



# *Pseudomonas aeruginosa* CAUTI

CAUTI Technology Workshop  
NIDDK

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# CAUTI is caused by specific pathogens associated with the microbiome

TABLE 4. Distribution and Rank Order of Selected Pathogens Associated With Cases of Healthcare-Associated Infection (HAI) Reported to the National Healthcare Safety Network, January 2006–October 2007, by Type of HAI

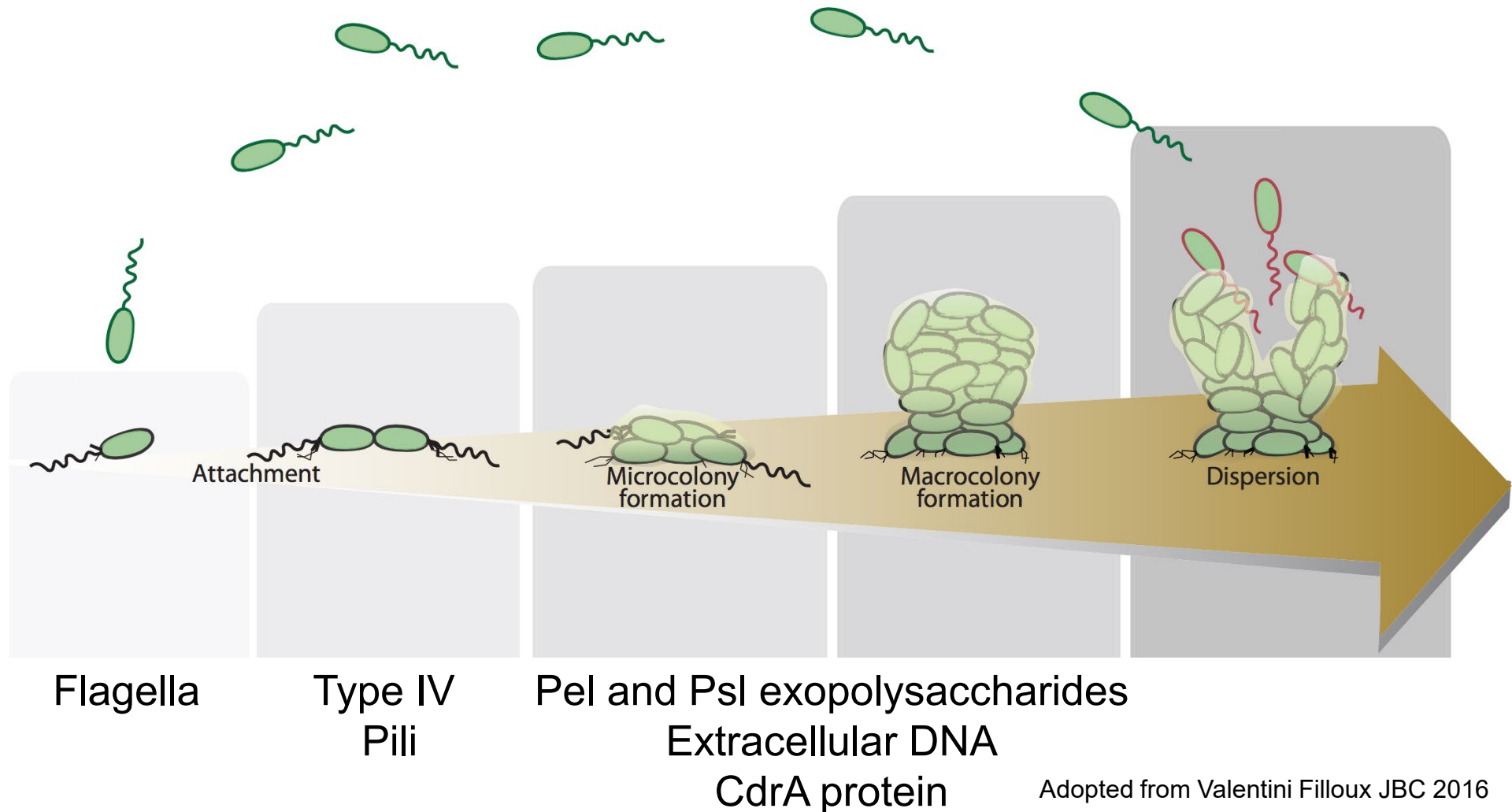
Pathogen	Overall <sup>a</sup>		CLABSI		CAUTI		VAP		SSI	
	No. (%) of pathogenic isolates	Rank	No. (%) of pathogenic isolates	Rank	No. (%) of pathogenic isolates	Rank	No. (%) of pathogenic isolates	Rank	No. (%) of pathogenic isolates	Rank
CoNS	5,178 (15.3)	1	3,900 (34.1)	1	234 (2.5)	7	79 (1.3)	9	965 (13.7)	2
<i>Staphylococcus aureus</i>	4,913 (14.5)	2	1,127 (9.9)	4	208 (2.2)	8	1,456 (24.4)	1	2,108 (30.0)	1
<i>Enterococcus</i> species		3		2		3		10		3
<i>E. faecalis</i>	1,177 (3.5)		627 (5.5)		335 (3.6)		21 (0.4)		194 (2.8)	
