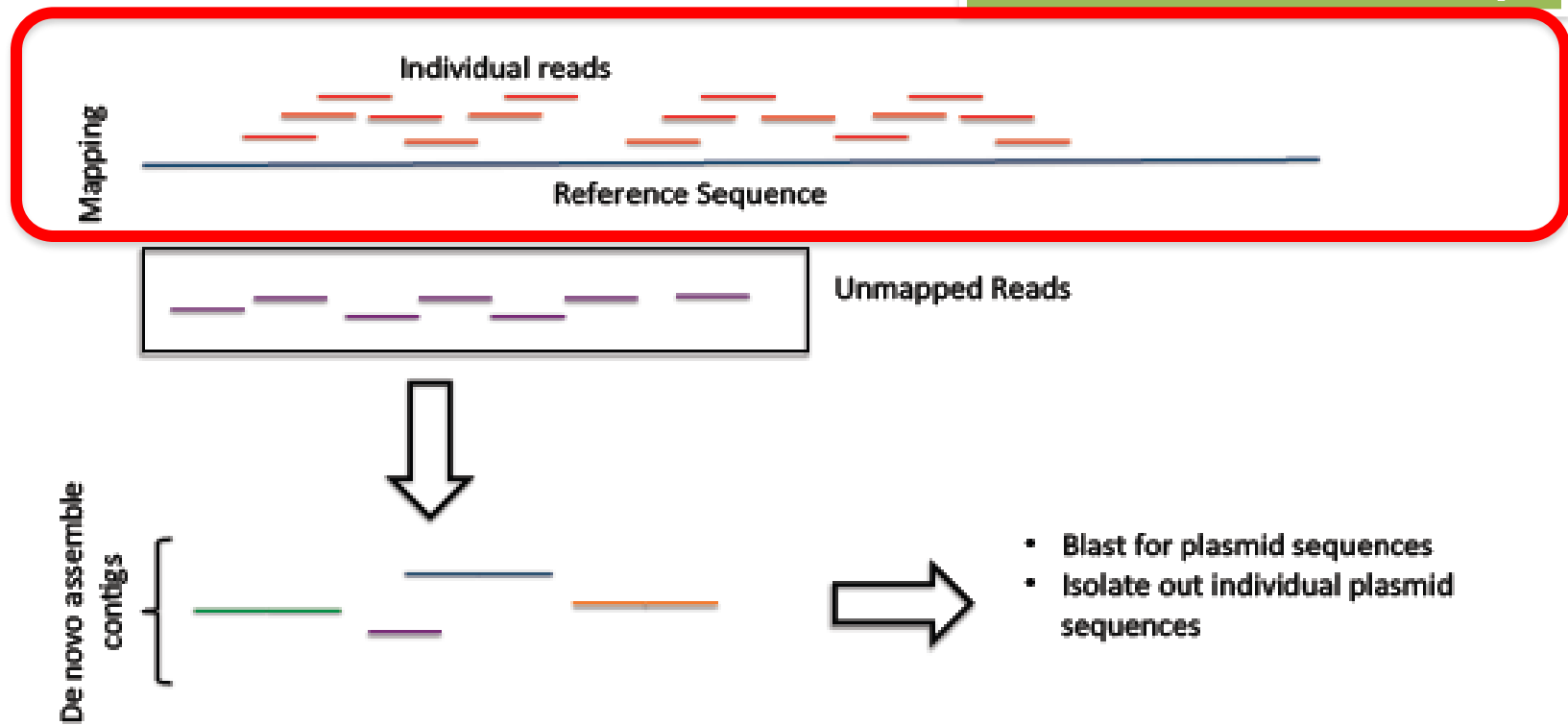
Isolate	Isolation date	Resistance pattern					3 rd	AmpC	Phylo	ST	Replicon	
R1	9/2006	AMC	CEF	COT	CIP	TET	R	+	A	10	FII I1	
R2	1/2008	AMC	CEF	COT		TET	R	+	n/t	46	FII I1	
R3	9/2010	AMC	CEF	COT	CIP	TET	R	+	A	744	FII I1	
R4	10/2010	AMC	CEF			TET	R	+	D	648	FII I1	
R5	3/2010	AMC	CEF			TET	R	+	D	963	FII I1	
R6	2/2011	AMC	CEF	COT		TET	R	+	D	N	FII I1	
R7	12/2007	AMC	CEF	COT	CIP	TET	R	+	B1	539	B/O I1	
R8	9/2011	AMC	CEF	COT	CIP	TET	GEN	S	+	B1	23	FII FIB
R9	9/2011	AMC	CEF	COT		TET		R	+	B1	101	I1
R10	3/2002	AMC	CEF	COT	CIP	TET		R	+	B2	167	FII FIA I1
R11a	2/2010	AMC	CEF	COT		TET		R	+	D	10	-
R11b	8/2010	AMC	CEF			TET		R	+	D	372	-
R12	7/2006	AMC	CEF	COT		TET	GEN	S	-	D	372	I2
R13	8/2009	AMC		COT	CIP	TET		S	-	A	10	FII FIA
R14	8/2008	AMC		COT	CIP	TET		S	-	A	10	-
R15	4/2009	AMC	CEF	COT	CIP	TET		S	-	A	998	-
R16a	4/2011	AMC	CEF		CIP	TET	GEN	R	-	B1	23	FII B/O
R16b	5/2011	AMC		COT	CIP	TET	GEN	S	-	B2	23	FII FIB

Wagner S et al. **Multidrug-resistant *Escherichia coli* from canine urinary tract infections tend to have commensal phylotypes, lower prevalence of virulence determinants and ampC-replicons.** *Vet. Microbiol.* (2014), <http://dx.doi.org/10.1016/j.vetmic.2014.01.003>

