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Individual Patterns of Complexity in Cystic Fibrosis Lung Microbiota, Including Predator Bacteria, over a 1-Year Period

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A wide range of bacterial species in the CF lung microbiota. Microbiological cultures of the samples demonstrated chronic lung colonization by CF pathogens, including *P. aeruginosa* (11 patients), *S. aureus* (11 patients), *Burkholderia* species (1 patient), and *Pandora* species (1 patient). *P. aeruginosa* and *S. aureus* cocolonization was observed in the eight patients with the poorest lung function (Table 1). MRSA isolates were not detected.

TABLE 1 Clinical characteristics of the patients included in this study with the chronic and acute antibiotic treatments received during the study

Lung function Impairment and patient no.	FEV ₁ (%)	Sex ^a	Age (yr)	Chronic treatment (route) ^b	Exacerbation treatment(s) (no. of incidents)			Cultured pathogens ^c
					Inhaled	Oral	Intravenous	
Mild								
1	90	F	40	TOB (inh), ATM (inh)		CIP (2), AZM (2)		Hp, Pa, Sm
2	87	M	39			MIN (2), MOX (2)	VAN, CFX	Sm, Hi, Sa, Hp
3	80	F	38	COL (inh)		CIP (6), FOS (3), SXT, AZM		Pa, Sw
4	80	M	19	COL (inh)		CFX (4), CIP		Sa, Hp, Hpitt, Pa
5	75	F	40	COL (inh)		CIP		Sa, Bv, Bc, Hp, Pa
Moderate								
6	73	M	36	COL (inh)	AMP	AMC (6), MOX (2)		Hp, Sm, Cp, SI
7	62	F	32	COL (inh)		SXT (3), AMC	CIP, AMK	Sa, Ps, Hp, Hp, Mm
8	61	F	34	AZM (p.o.), ATM (inh)		AZM, FOS, LEV	TOB (2), PTZ, CFT	Hp, Pa, Sw, Sm
9	61	F	29	AZM (p.o.)	AMP	AMC (4)	MER, AMC	Sa, Hp, Hpitt, A
10	60	F	49		TOB	MOX (3), AMC, SXT (7), CLO (7), CIP		Sa, Sm, Ca, Pa, Af
11	56	M	39	AZM (p.o.), COL (inh)		SXT (2)		Sa, Pa, Hp
12	52	F	21	TOB (inh)		CIP (3), AMC (2), AZM		Sa, Pa
13	52	F	19	COL (inh)		AZM		Pa, Sa
14	46	F	22	TOB (inh), AZM (p.o.)		AMC (2), SXT, LNZ (2)	TOB, PTZ	Pa, Sa, Cg
Severe								
15	28	F	28	COL (inh)	Col, ATM	CIP (3), LEV, SXT, ATM	MER (3), TOB (4), FOS, PTZ (3)	Hp, Sa, Pa

???

analysis to better monitor the lung microbiota (Fig. 1 to 3). The median number of operational taxonomic units (OTUs) in all of the samples was $16,780 \pm 14,670$ (range, 711 to 82,507); as expected, the lower number of reads corresponded to the patients with the poorest lung function (Fig. 1). Taxonomic genus assignment was incomplete in 10% of the total reads, and only the family taxon was ascribed to these sequences.

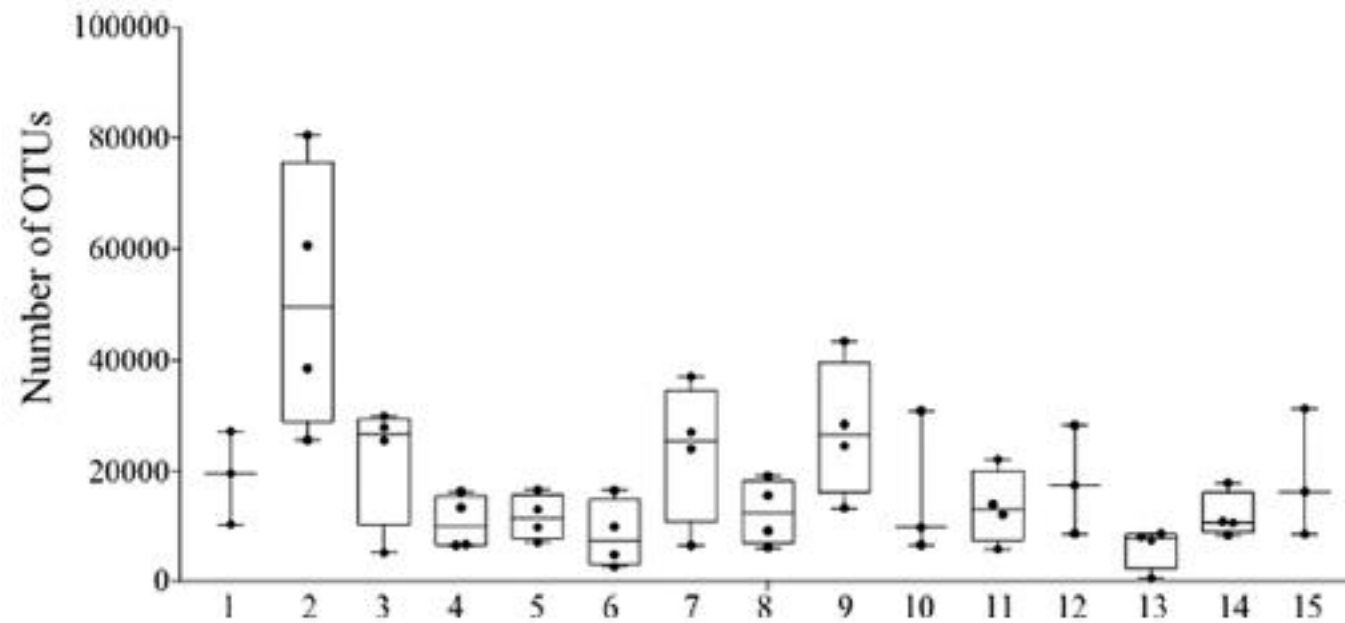


FIG 1 Biodiversity of the sputum samples used in this study. The median, minimum, and maximum numbers of OTUs in the samples are represented.