<i>E. faecium</i>	1,888 (5.6)		942 (8.2)		562 (6.0)		38 (0.6)		345 (4.9)	
NOS	1,028 (3.0)		265 (2.3)		496 (5.3)		18 (0.3)		249 (3.5)	
<i>Candida</i> species		4		3		2		7		8
<i>C. albicans</i>	2,295 (6.8)		673 (5.9)		1,361 (14.5)		140 (2.4)		115 (1.6)	
Other <i>Candida</i> spp. or NOS	1,333 (3.9)		669 (5.9)		613 (6.5)		20 (0.3)		30 (0.4)	
<i>Escherichia coli</i>	3,264 (9.6)	5	310 (2.7)	8	2,009 (21.4)	1	271 (4.6)	6	671 (9.6)	4
<i>Pseudomonas aeruginosa</i>	2,664 (7.9)	6	357 (3.1)	7	938 (10.0)	4	972 (16.3)	2	390 (5.6)	5
<i>Klebsiella pneumoniae</i>	1,956 (5.8)	7	563 (4.9)	5	722 (7.7)	5	446 (7.5)	5	213 (3.0)	7
<i>Enterobacter</i> species	1,624 (4.8)	8	443 (3.9)	6	384 (4.1)	6	498 (8.4)	3	293 (4.2)	6
<i>Acinetobacter baumannii</i>	902 (2.7)	9	252 (2.2)	9	109 (1.2)	9	498 (8.4)	3	42 (0.6)	9
<i>Klebsiella oxytoca</i>	359 (1.1)	10	99 (0.9)	10	85 (0.9)	10	128 (2.2)	8	47 (0.7)	9
Other	5,267 (15.6)		1,201 (10.5)		1,321 (14.1)		1,375 (23.1)		1,363 (19.4)	
Total	33,848 (100)		11,428 (100)		9,377 (100)		5,960 (100)		7,025 (100)	