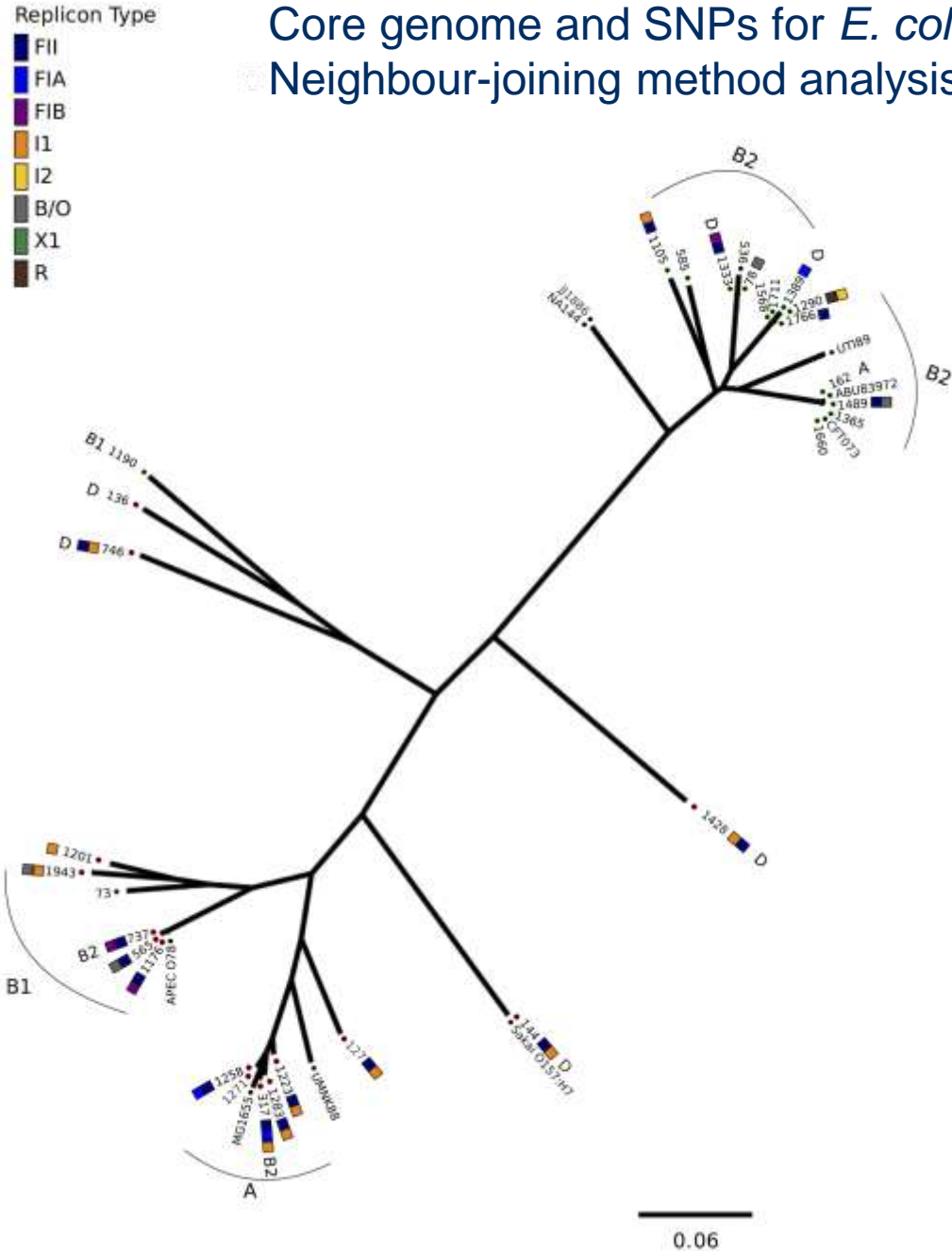


Sequence entire genome of our isolates

ILLUMINA hi-seq

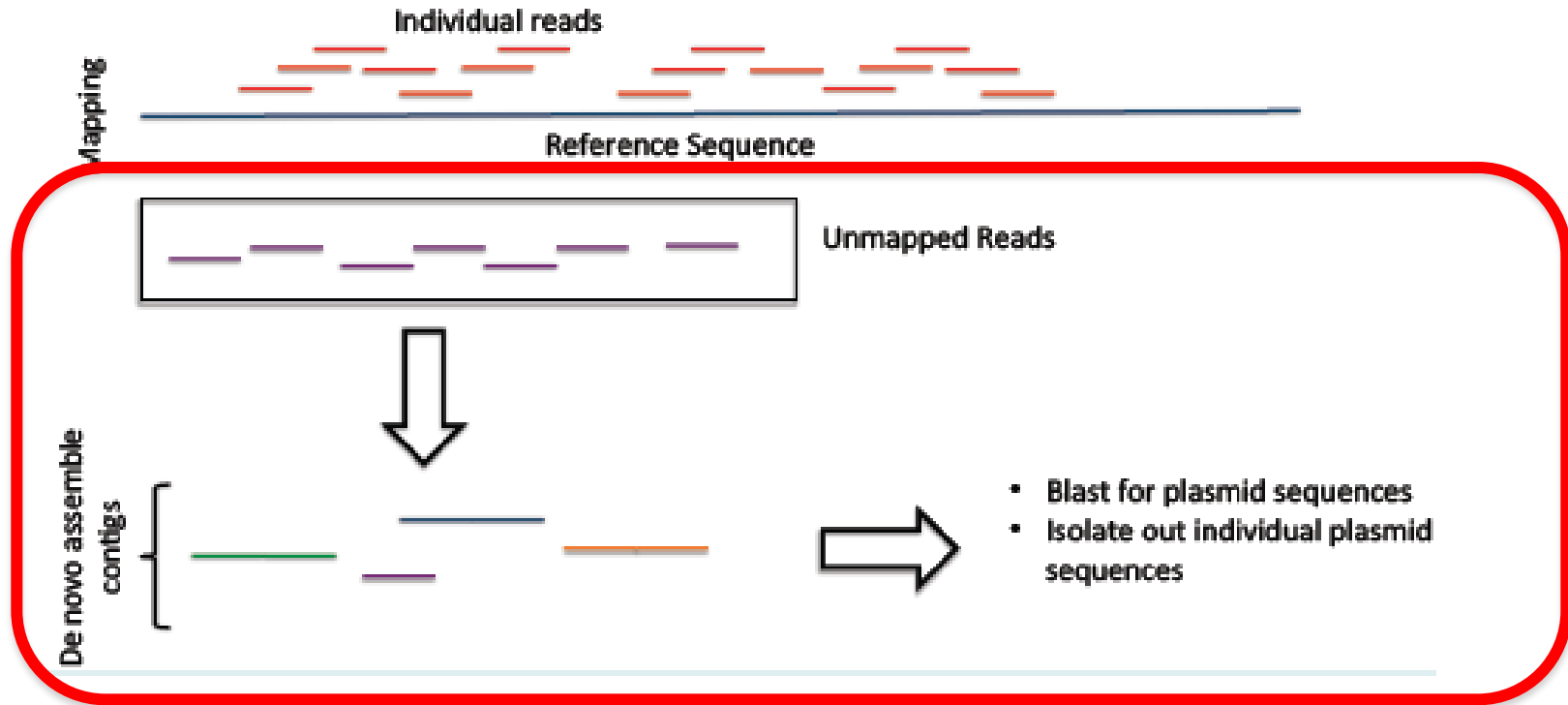


Core genome and SNPs for *E. coli* comparisons using Neighbour-joining method analysis