Phylum distribution of lung microbiome vary between patients and can fluctuate in patients over time

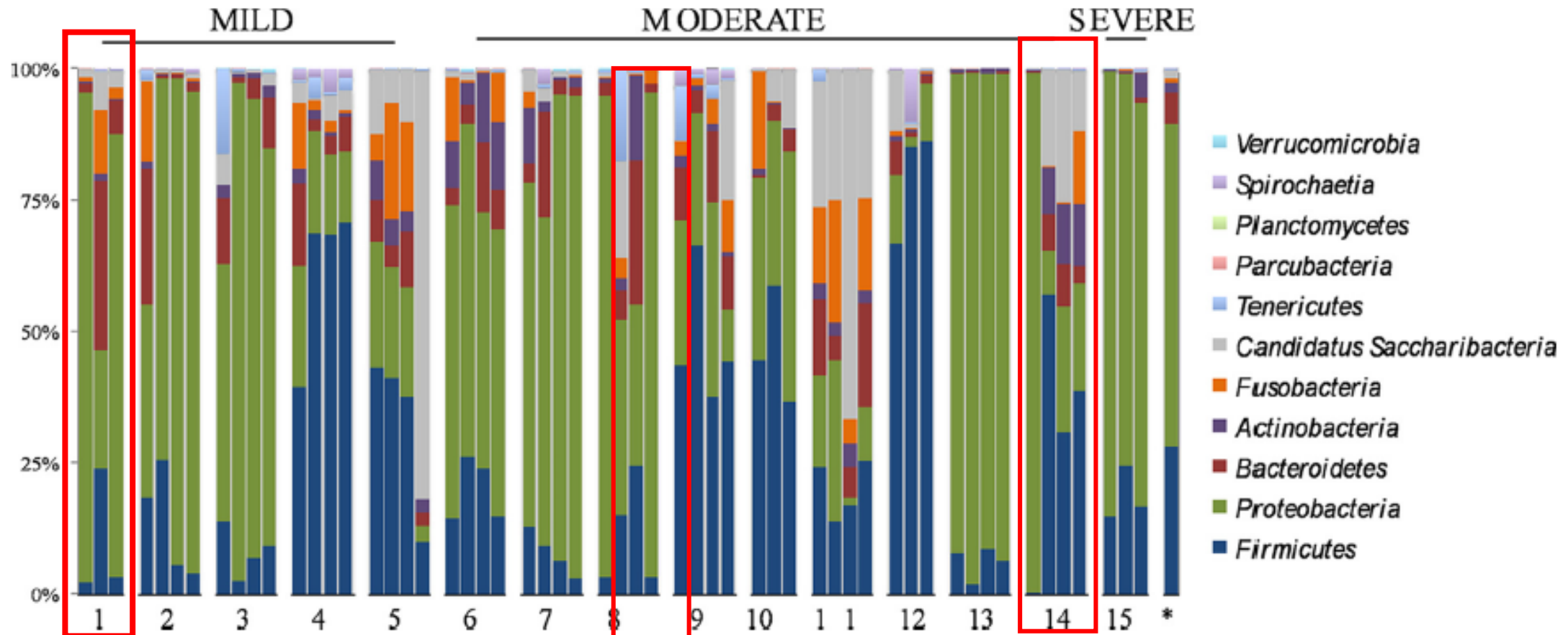


FIG 2 Phylum distribution in the samples from the 15 CF patients in this study. The last column (*) represents the median value of all 56 samples.

No association between detection of Predatory Bacteria and relative abundance of pathogens