NOTE. Of the 28,502 cases of HAI reported, 4,671 (16.4%) were polymicrobial. CAUTI, catheter-associated urinary tract infection; CLABSI, central line-associated bloodstream infection; CoNS, coagulase-negative staphylococci; NOS, not otherwise specified; SSI, surgical site infection; VAP, ventilator-associated pneumonia.

*P. aeruginosa* is an important CAUTI pathogen that is NOT associated with the microbiome



# *P. aeruginosa* as a model for biofilm formation



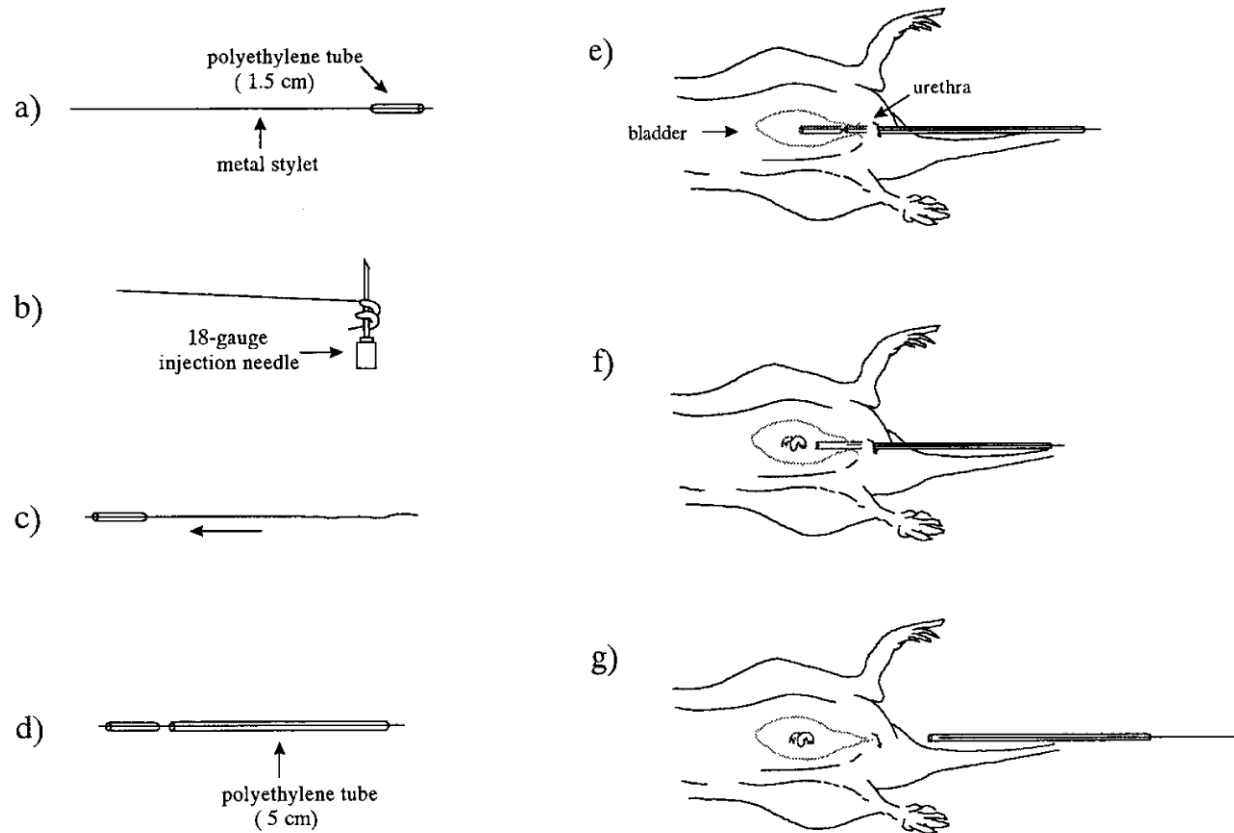


# Key questions

- Does *P. aeruginosa* form a biofilm on the catheter during CAUTI?
- How does *P. aeruginosa* form a biofilm on the catheter? What biofilm factors are used?
- What is the response of *P. aeruginosa* to urine?
- What is role of quorum-sensing for *P. aeruginosa* CAUTI?



