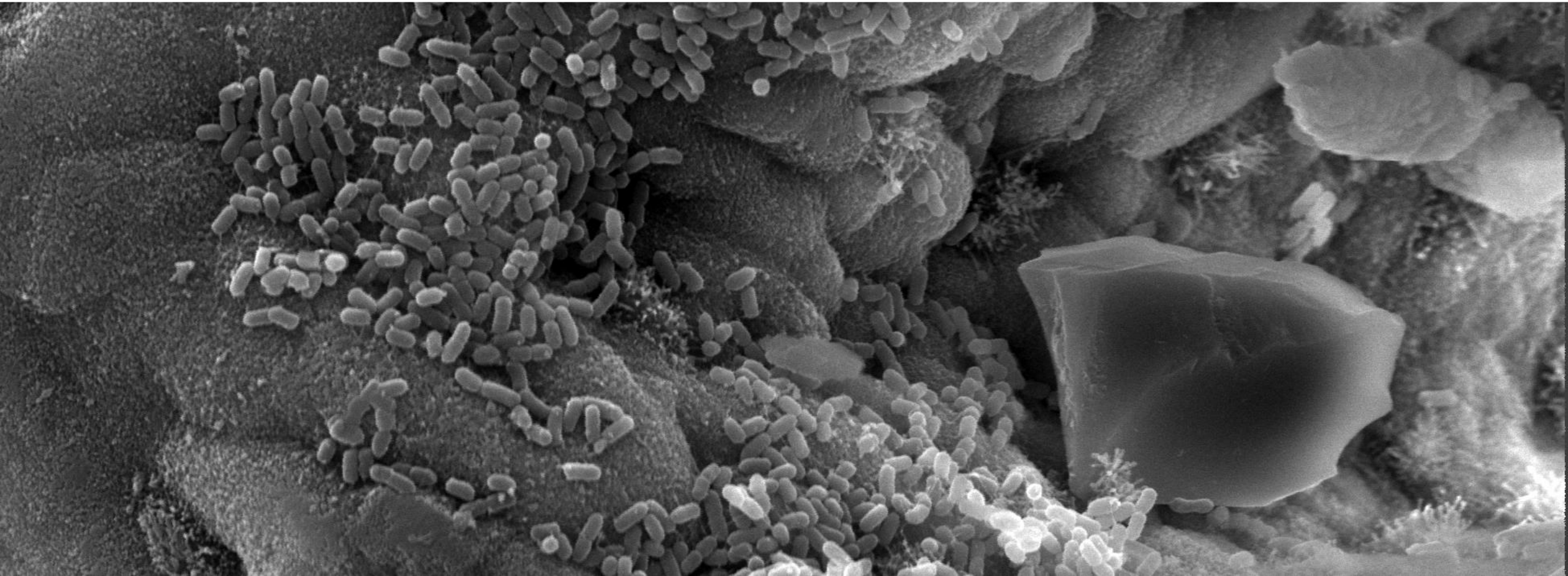


Oxygen and contact with human intestinal epithelium independently stimulate virulence gene expression in enteroaggregative *E. coli*



Samuel J. Ellis, Muhammad Yasir, Douglas F. Browning, Stephen J. W. Busby, and Stephanie Schüller
Cell Microbiol. 2019 Jun;21(6):e13012.



Enteroaggregative *E. coli* (EAEC)

Aggregative adherence to HEp-2 cells (Nataro et al., 1987)

