

# *Pertussis vaccine: does strain variation matter?*

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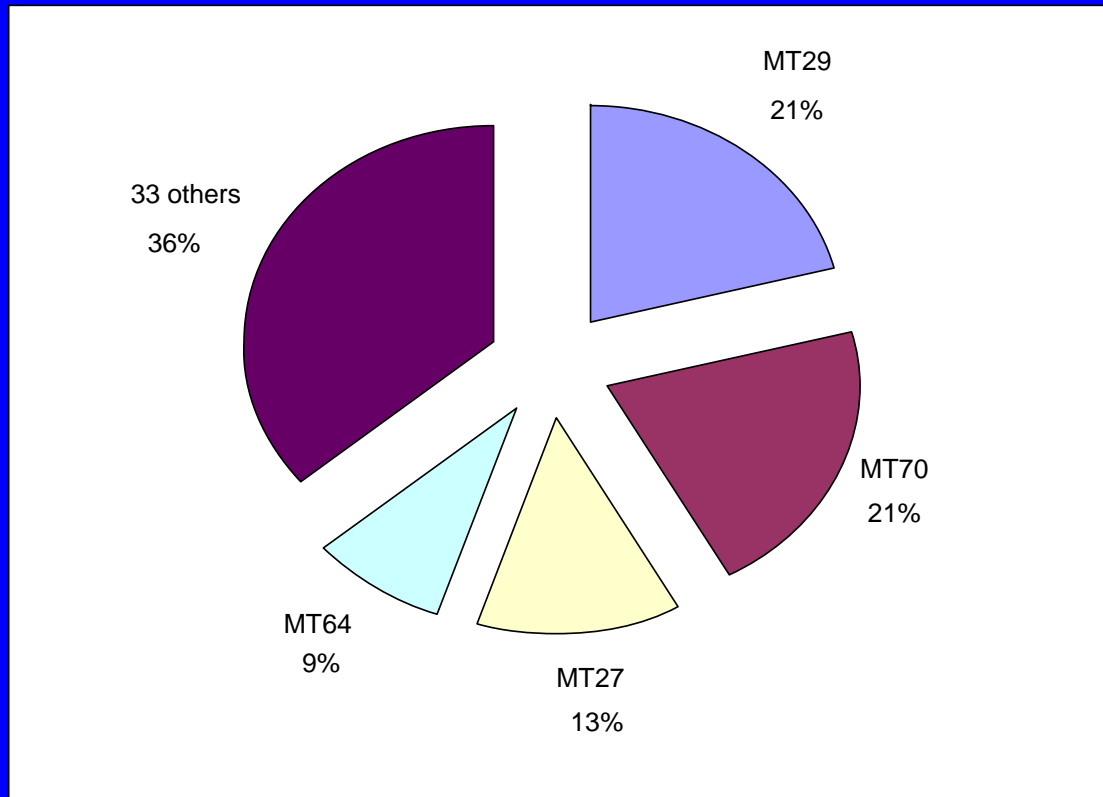
# 4 questions

- Is *B. pertussis* changing?
- Are the changes in response to vaccination?
- Are these changes advantageous to the bacterium?
- How can we use this information to control pertussis?