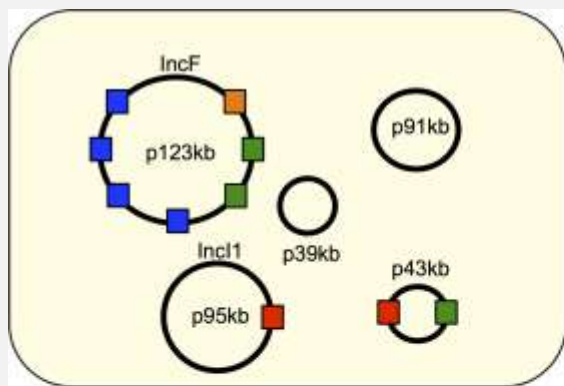
Sequence entire genome of our isolates

ILLUMINA hi-seq

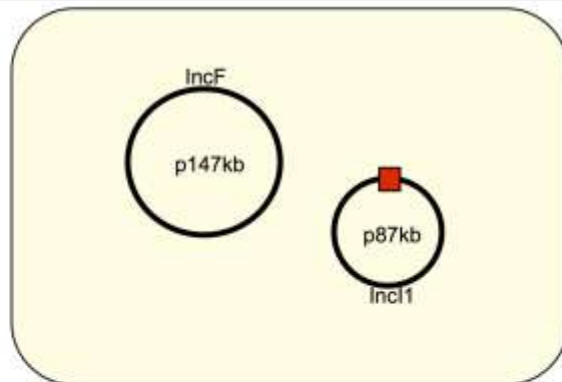


SMRT PacBio sequencing

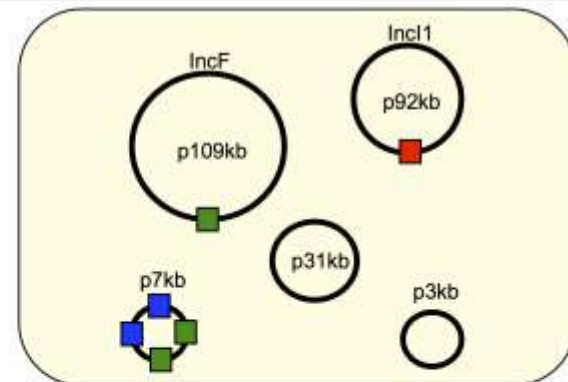
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R16a	4/2011	AMC	CEF		CIP	TET	GEN	R	-	B1	23	FII B/O
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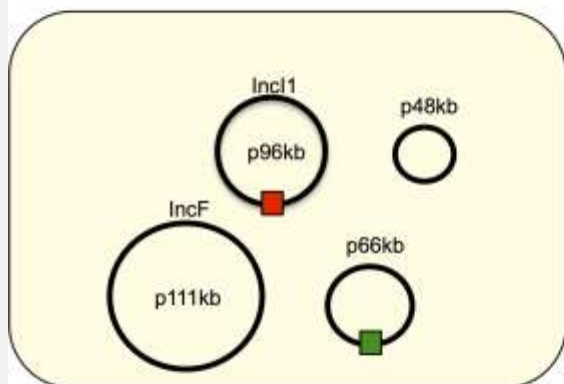
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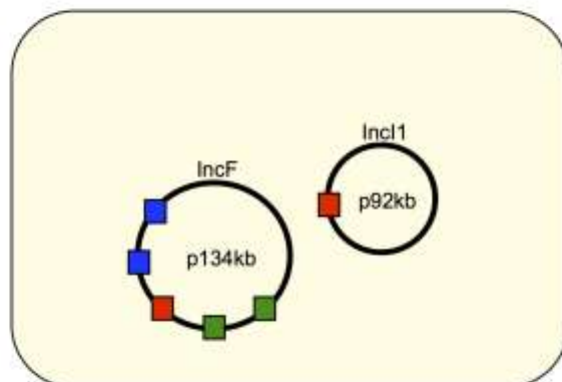