Persistent infantile diarrhoea in developing world

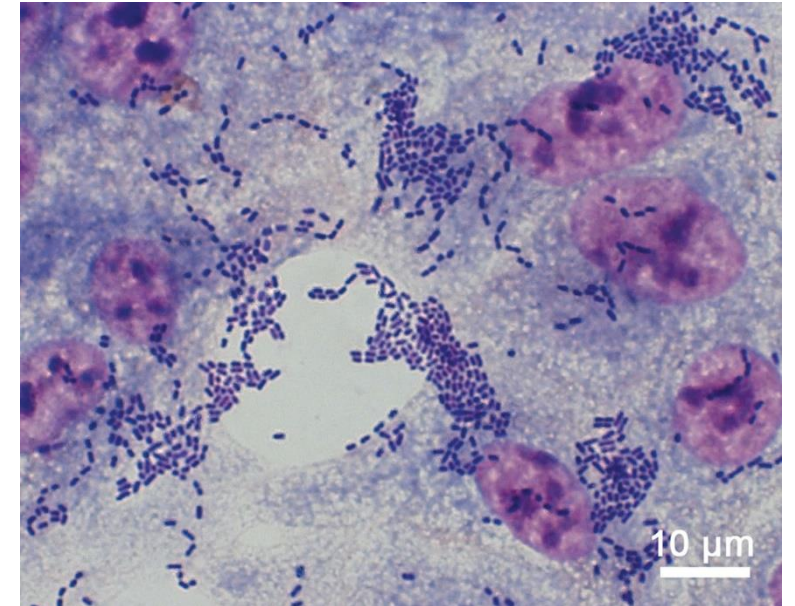
Traveller's diarrhoea in adults

Enteric infections in HIV/AIDS patients

Second most common bacterial cause of diarrhoea in UK

E. coli O104:H4 outbreak in Germany in 2011:

4,000 cases; 1,000 hospitalisations; 50 deaths

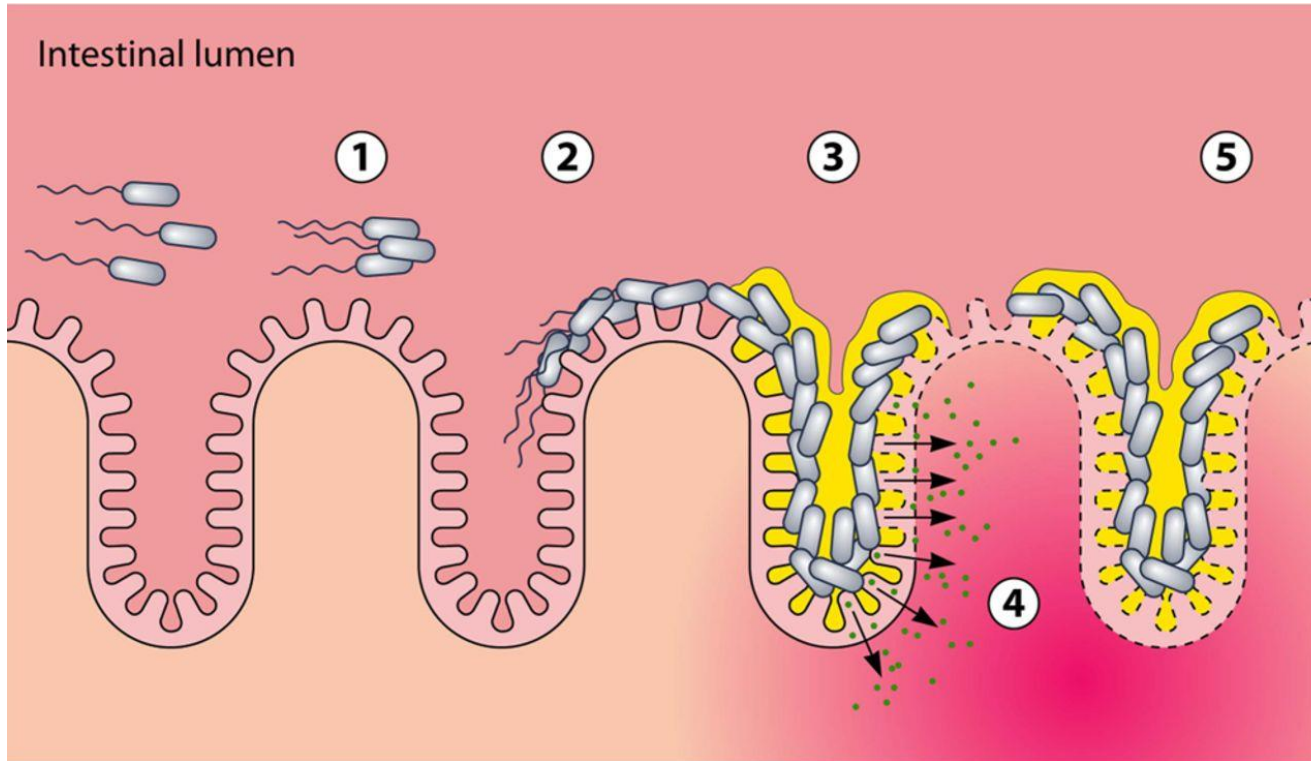


Karch et al., 2012

Identification of virulence factors difficult due to heterogeneity of EAEC strains

EAEC pathogenesis and putative virulence factors

Aggregative adherence and biofilm formation
Toxin release → mucus secretion, epithelial damage and inflammation



Hebbelstrup Jensen et al., 2014

Adhesins:

Aggregative adherence fimbriae (AAF)
Dispersin
E. coli common pilus (ECP)