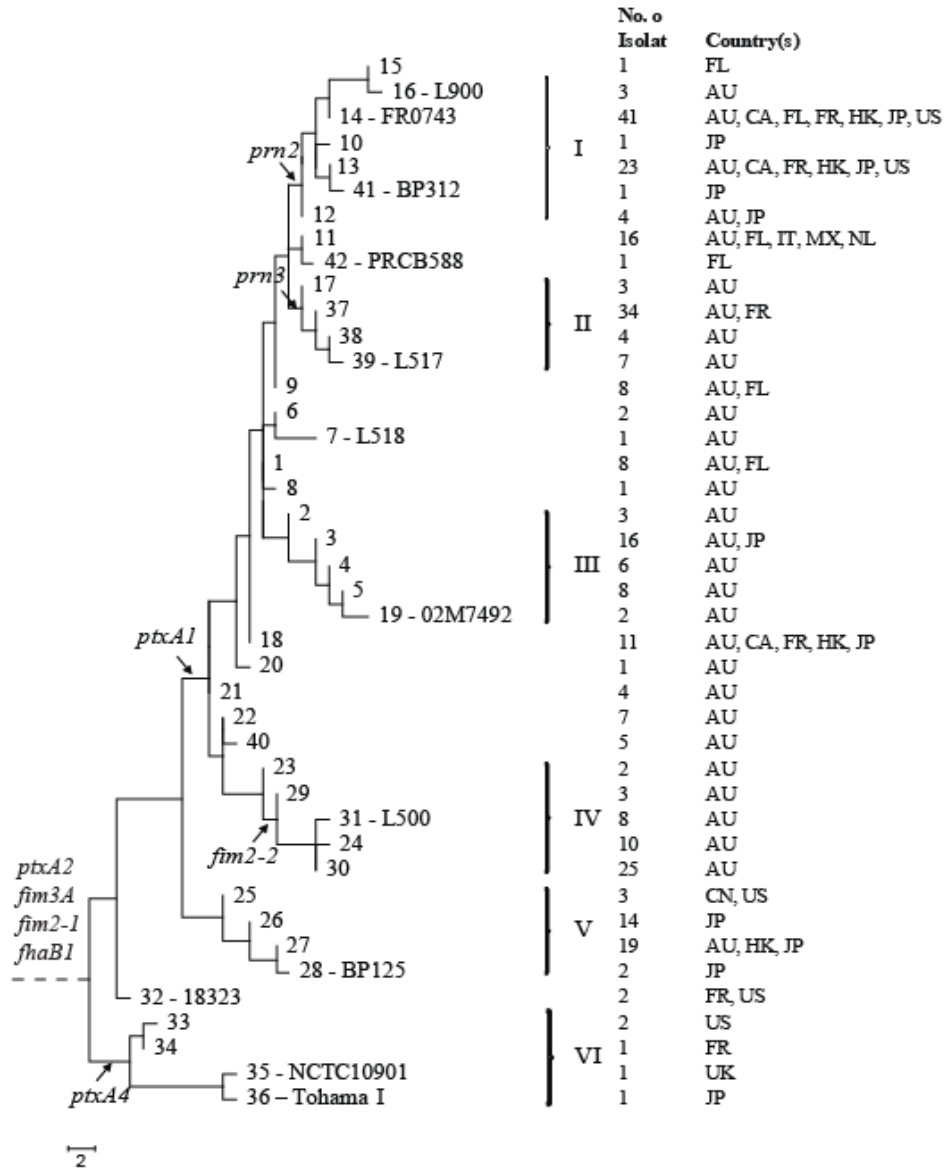
# Is *B. pertussis* changing?

- Neutral markers:
  - Multilocus variable number tandem repeats analysis (MLVA)
  - Single nucleotide polymorphism typing (SNP typing)
- Isolates from over 40 years
- Isolates from the recent epidemic