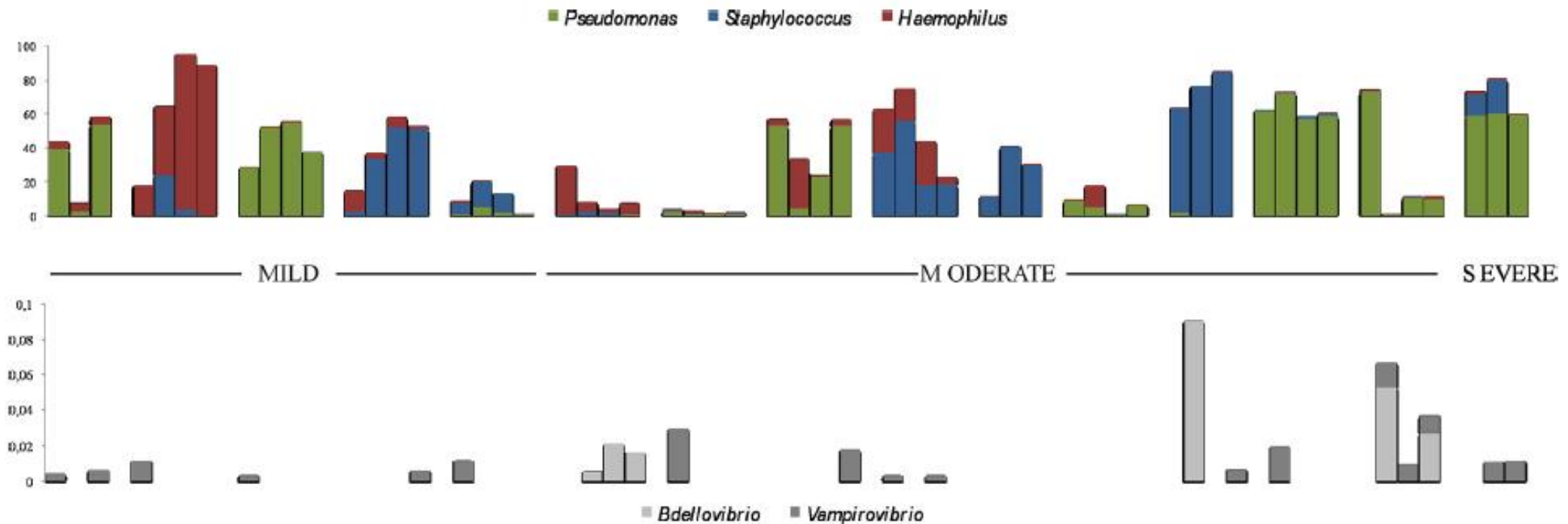


FIG 4 Numbers of OTUs of the main CF pathogens and predator species detected in the sputum samples.

Microbial predators can be periplasmic (penetrate and attach to the inner membrane), epibiotic (attach to the outside), endobiotic (penetrate the cytoplasm) or wolf-pack (swarming as a 'wolf-pack' towards prey, which they kill and degrade) --Soo *et al* 2015

Spatial Simulation using relative abundances of Pathogens and Predatory Bacteria predicts coexistence of *Pseudomonas* and *Bdellovibrio*

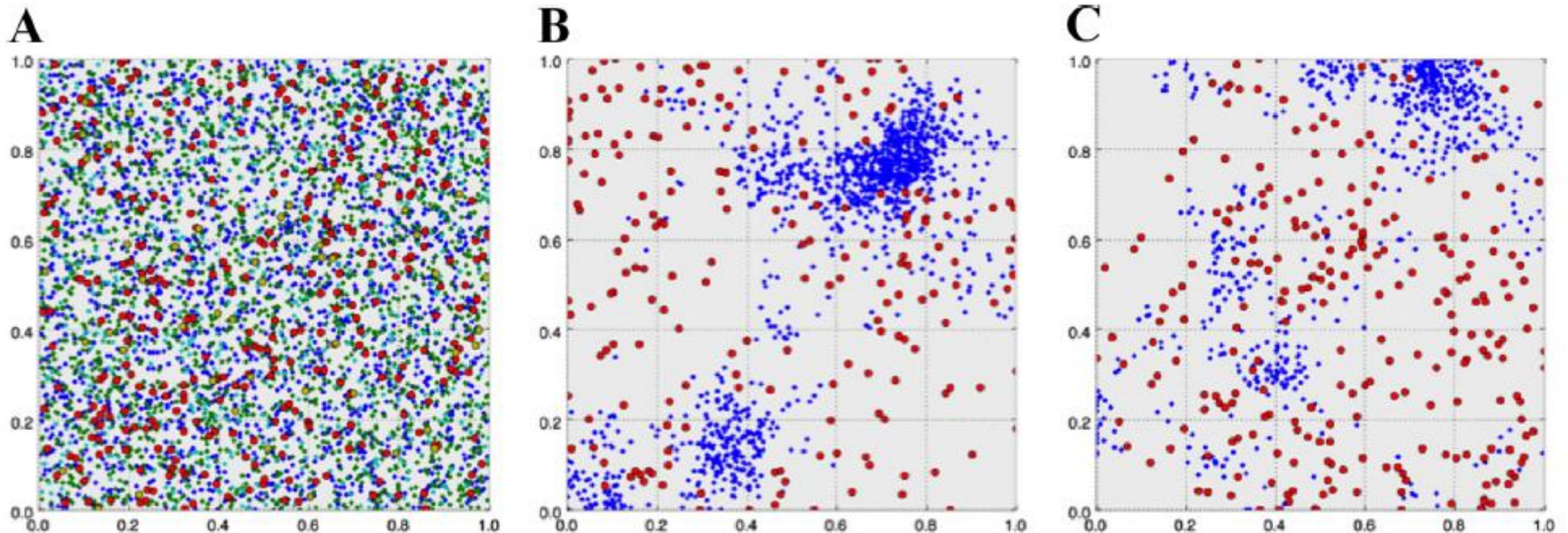


FIG 5 Spatial distribution of the bacteria in the computational model and evolution in time. (A) Random initial distribution of 5,000 bacteria of five different species (3,500 *Pseudomonas* [blue], 1,000 *Staphylococcus* [green], 350 *Haemophilus* [light blue], 100 *Bdellovibrio* [red], and 50 SPP [yellow] bacteria). (B) Spatial distribution at 2,500 arbitrary time units. (C) Spatial distribution at 5,000 arbitrary time units. Coexistence of *Pseudomonas* and *Bdellovibrio* was observed in evolved panels B and C after the other bacterial species disappeared.