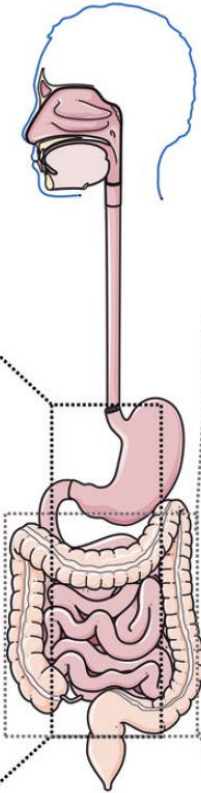
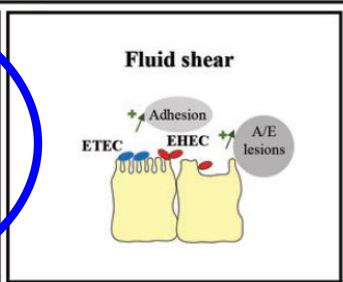
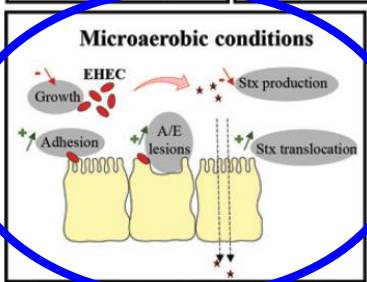
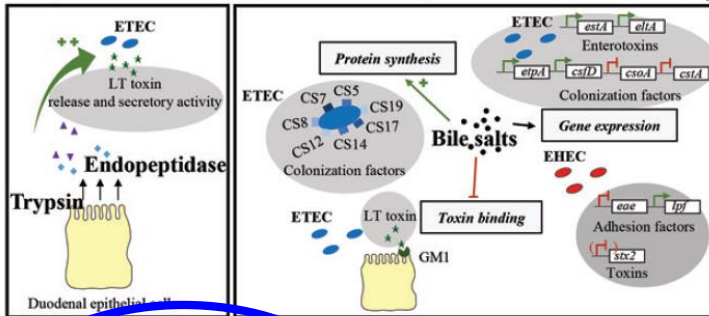
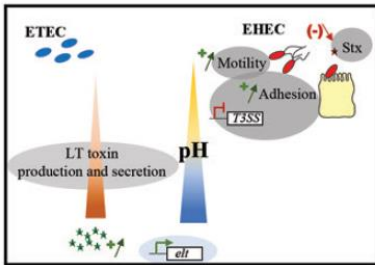
Toxins:

Heat-stable enterotoxin EAST-1
cGMP signalling and anion secretion
Haemolysin E (HlyE) pore formation
Plasmid-encoded toxin Pet
Cytoskeletal disruption

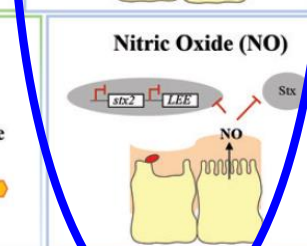
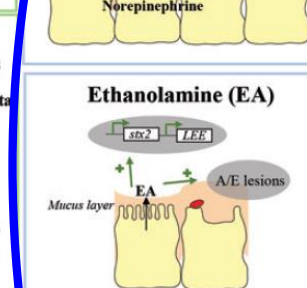
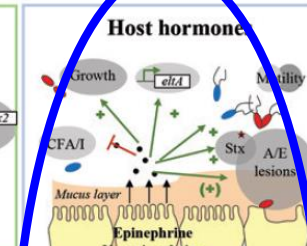
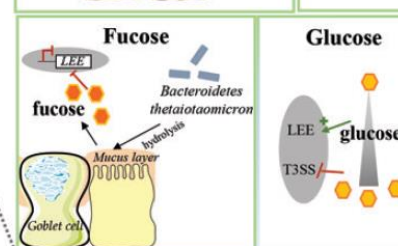
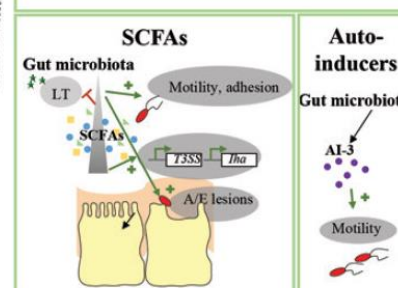
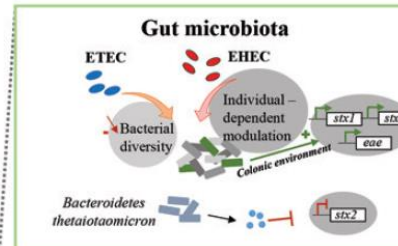
Serine protease Pic
Mucus degradation & secretion
Global regulator AggR

Environmental cues modulate bacterial pathogenesis

Physicochemical parameters



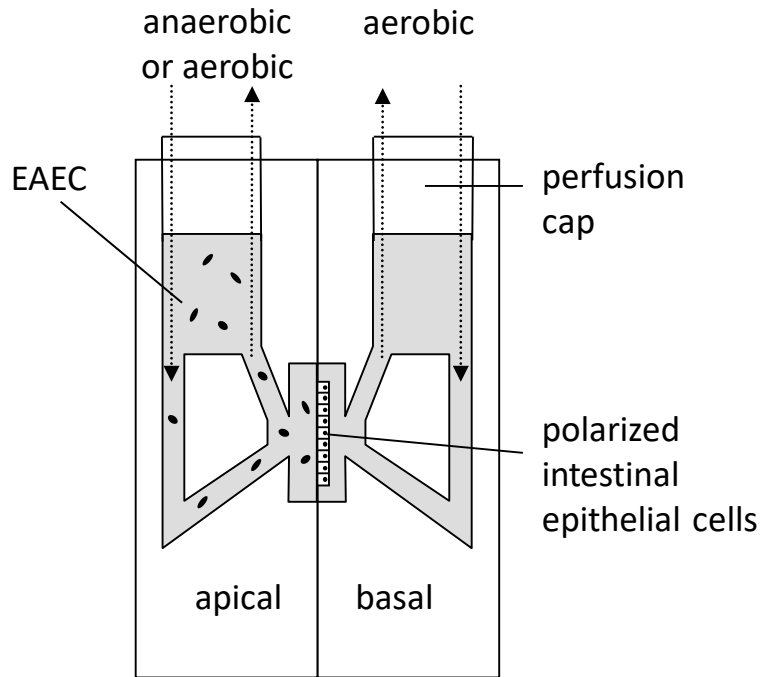
Biotic factors



Which EAEC virulence genes are switched on in an intestinal environment?