# Major Australian MLVA types



# SNP types

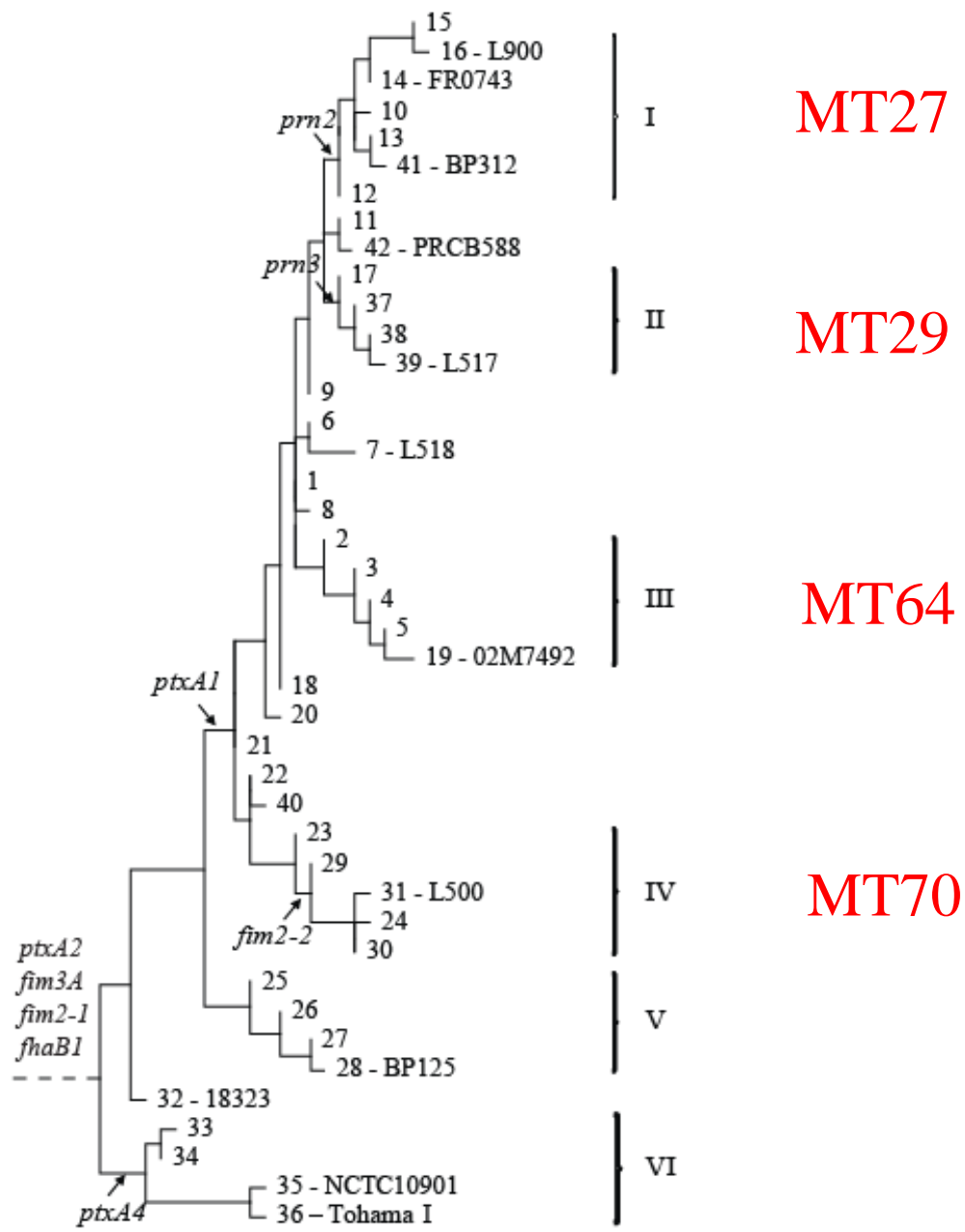


Australian  
isolates

Other  
international  
isolates

Japan isolates

Old isolates

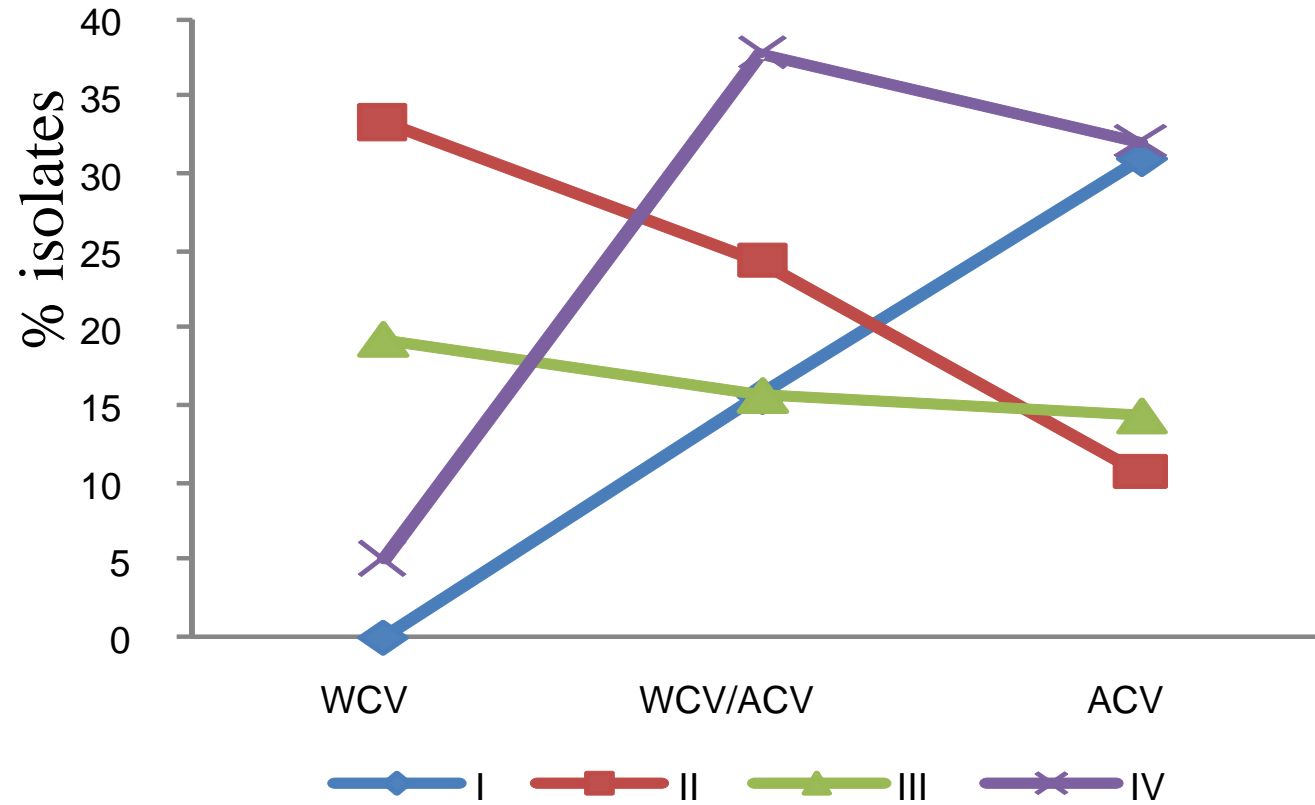


Are the changes in response to  
vaccination?

# Vaccines

- Whole cell vaccine (WCV): 1950s to 1997
- Acellular vaccine (ACV): 2000 onwards
- Transition period, WCV or ACV: 1997-1999

# Frequency of SNP clusters by vaccine period in Australia



# Variation in genes encoding acellular vaccine antigens

- Acellular vaccine (ACV) components:
  - Pertactin (Prn)
  - Pertussis toxin (PTX)
  - Filamentous haemagglutinin (FHA)
  - Fimbriae (Fim2 and Fim3)
- *ptxP* – pertussis toxin promoter

# Antigenic gene variation

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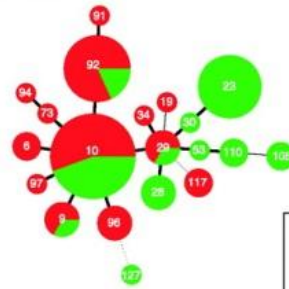
	Prn	Ptx(A)	FhaB	Fim2	Fim3
ACV	1	A2	1	2-1	3-A
Cluster I	2	A1	1	2-1	3-A/B
Cluster II	3	A1	1	2-1	3-A
Cluster III	1	A1	1	2-1	3-A
Cluster IV	1	A1	1	2-2	3-A

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# Strain variation in other parts of the world