# Murine model of catheter-associated urinary tract infection (CAUTI)



Mice are CF-1 outbred mouse to better mimic human populations

Infect for 7-14 days (time when *P. aeruginosa* is cleared in the absence of catheter)



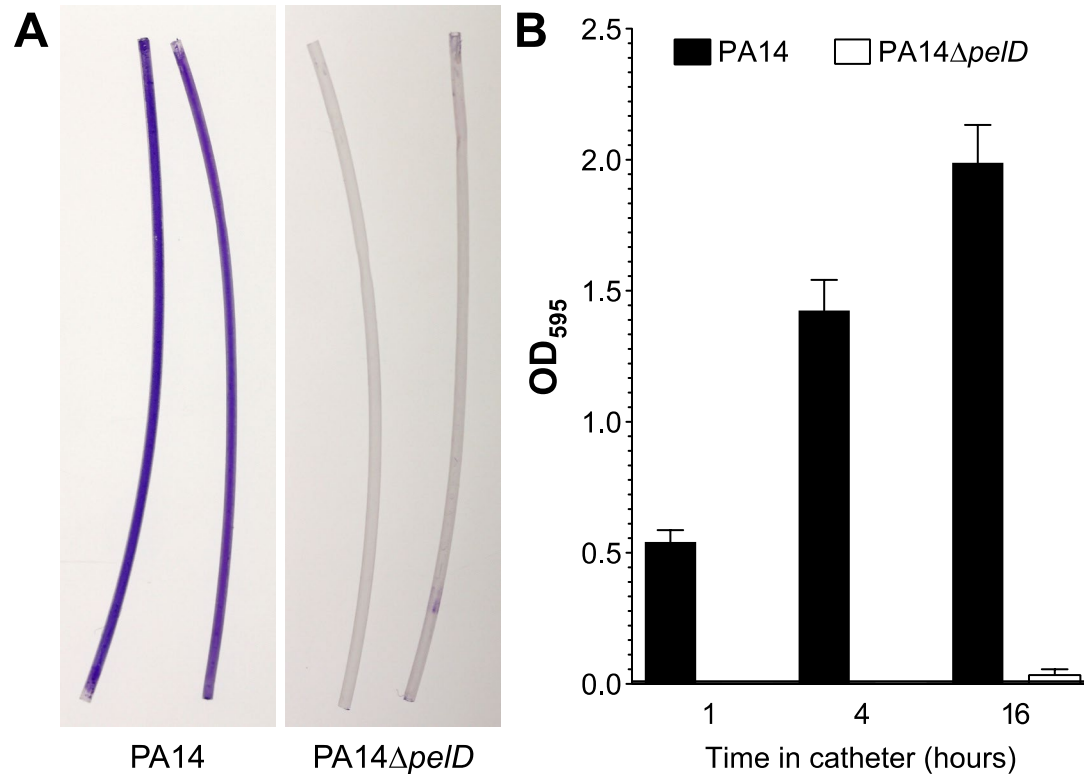
# *P. aeruginosa* uses exopolysaccharides to form biofilm on catheters *in vitro*