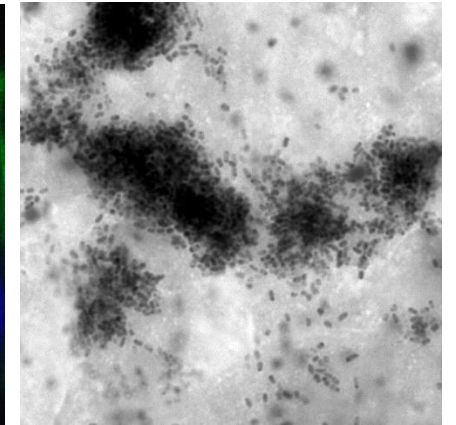
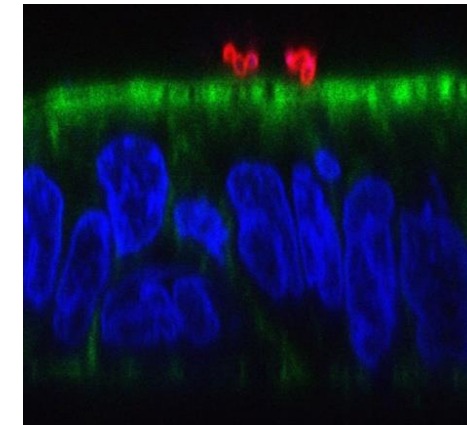
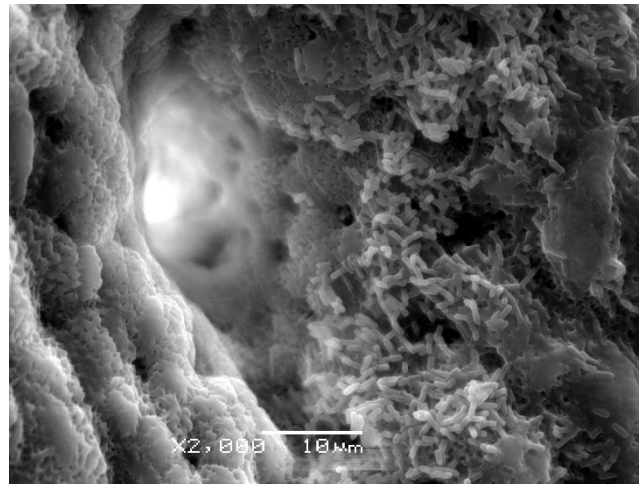
Microaerobic Vertical Diffusion Chamber (VDC)

In vitro organ culture of endoscopic biopsies



Schüller & Phillips, 2010

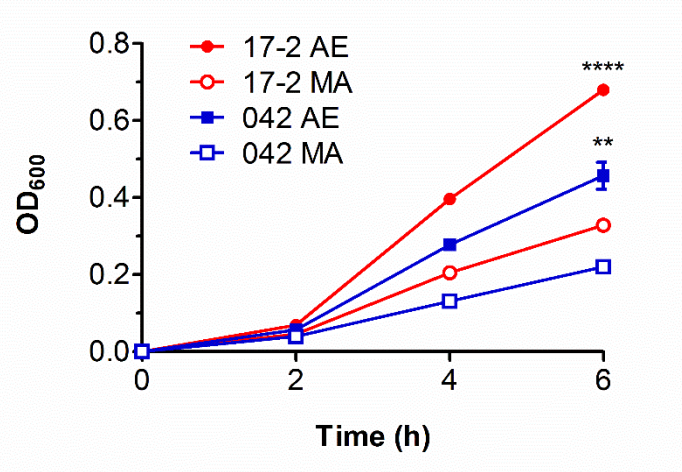
Region	EAEC strain	
	042	17-2
Duodenum	0/8 (0)	0/8 (0)
Terminal ileum	4/7 (57) ^a	3/7 (43) ^a
Transverse colon	6/7 (86)	4/7 (57)
Sigmoid colon	6/7 (86)	2/6 (33)