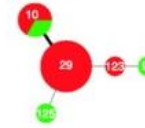
# UK

a) Pre-vaccine



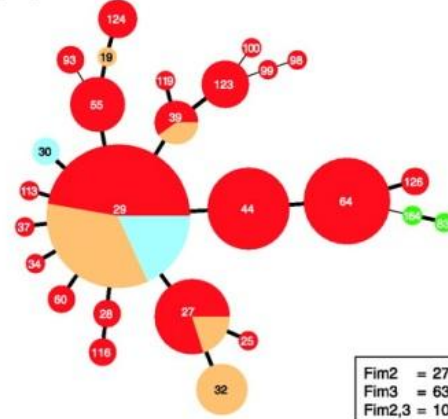
Fim2	= 58%
Fim3	= 2%
Fim2,3	= 13%
Fim <sup>-</sup>	= 21%

b) Early post-vaccine



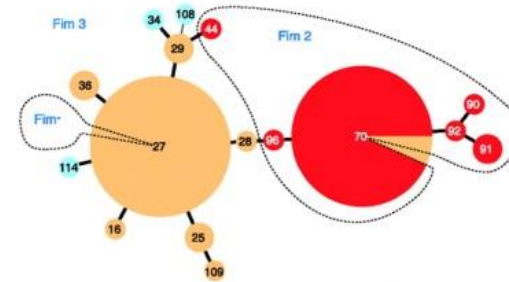
Fim2	= 16%
Fim3	= 38%
Fim2,3	= 38%
Fim <sup>-</sup>	= 8%

c) Epidemic



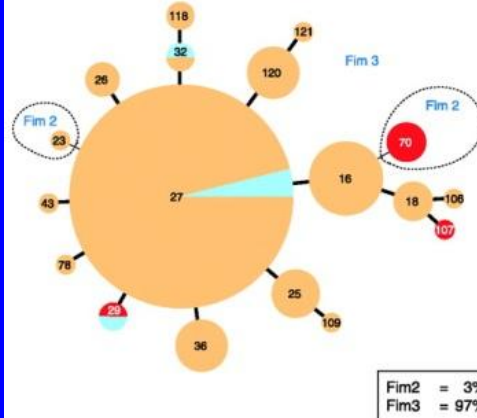
Fim2	= 27%
Fim3	= 63%
Fim2,3	= 10%

d) Vaccination recovery



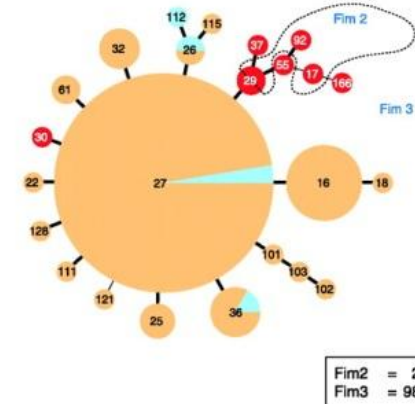
Fim2	= 47%
Fim3	= 52%
Fim <sup>-</sup>	= 1%