Angela Records



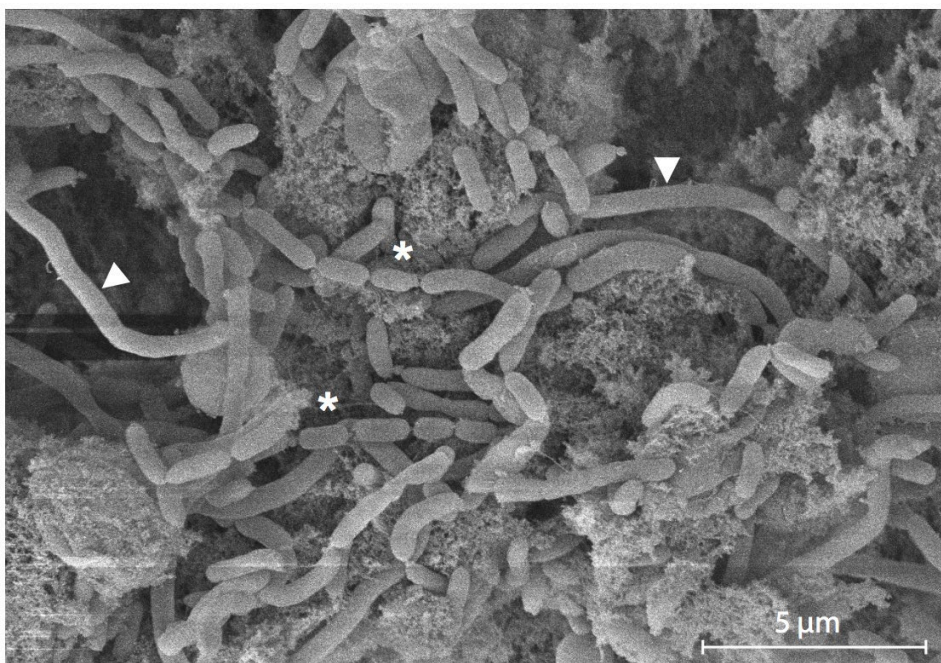
Stephanie Cole



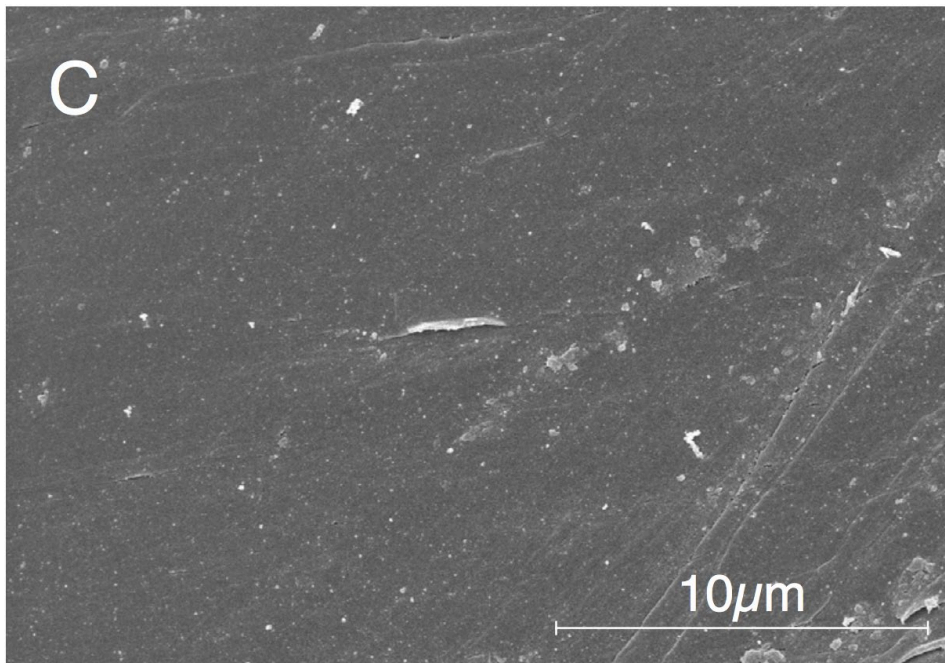


# *P. aeruginosa* forms a biofilm in the catheter during infection

Interior of catheter



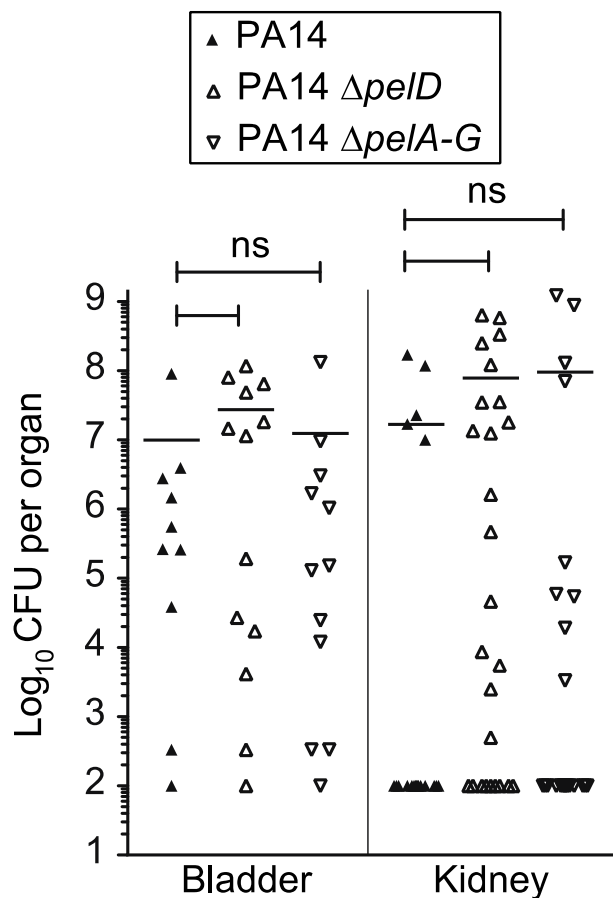
Exterior of catheter



SEM of the catheter and bladder reveals *P. aeruginosa* only  
in the interior of the catheter



# *P. aeruginosa* do not use Pel and Psl exopolysaccharides during CAUTI



1. There is a wide distribution of CFU/organ in outbred mice