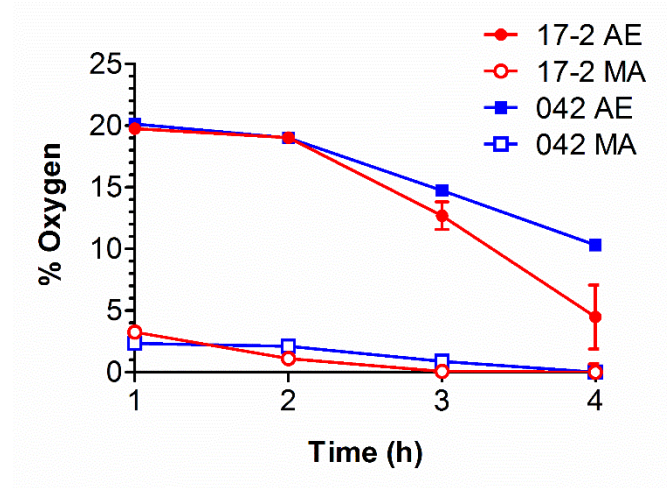
T84 colon carcinoma

Optimisation of VDC infection protocol

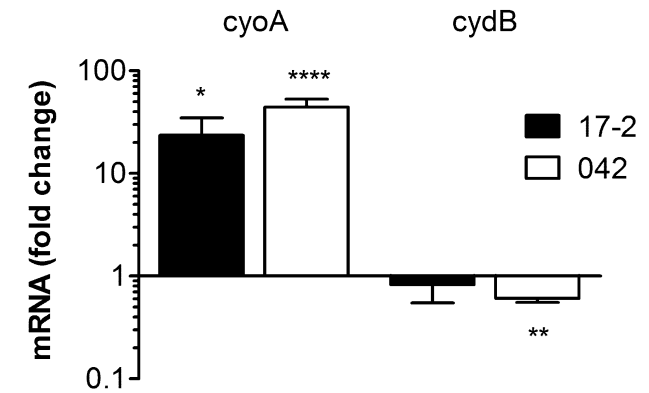
Bacterial growth



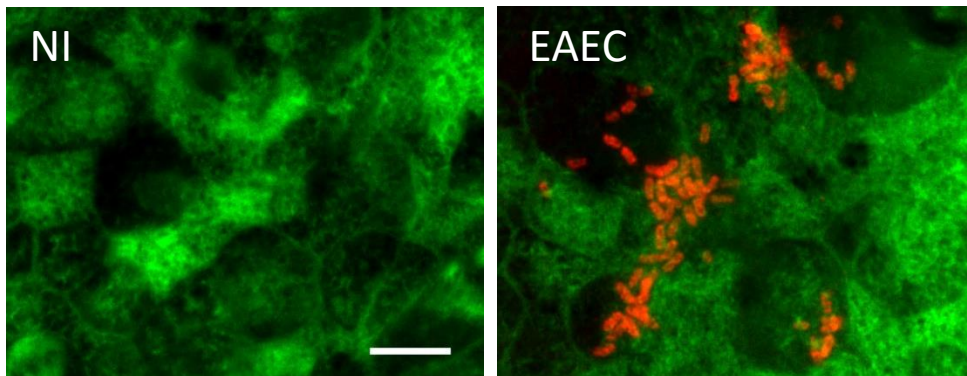
Oxygen consumption



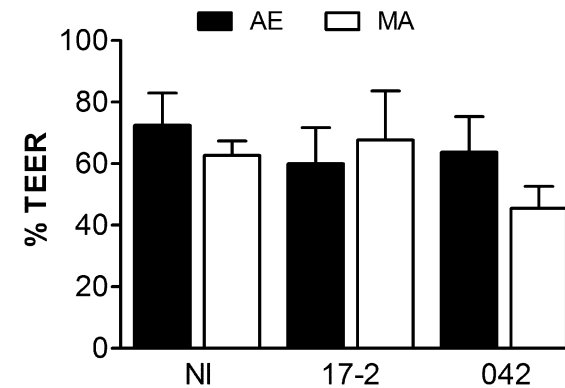
Respiration status



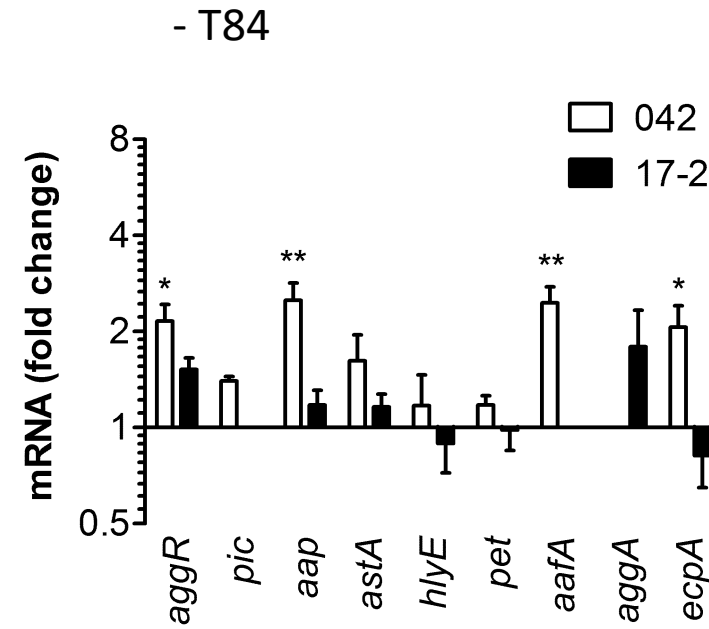
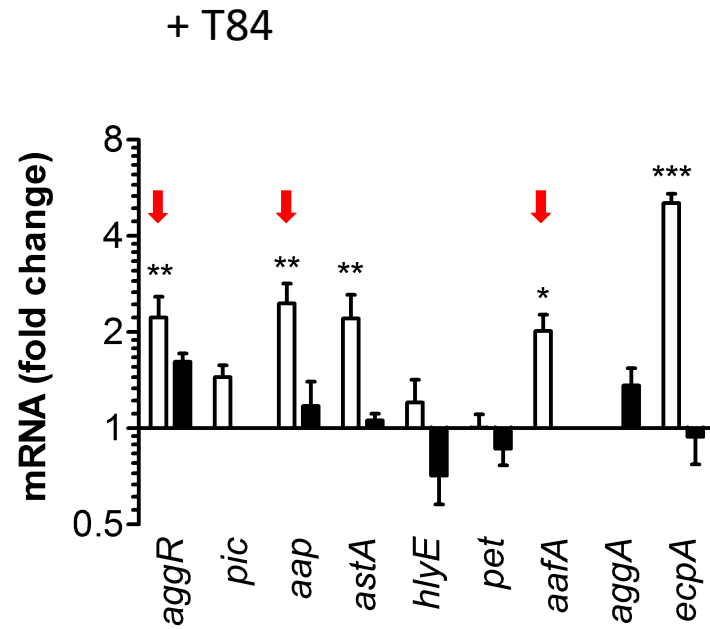
Epithelial integrity