e) Post addition of ACV booster



Fim2	= 3%
Fim3	= 97%

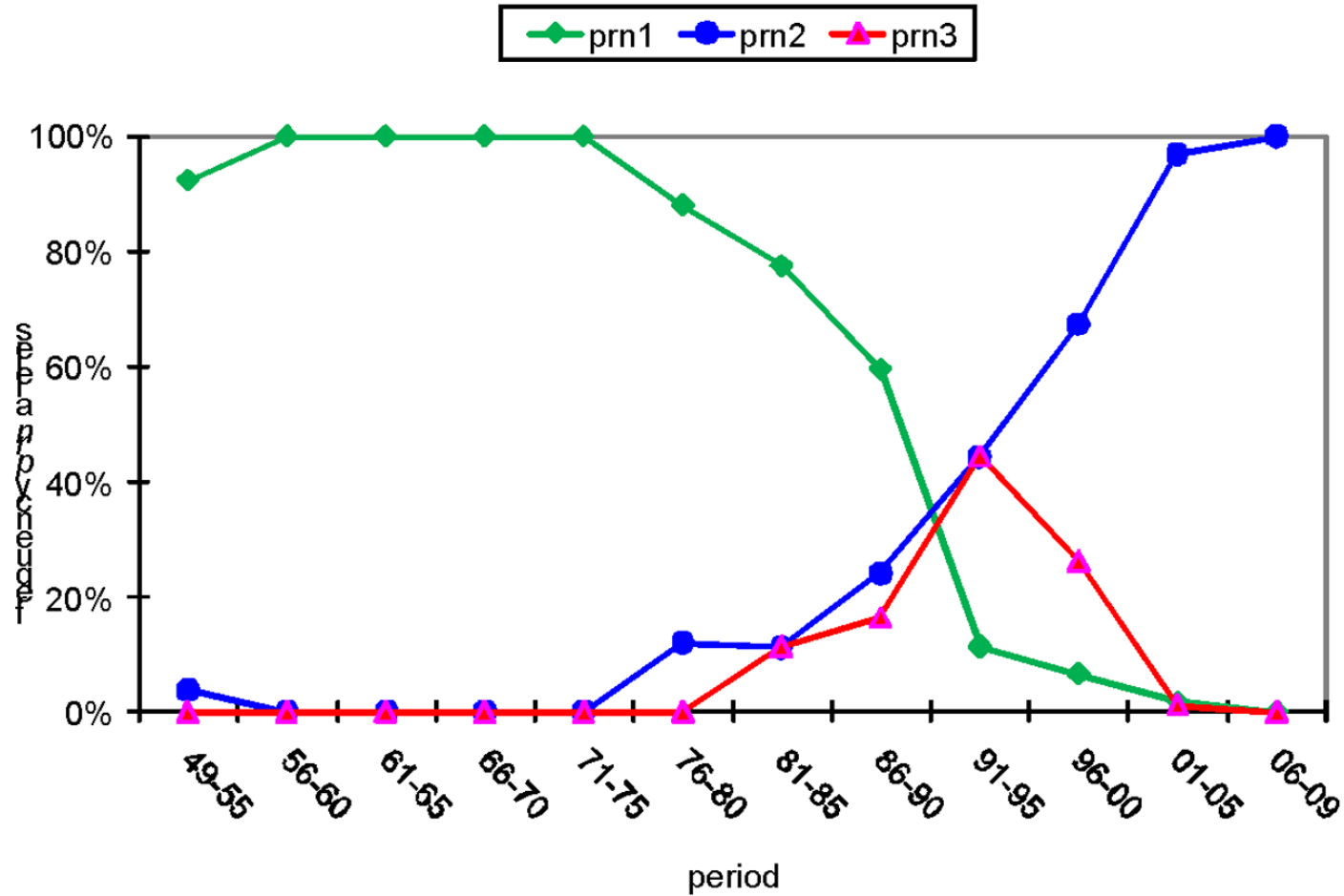
f) Post complete switch to ACV



Fim2	= 2%
Fim3	= 98%

● *prnA(1) + ptxA(1)*   ● *prnA(2) + ptxA(1)*   ● *prnA(3) + ptxA(1)*   ● *prnA(1) + ptxA(2)*