2. Most mice with pyelonephritis have bacteria in the bladder
3. Most CFU in the bladder are associated with the catheter
4. *P. aeruginosa* forms biofilm independent of known biofilm exopolysaccharides

Similar results were obtained for PAO1





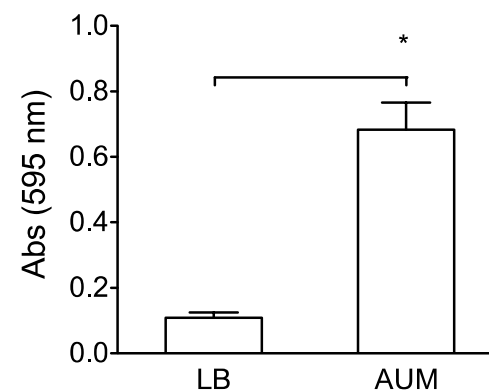
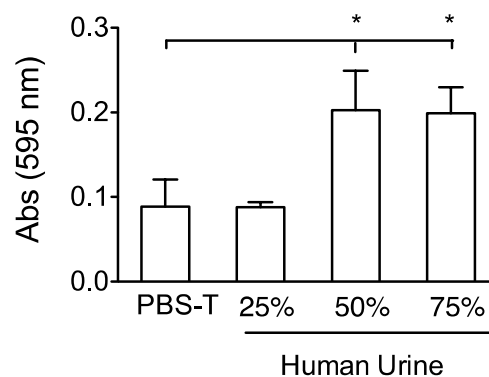
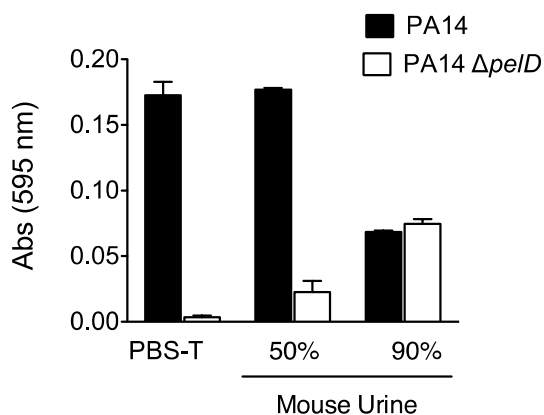
# What is triggering PA14 $\Delta peiD$ to form a PEL and PSL independent biofilm?