If initial percentage of predatory bacteria is high enough, everyone dies

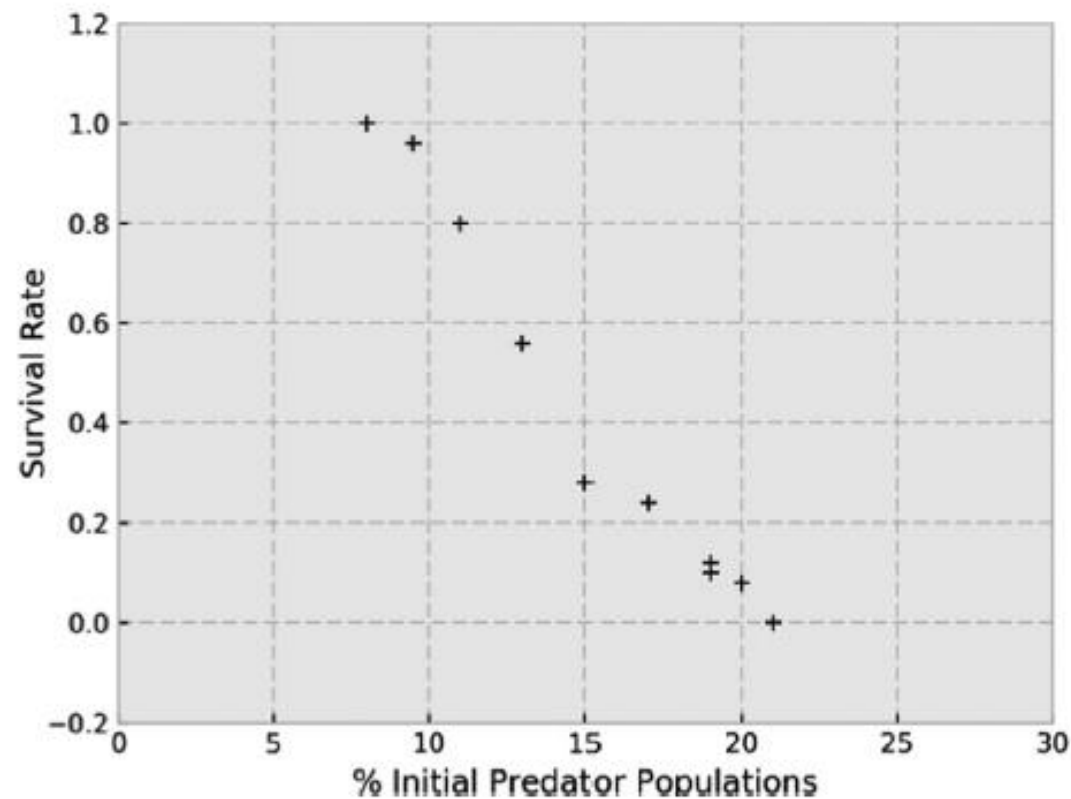