# The Netherlands

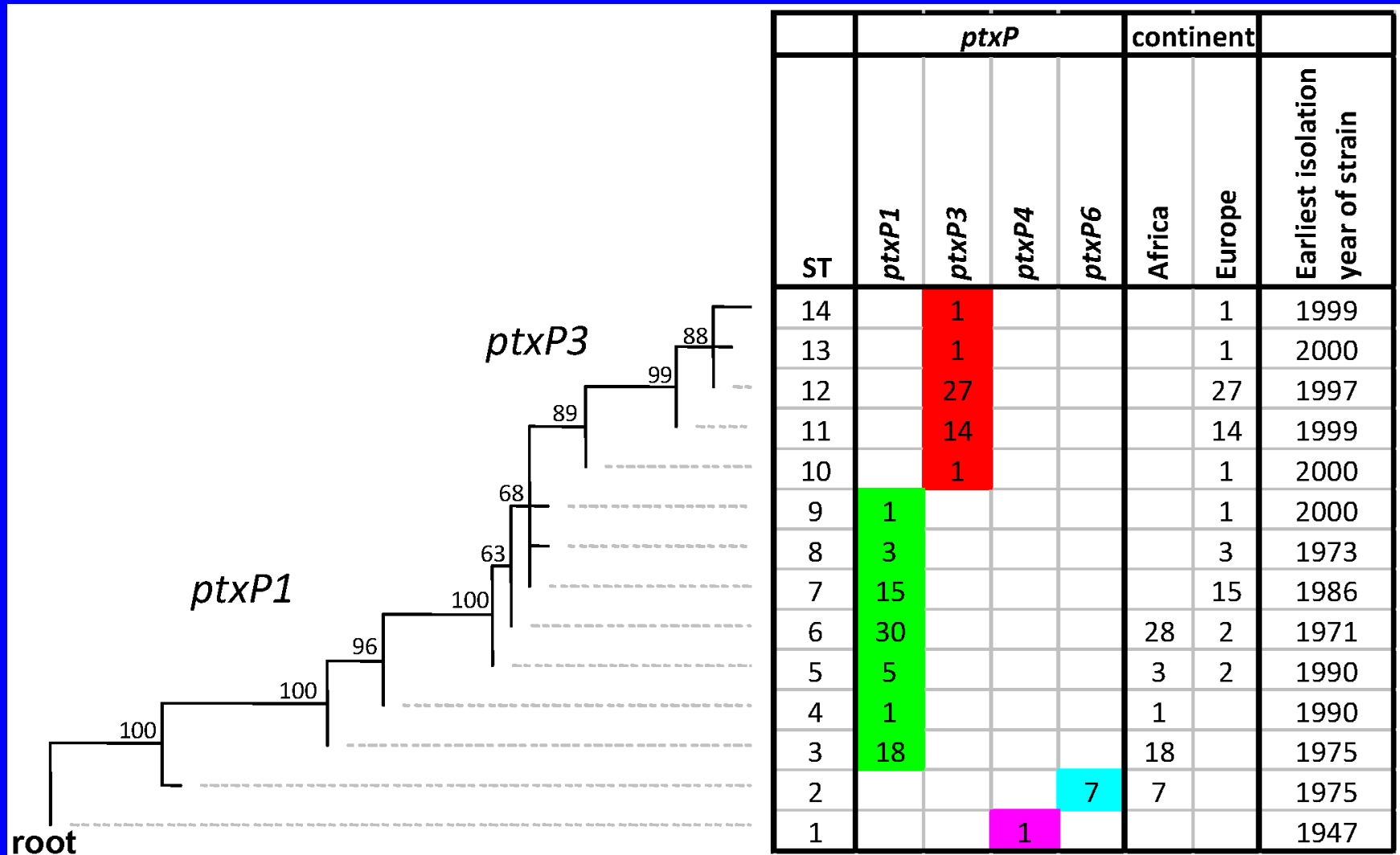


# Sweden

Distribution of *ptxP* alleles in strains collected during 1997 until 2006 in the Gothenburg area and in the Rest of Sweden.

		Area for sample		Total
		Gothenburg	Rest of Sweden	
<i>ptxP</i> allele	1	109 (21)	998 (33)	1107 (32)
Number (%)	3	403 (79)	2001 (67)	2404 (69)
Total		512 (100)	2999 (100)	3511 (100)

# Europe (Netherlands and Sweden)



Are the changes advantageous?