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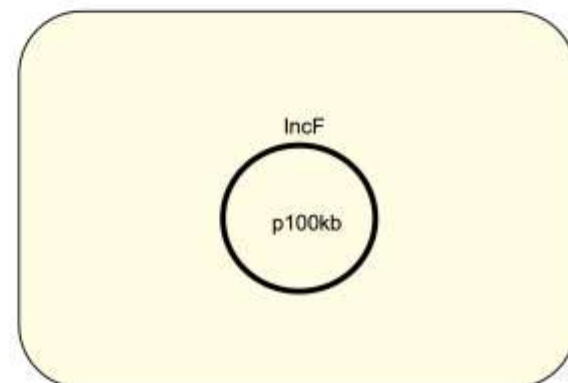
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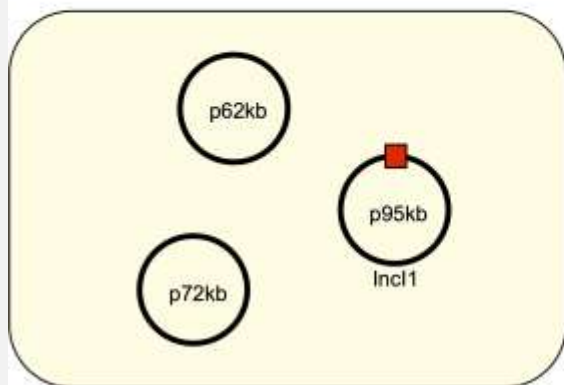
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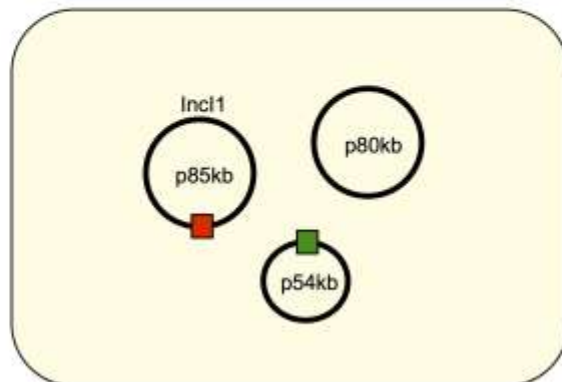
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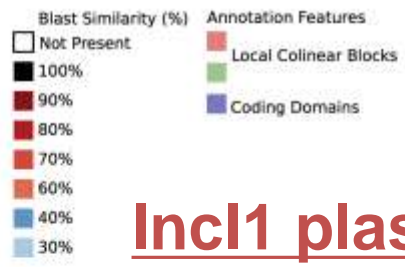
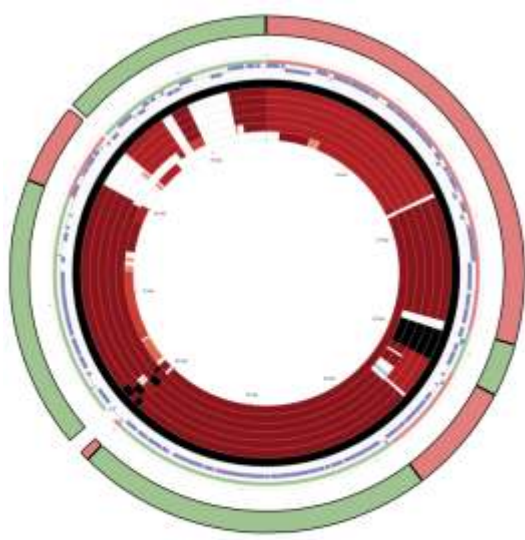


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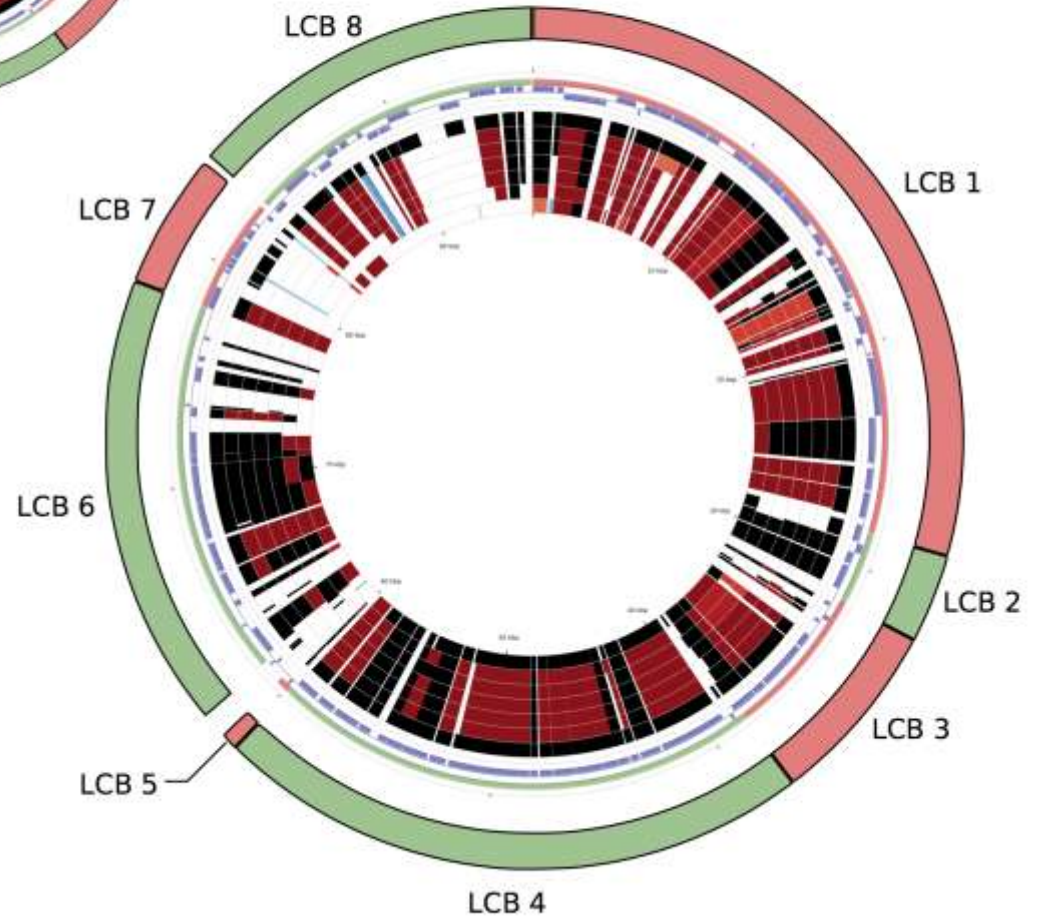