Barrier function

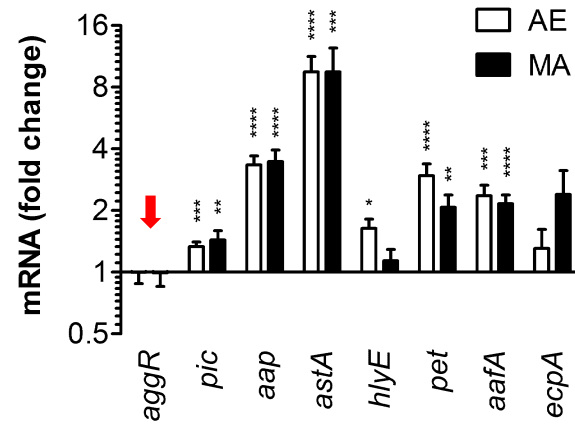


Oxygen enhances virulence gene expression in EAEC 042

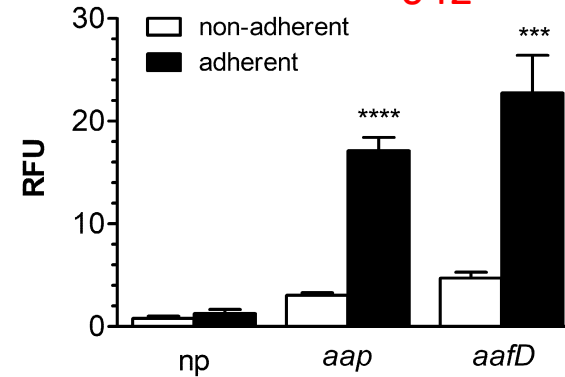


EAEC virulence gene expression is enhanced by host cell contact

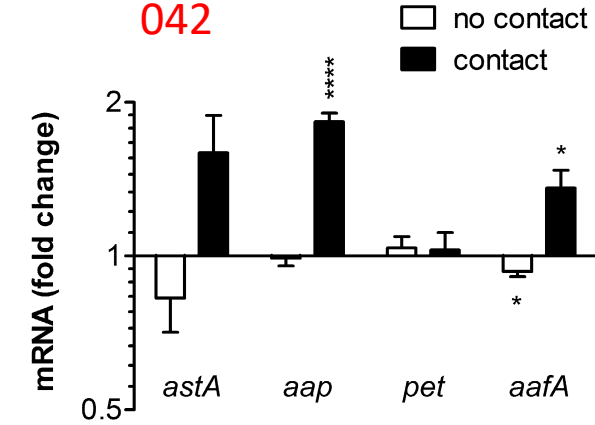
042



042



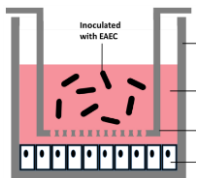
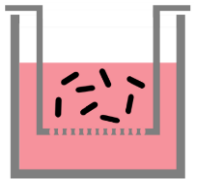
042