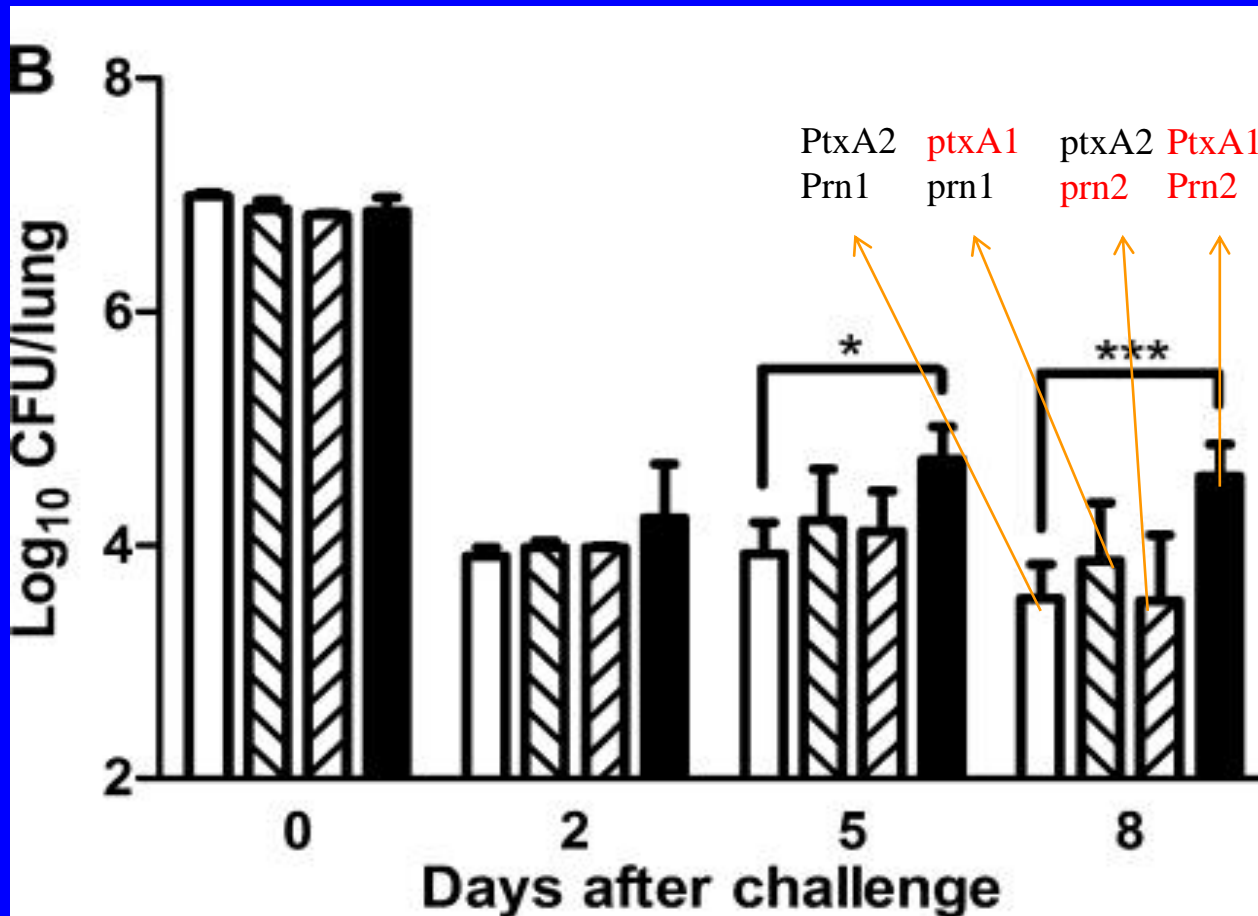
# Prn2

- Allelic specific epitope
  - Prn type-specific antibodies (He *et al.* 2003)
  - advantage
- Mouse colonisation
  - Prn1>Prn2 and Prn3 (van Gent *et al.* 2011)
  - Disadvantage

# *ptxP3* and pertussis toxin

- *ptxp3* versus *ptxp1* [Mooi *et al.* (2009)]
  - Increases Ptx production (PtxA1) 1.6x
  - More virulent

# Mouse challenge experiments



# How can we use this information to control pertussis?

## Vaccine

- Prn1
- PtxA2

## Strain

- Prn2
- PtxA1
- *ptxP3*

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