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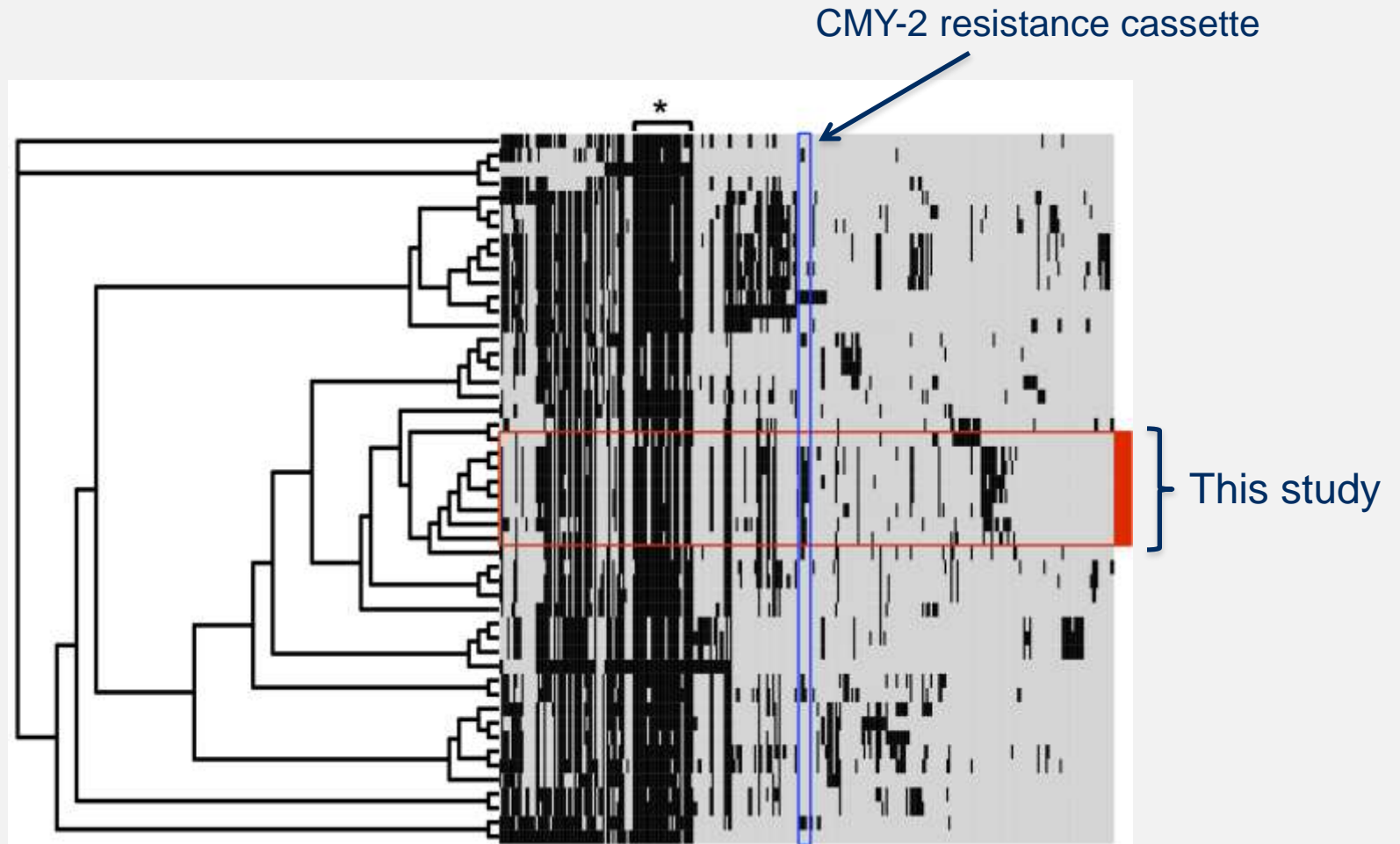
- Aminoglycoside
- Beta-Lactamase
- Potentiated Sulfonamides
- Chloramphenicol