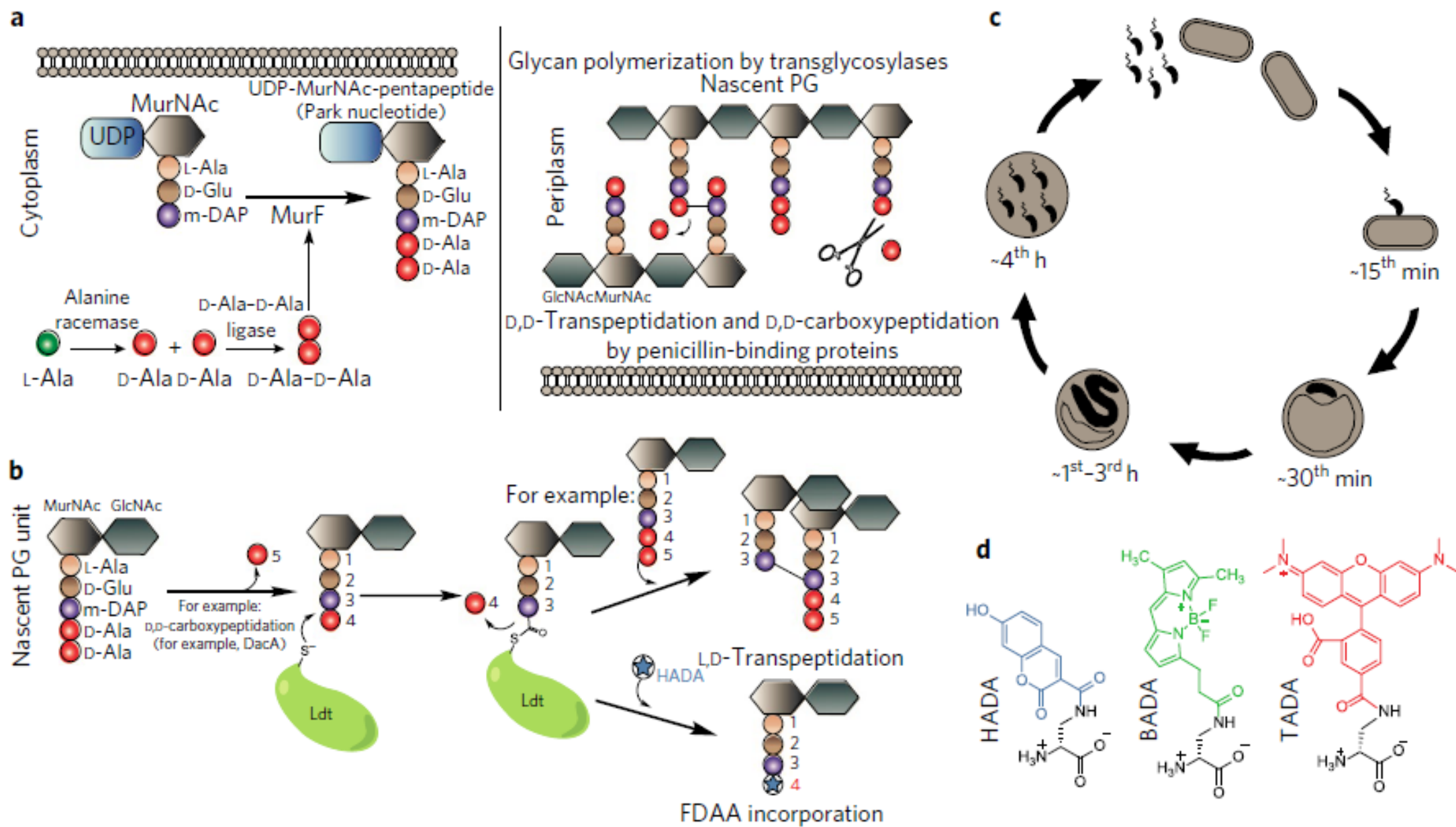
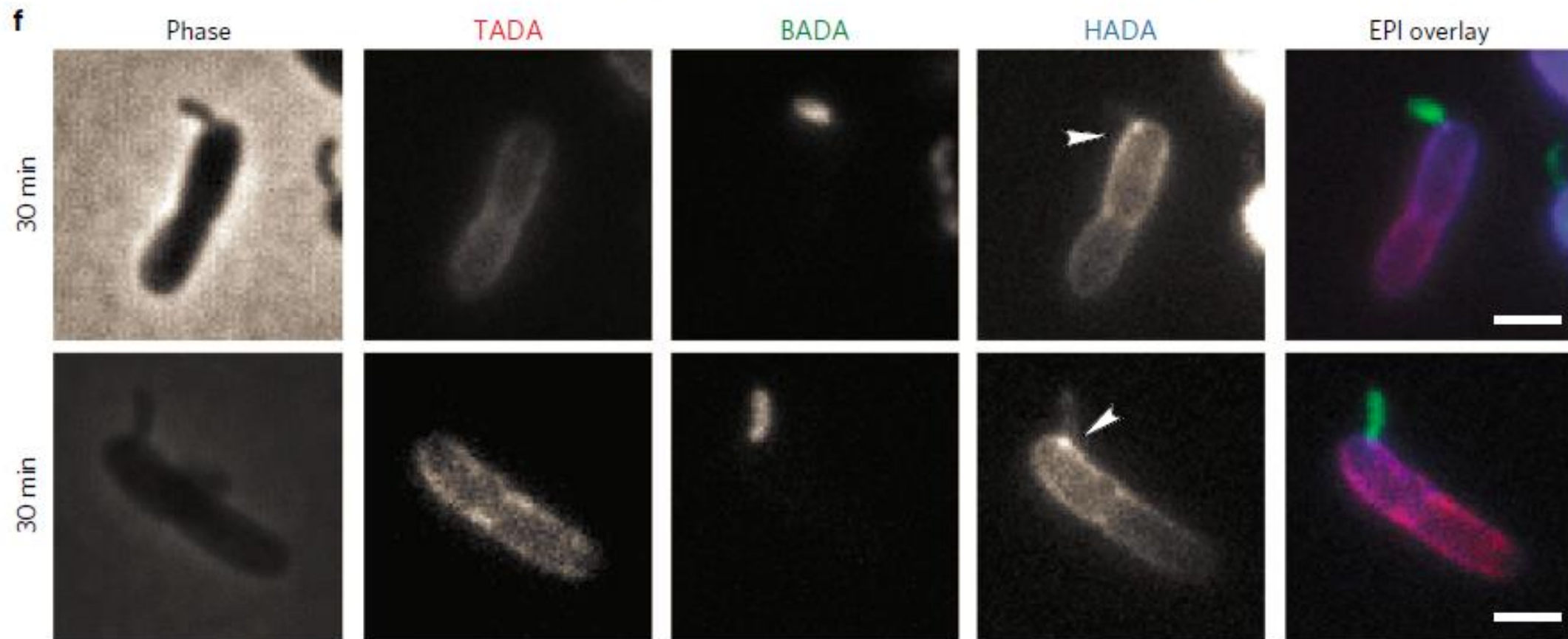
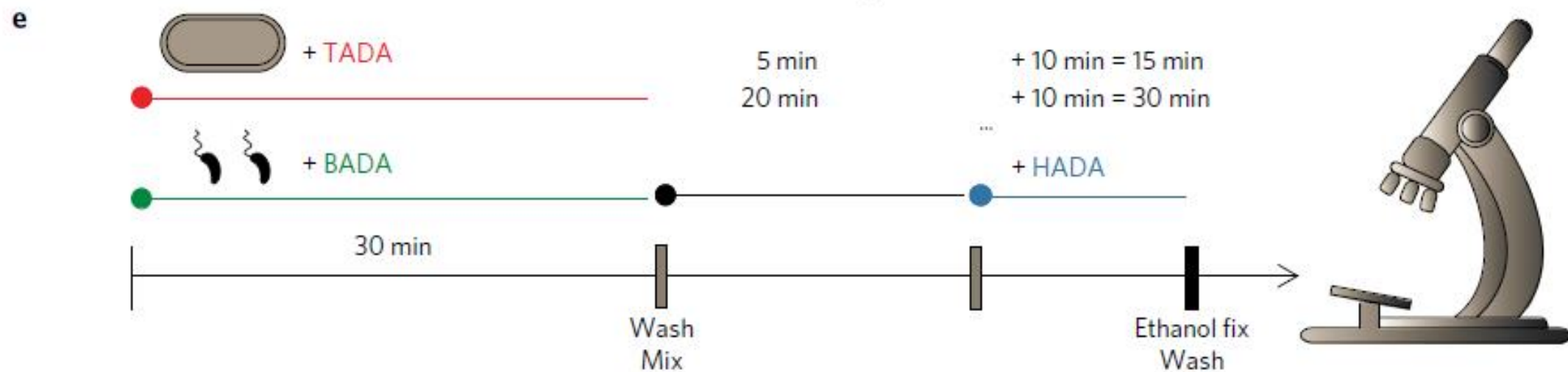