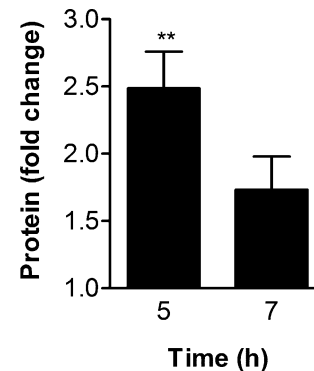
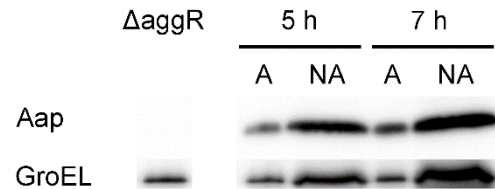
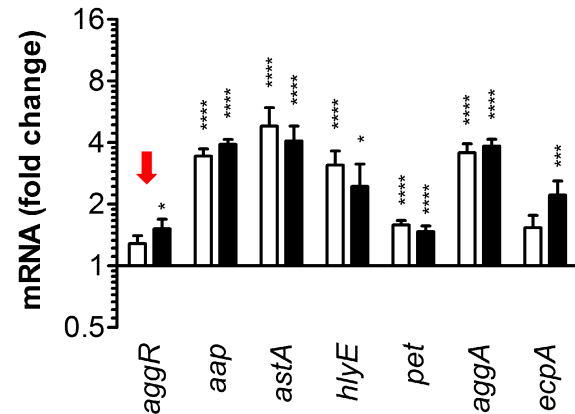
contact



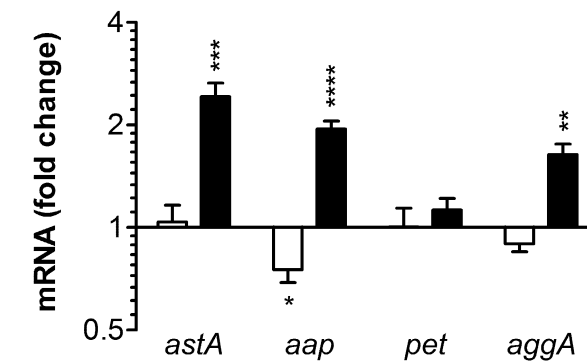
no contact



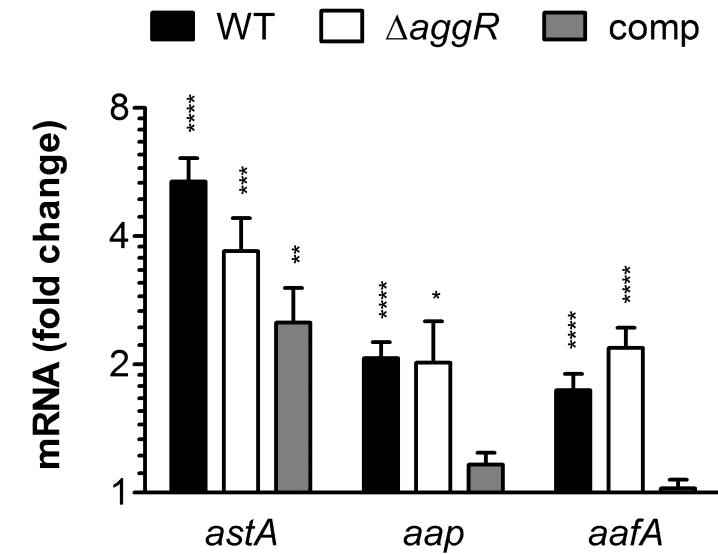
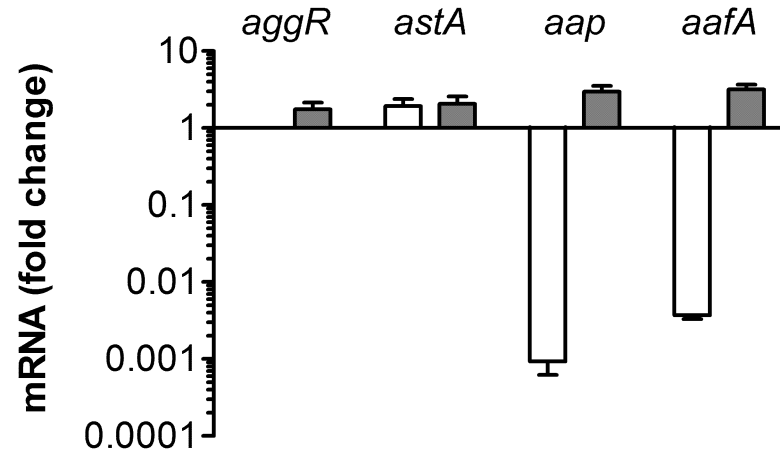
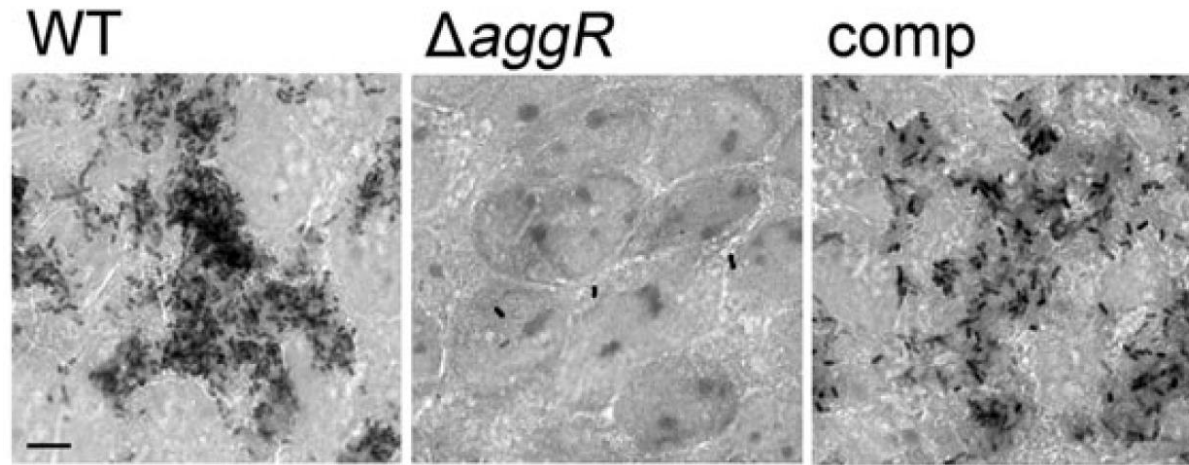
17-2