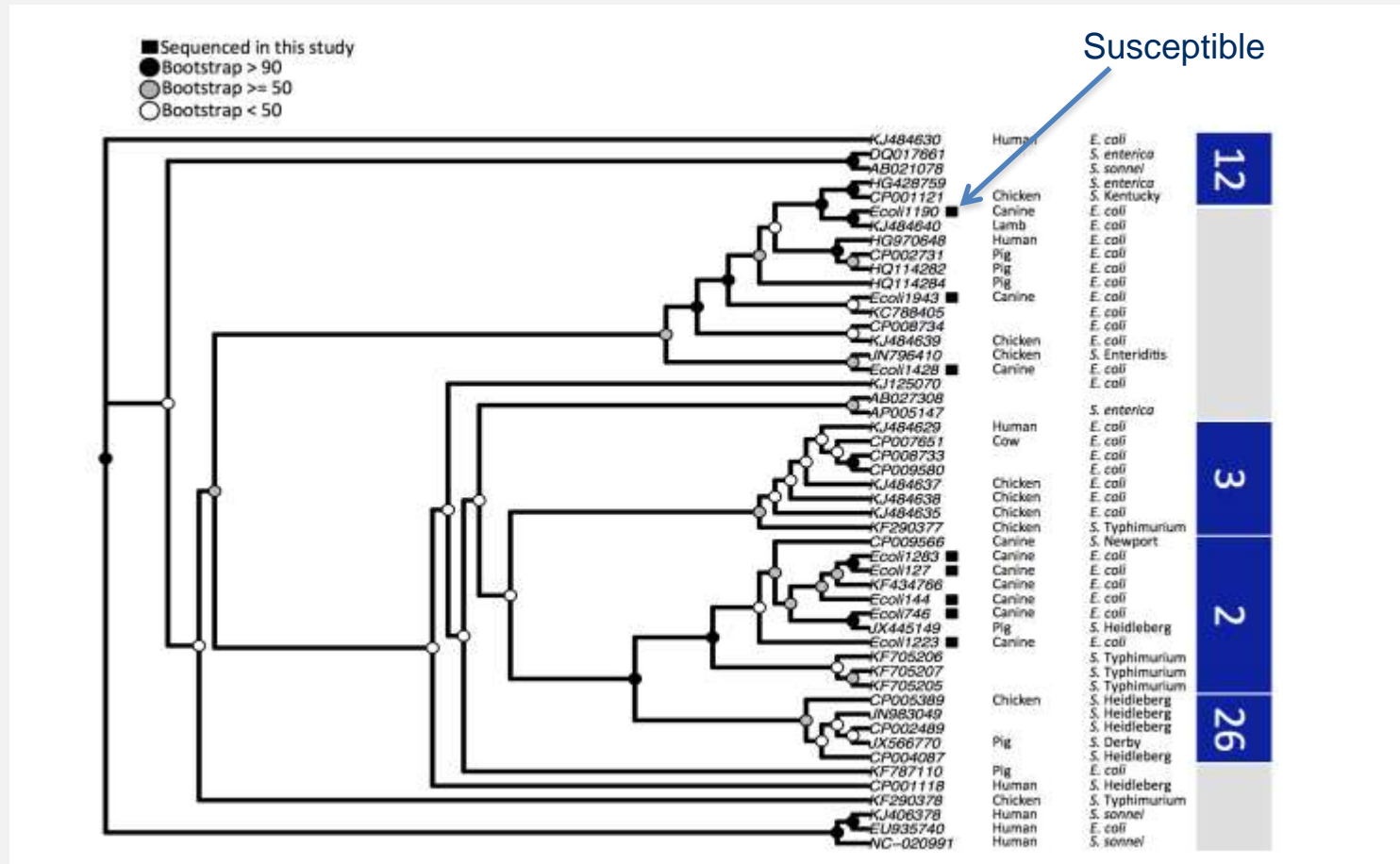
Incl1 plasmid comparisons

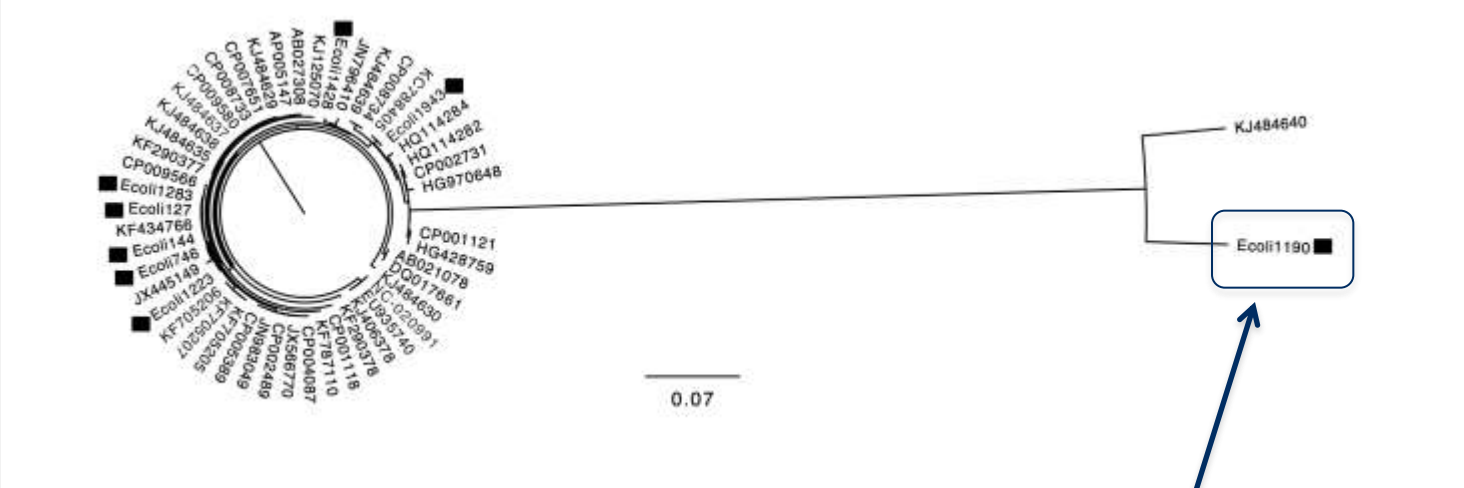


Pangenomic analysis of IncI1 plasmids



Maximum likelihood analysis, core genome IncI1 plasmids

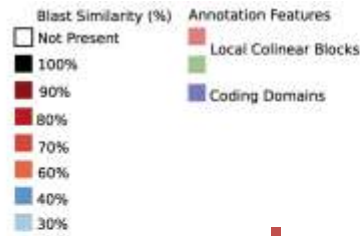
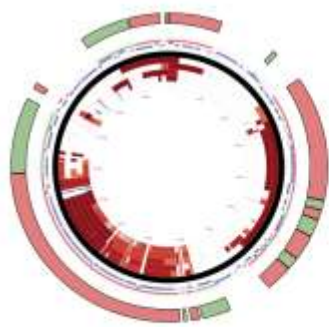