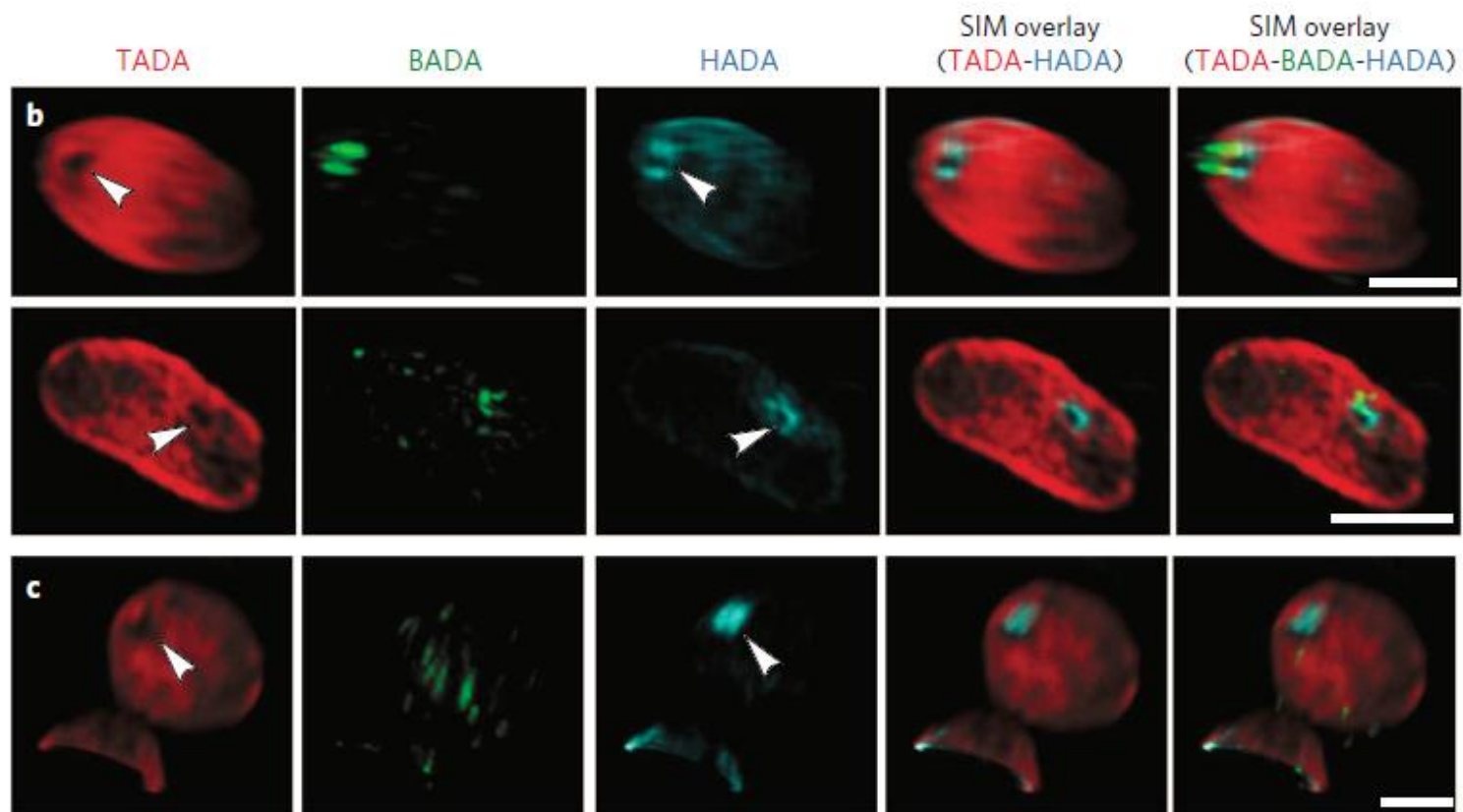
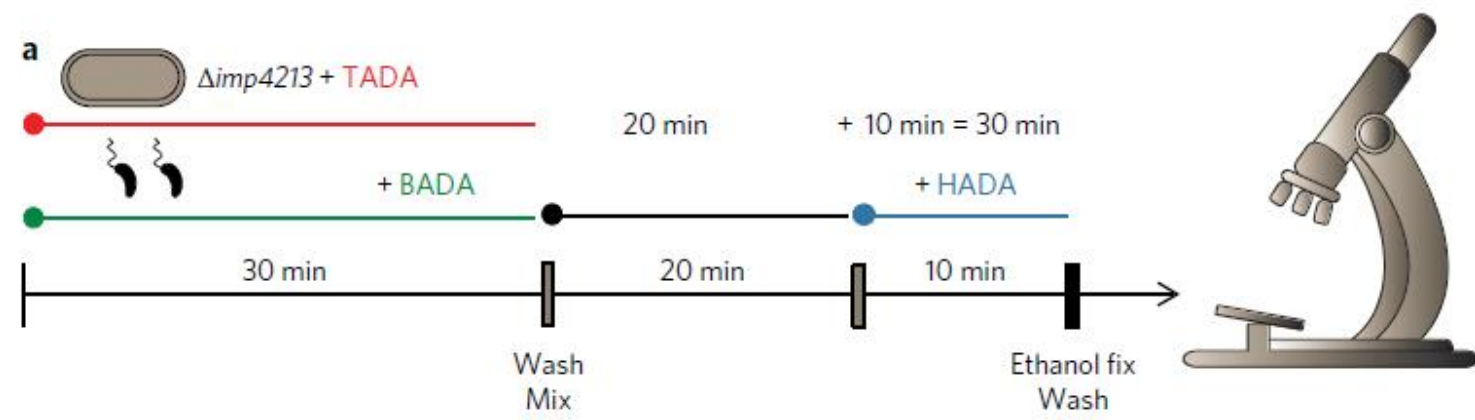
FIG 7 Survival rate versus initial percentage of predators to 50 repetitions. Initial populations that are <8% of the total bacteria in the simulations always survive, whereas initial populations that are >20% of the total bacteria always die.