Two possibilities (that are not mutually exclusive):

1. The luminal contents of the bladder triggers a novel biofilm pathway
2. The host response triggers a novel biofilm pathway

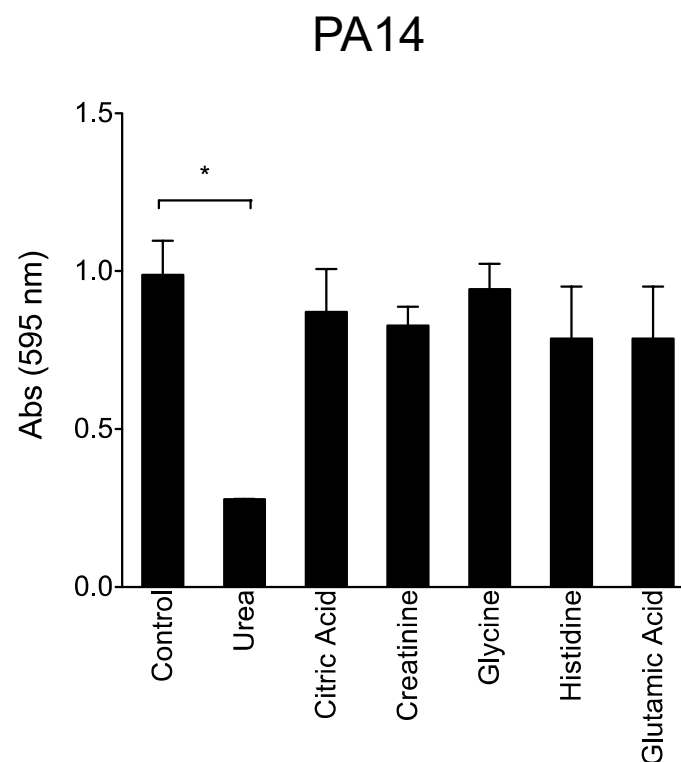
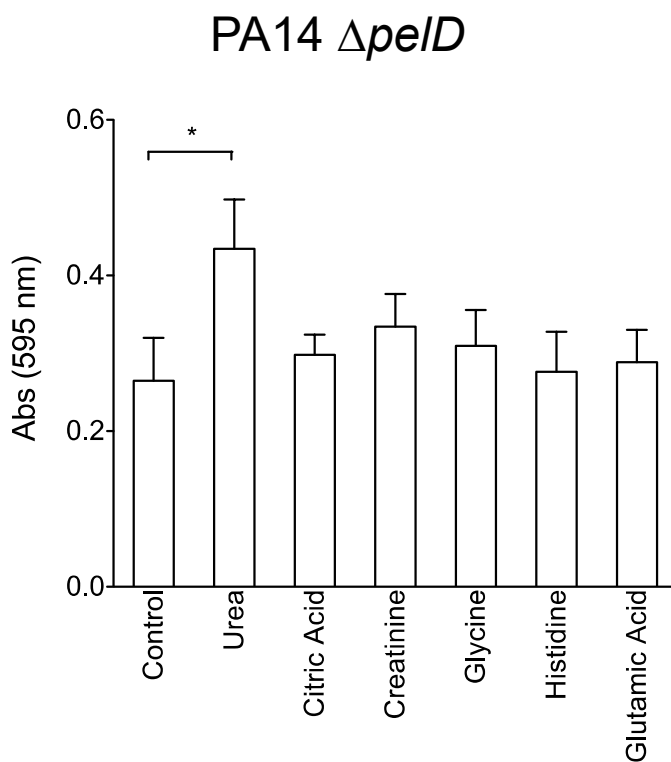