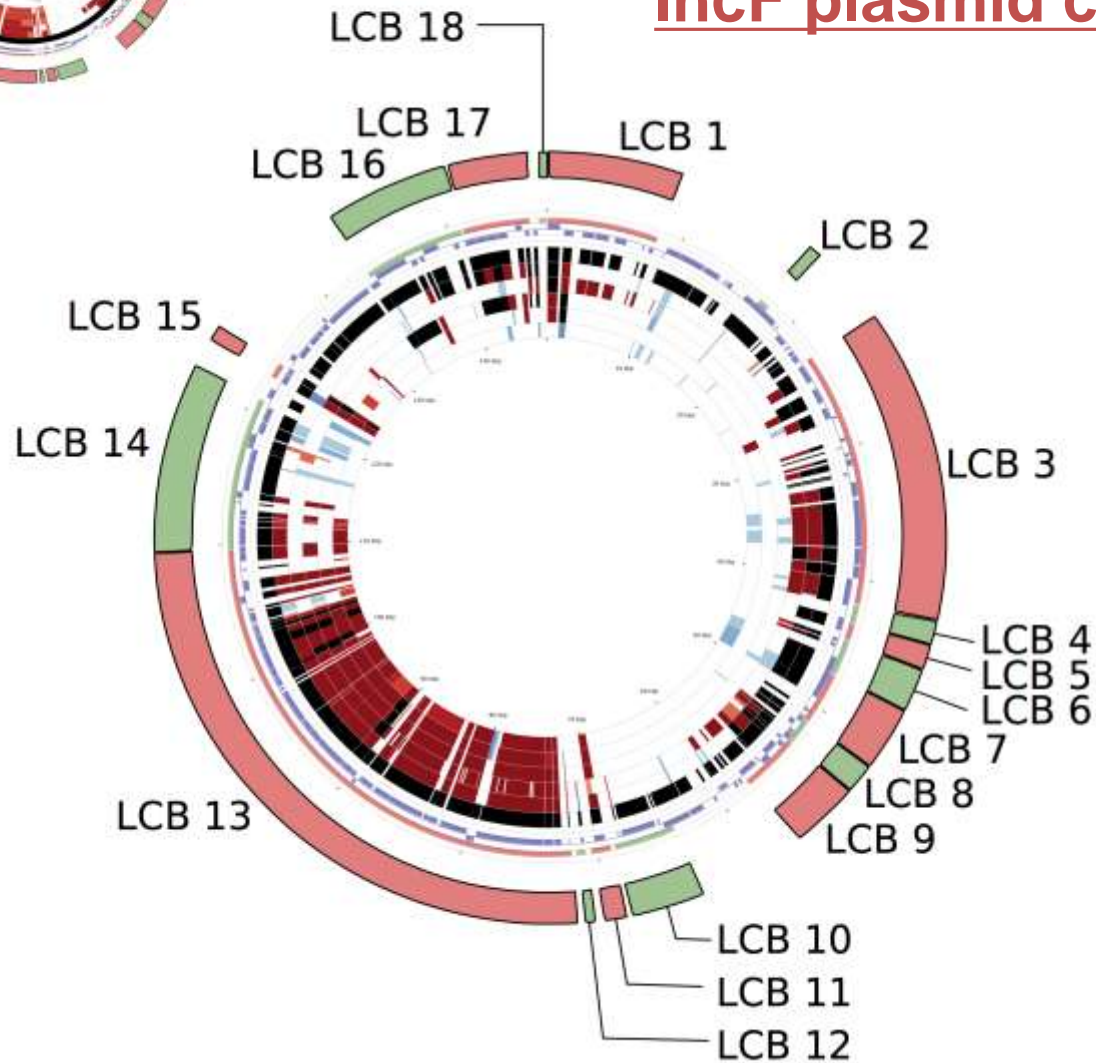
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Ecoli1190