Fluorescent D-amino-acids reveal bi-cellular cell wall modifications important for *Bdellovibrio bacteriovorus* predation

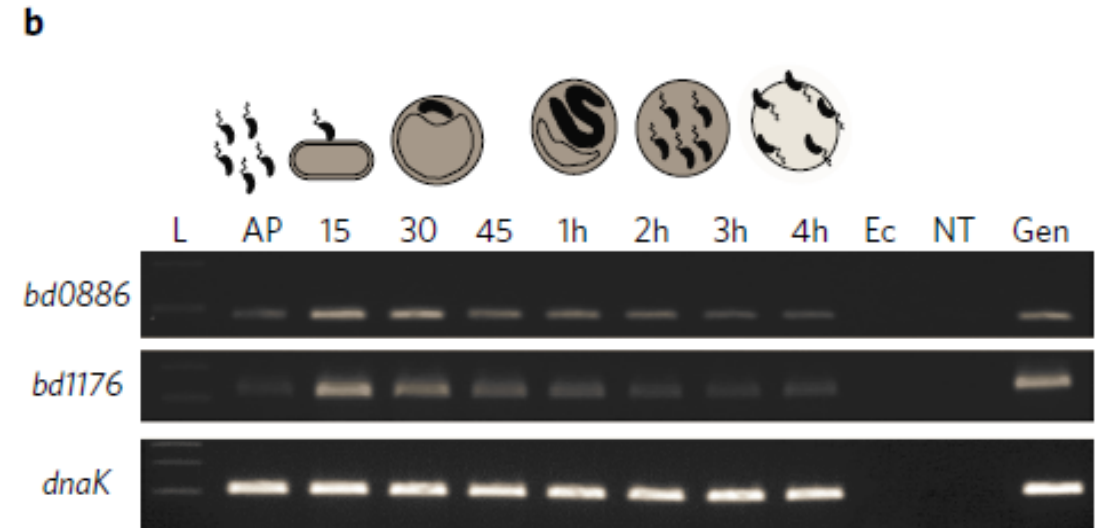
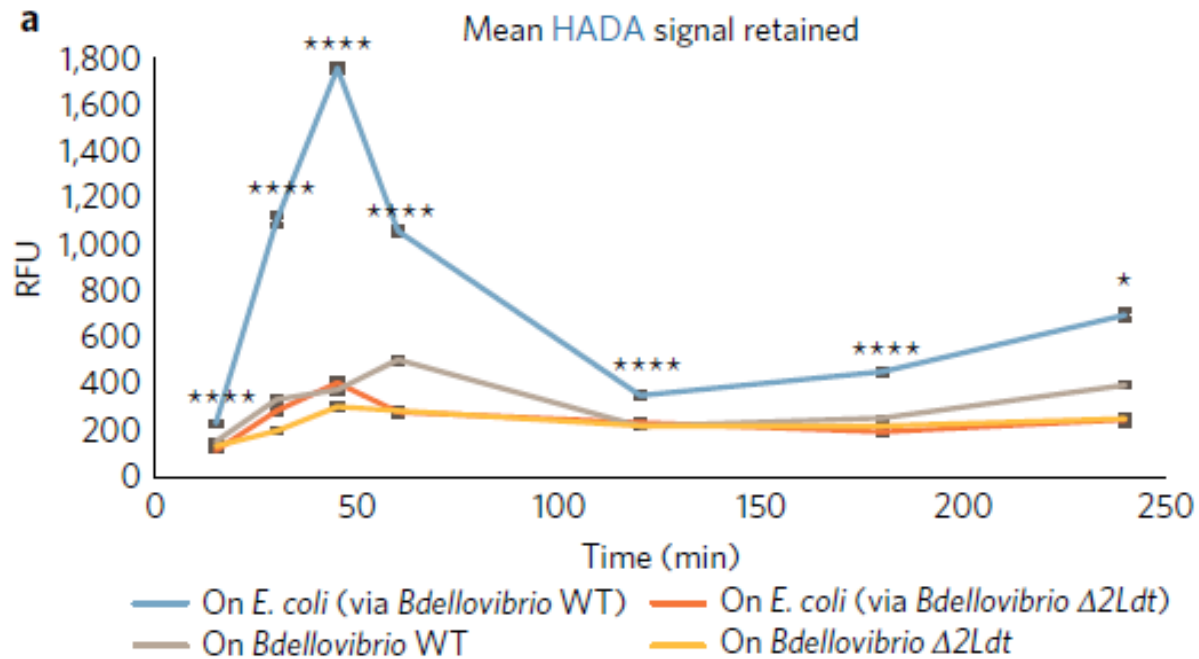