# Urine can induce PA14 $\Delta pe/D$ to form biofilm



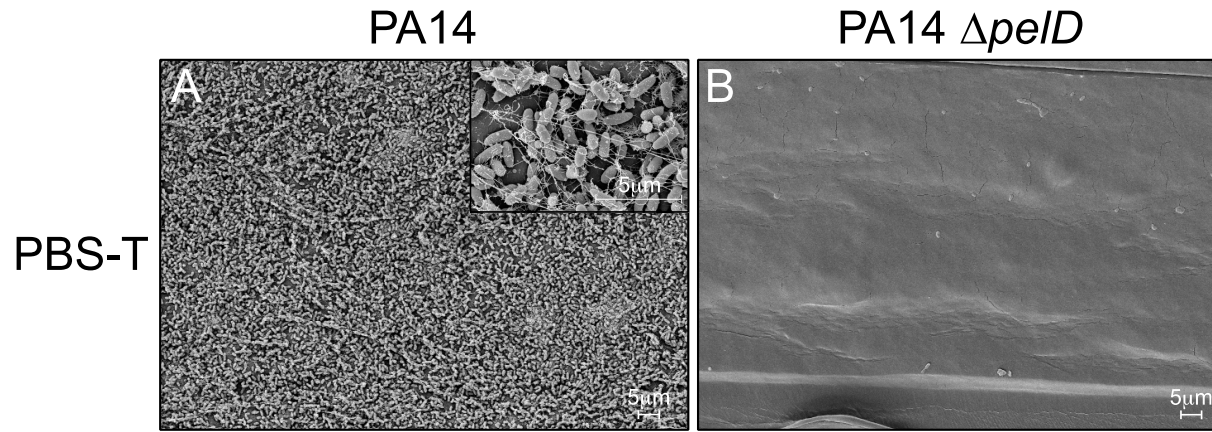


# Urea in urine triggers the alternate *P. aeruginosa* biofilm pathway





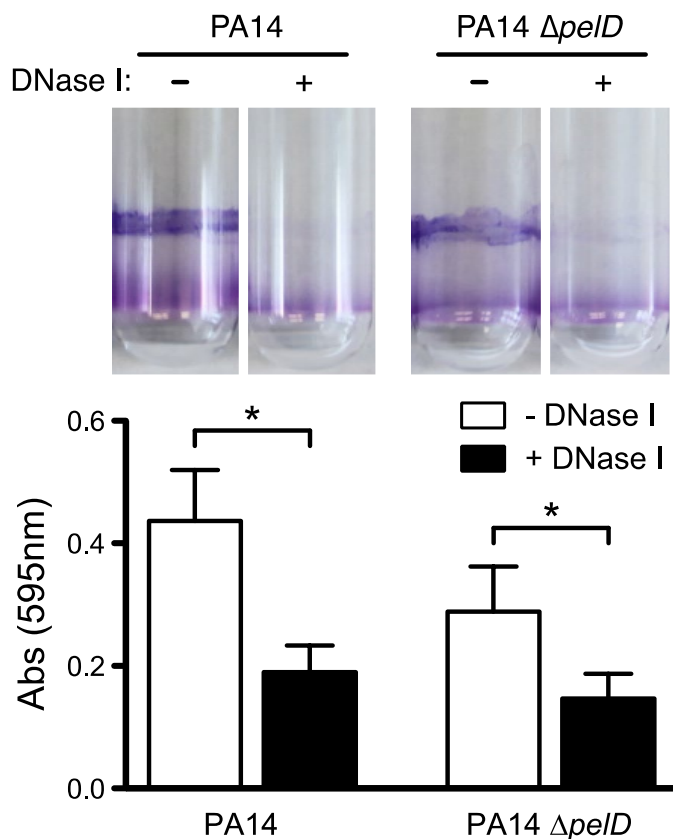
# Urea alters *P. aeruginosa* biofilms morphology



Urea triggers a heterogeneous biofilm for both PA14 and the  $\Delta peiD$  mutant



# Urea induced *P. aeruginosa* biofilms are sensitive to Dnase I



Conclusion: Urea in urine induces *P. aeruginosa* to form a DNA dependent biofilm