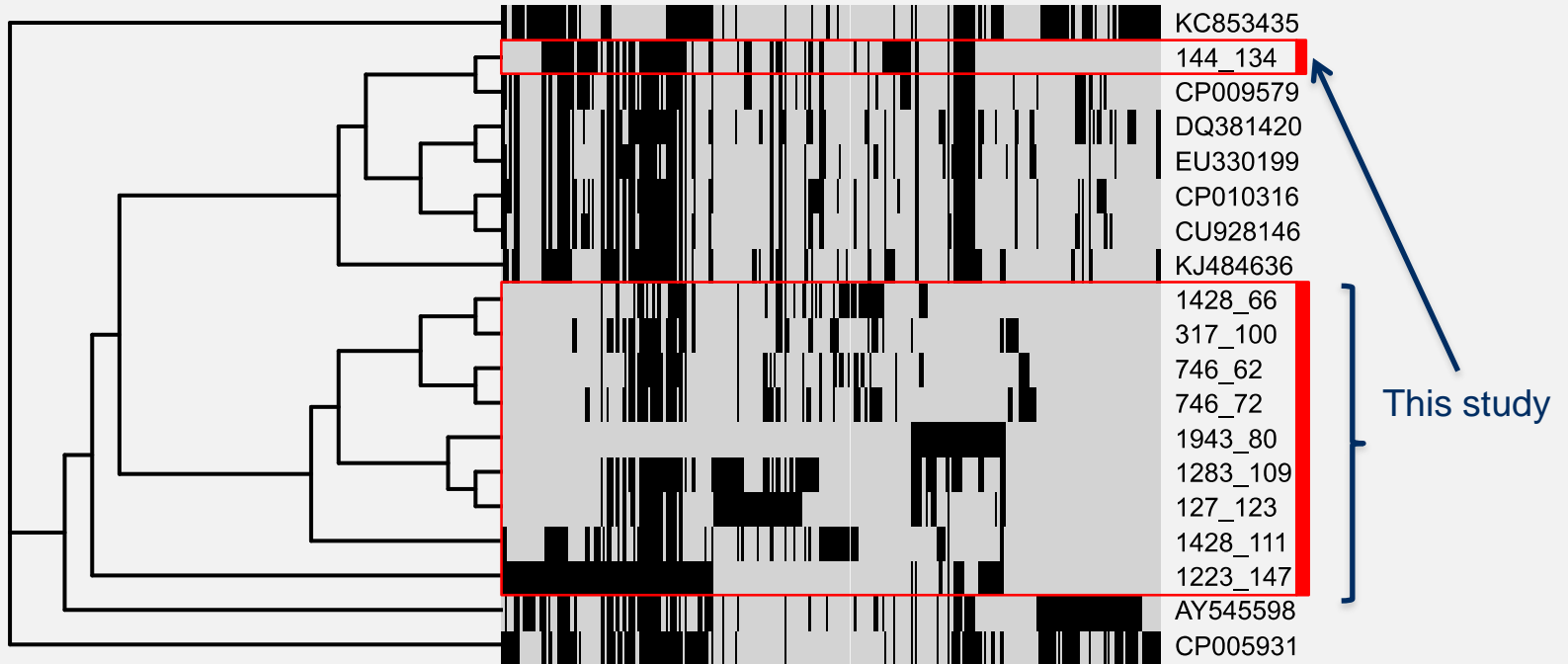
susceptible



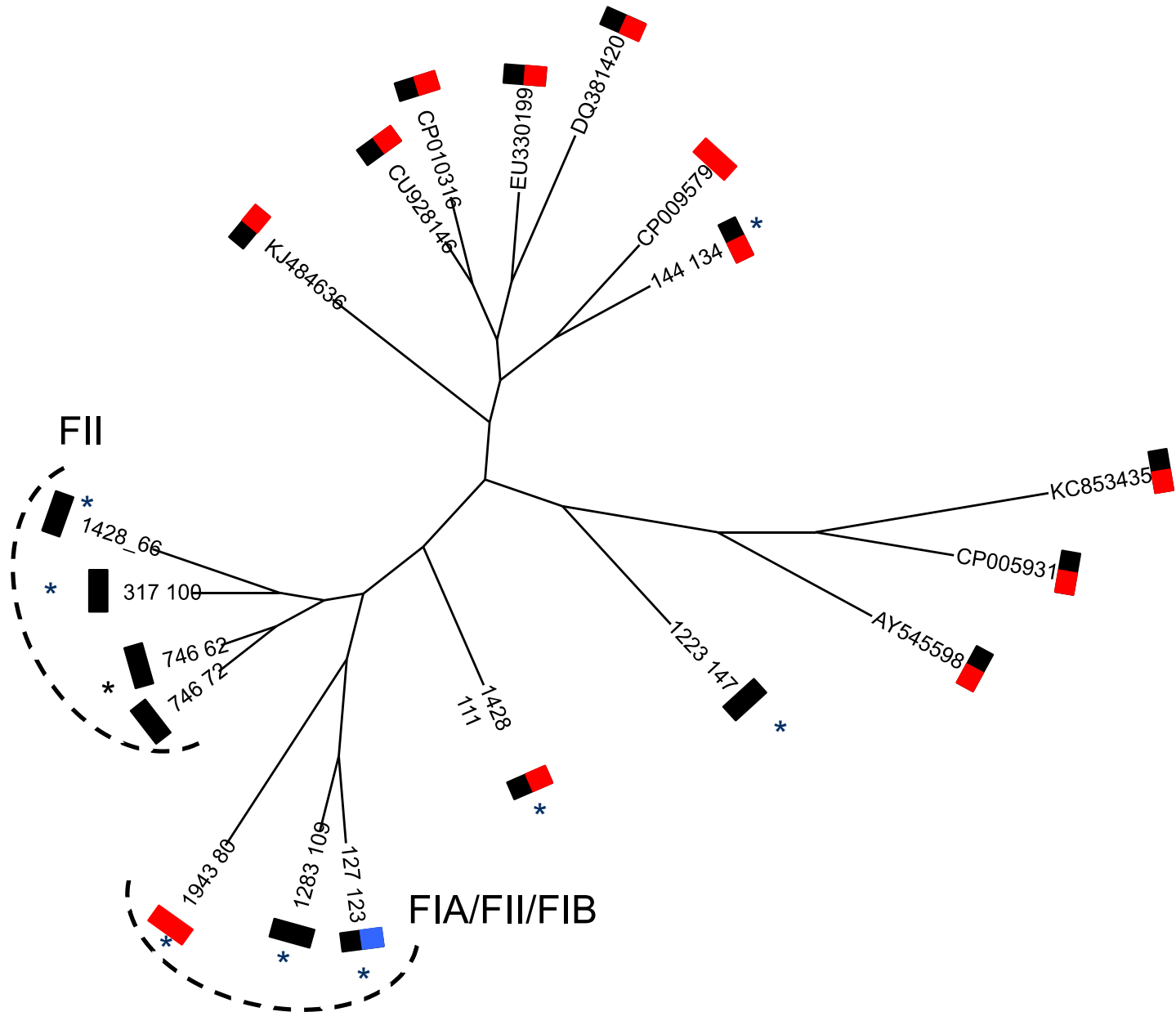
IncF plasmid comparisons



Pangenomic analysis of IncF plasmids



Maximum likelihood analysis, core genome IncF plasmids



Some conclusions

- Consider the clinical history of the dogs with MDR *E. coli* UTIs
- MDR *E. coli* associated with UTI in dogs in this study align more closely with commensal *E. coli* strains. Antibiotic susceptible *E. coli* also associated with UTIs align more closely with uropathogenic strains.
- Resistance to 3rd generation cephalosporins was exclusively pAmpC mediated (CMY-2 specifically)
- SMRT sequencing revealed multiple plasmids (up to 5)
- The CMY-2 gene was exclusive to the IncI1 plasmid
- The IncFII plasmid contributed additional resistance and virulence?
- **Is this the rise of the commensals?**



Acknowledgements

- Sam Wagner
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- Jim Bono