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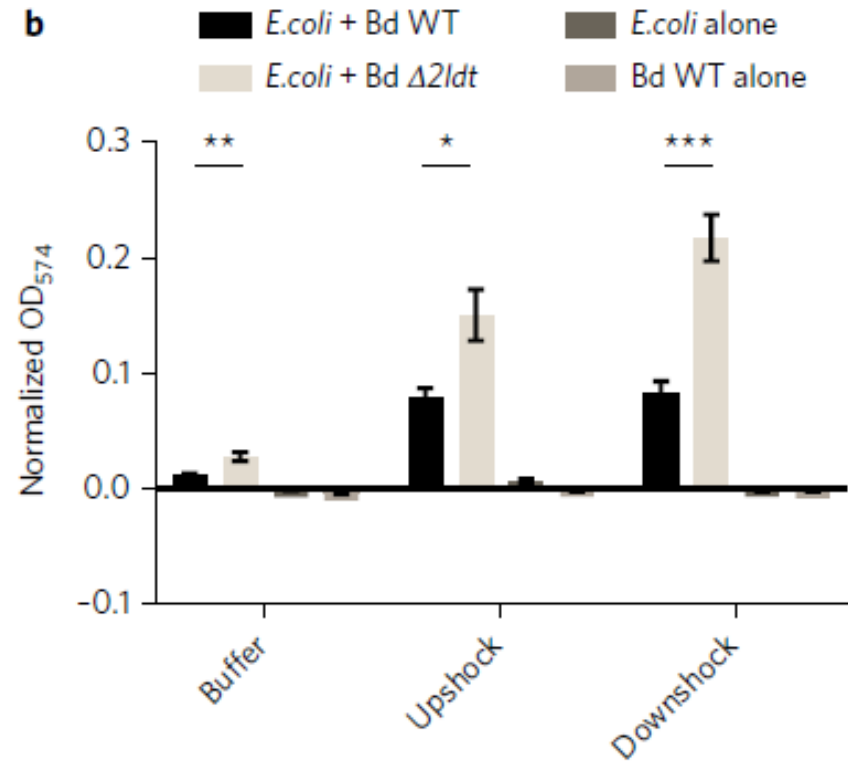
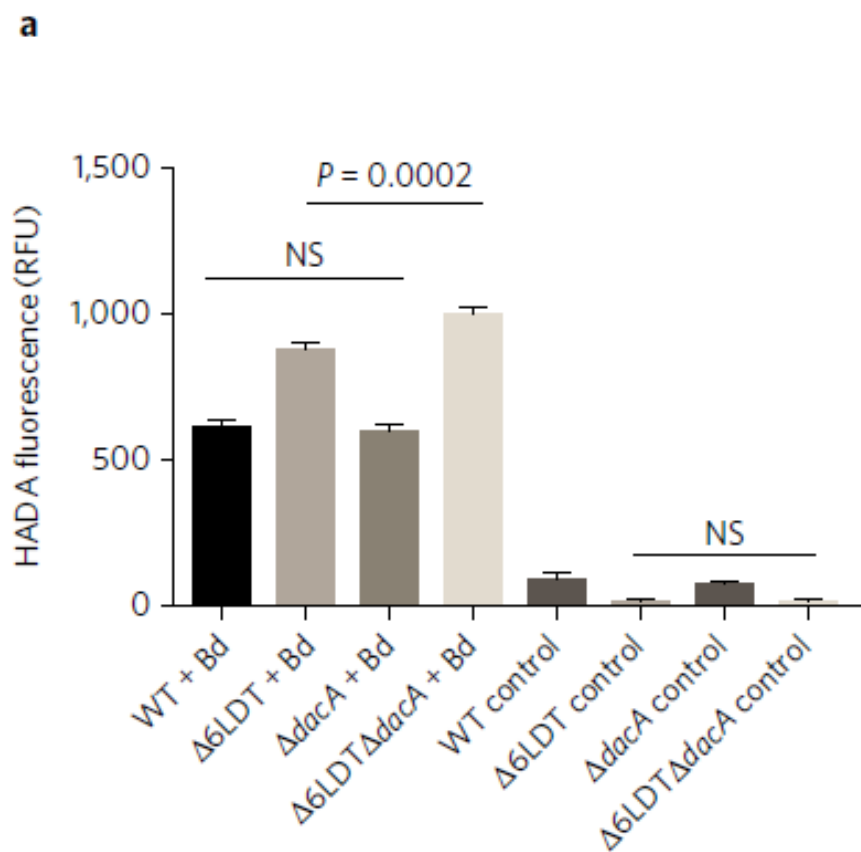
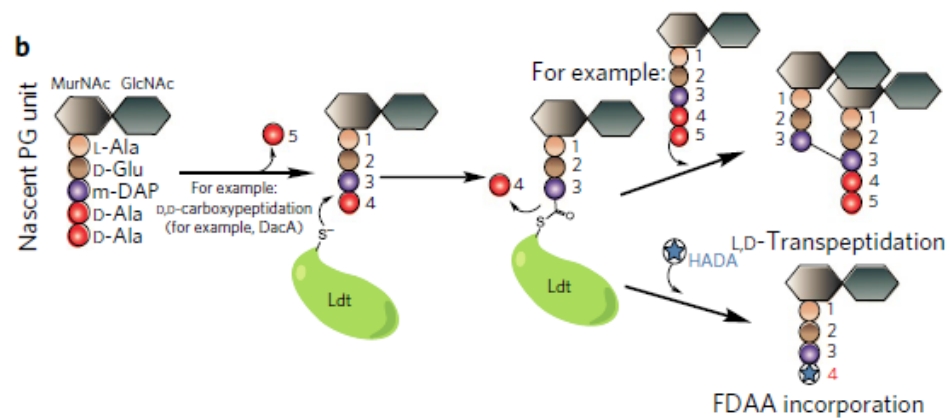






LD transpeptidase activity is important for Bdelloplast formation





More fun...