17-2

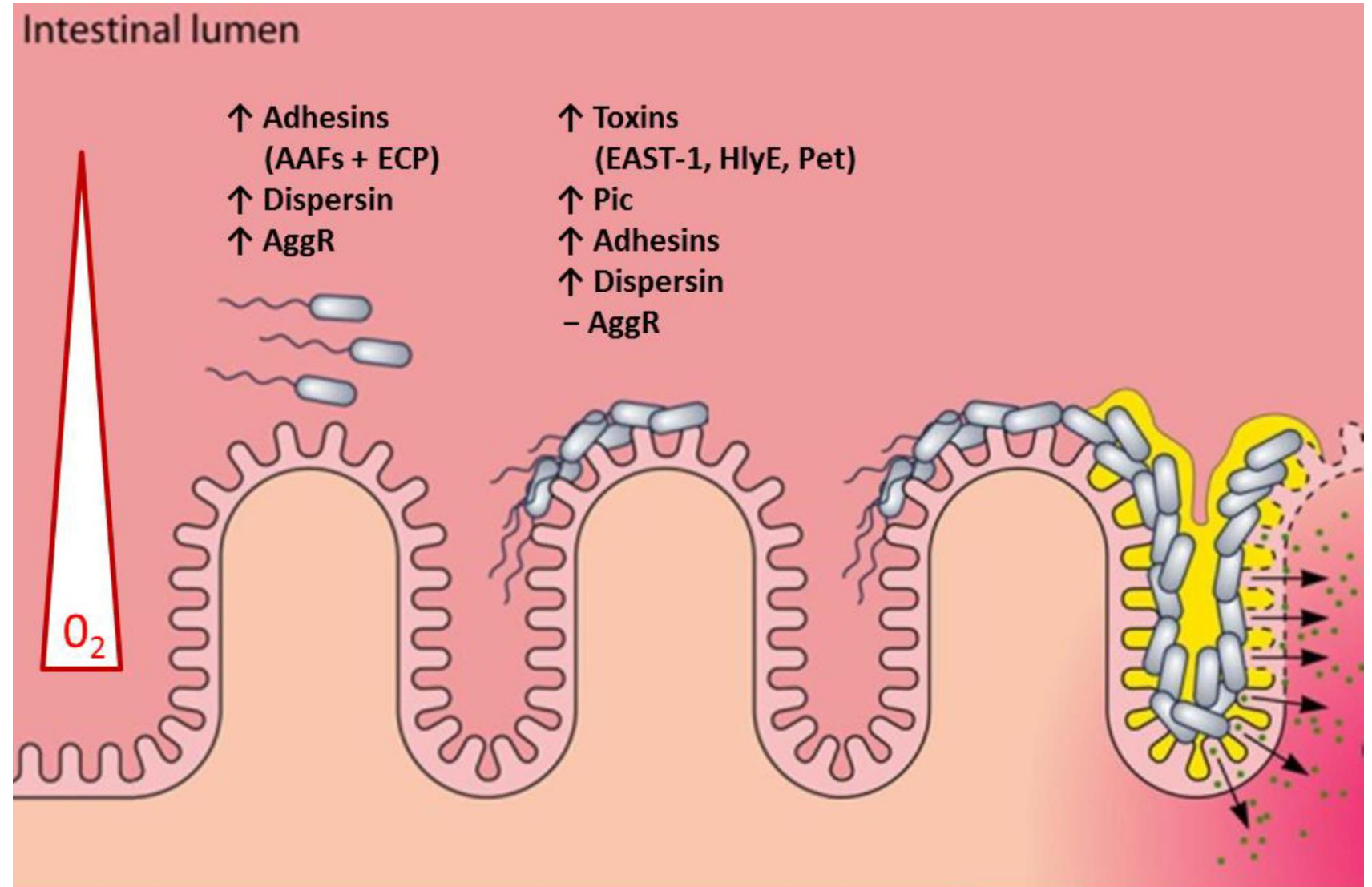


Host cell-induced virulence gene expression is not dependent on AggR



Oxygen & host cell contact provide separate signals for EAEC colonisation of the human gut

- 1) Mucosal oxygen gradient primes bacteria for adherence
- 2) Epithelial contact induces additional virulence factors important for mucus secretion, biofilm formation, cell damage and inflammation



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