Pathogenesis of bacteria and viruses





Jacques, D., McEwan, W., Hilditch, L., Price, A., Towers, G. and

James, L. (2016). HIV-1 uses dynamic capsid pores to import

http://www.bbc.com/news/health-28804267

nucleotides and fuel encapsidated DNA synthesis. Nature,

Vi**Bacteria**rs



Regulation of virulence factors: two-component systems (TSS)



A bit of synthetic biology...



Schmidl, S., Sheth, R., Wu, A. and Tabor, J. (2014). Refactoring and

Optimization of Light-SwitchableEscherichia coliTwo-Component

Systems. ACS Synthetic Biology, 3(11), pp.820-831.

Key events of pathogen-host interaction

- 1. Colonisation invasion
- 2. Multiplication
- 3. Transmission
- 4. Damage



Uropathogenic E. coli binding a kidney receptor with adhesins at the top of P-pili



scanning electron microscopy



cytoskeleton enteropathogenic *E.coli*

Enteropathogenic *E. coli* build specialised structures for adhesion

Biofilms



Invasion

"Zipper mechanism". Listeria invading non-phagocytic cells.





Bonazzi, M. and Cossart, P. (2006). Bacterial entry into

cells: A role for the endocytic machinery. FEBS Letters,

580(12), pp.2962-2967.

"Trigger mechanism". Salmonella.

Type III Secretion System



Transmission EM micrograph of *Salmonella* possessing T3SS



Cryo-EM micrograph of T3SS



Abbreviations used: OR, outer ring; IR, inner ring; OM, outer membrane; IM, inner

membrane. (B) An axial section through the map in (A). (C) Transverse sections

through the map in (A) at the level of the neck (top) and IR1 (bottom).

Type III Secretion Systems. Virulence Mechanisms of Bacterial

Pathogens, Fifth Edition, pp.241-264.

nature REVIEWS MICROBIOLOGY

Type IV secretion

Anja Seubert, Rino Rappuoli and Antonello Covacci

The type IV secretion systems of Gran-regative bacteria are evolutionarily random to bacteriar conjugation systems. Ensurine gatives use type for secretion systems for a variety of totograf the transitional methods secreting of grantic material with other bacteria and the transaction of oncogene that are effective presents into exclusion that calls. The secretion apparatus teel type totage methods as many other comprise. that generate the bacterial inverted cover methods are induced and also generate the secretion apparatus to a secretion of the secretion of a secretion of that generate the bacterial inverted cover methods are set as the secretion apparatus to a secretion of the bacterial inverted cover methods are set of the secretion of the secre membrane of subsystic host only. This assembly is typically composed of up to 10 proteins, and women research has revealed betated into which on the structure and assembly of the exercision appears. It is the coming increasingly clear that the type N accorded effections play important takes in the volumes of some Samir negative participers. The poster summarises our current increasing of the type in accorded effections of sameted Samirangable pathogens and here offices on hom cells.

CHIRON

Helicobacter pylori

The gestric pathogen N, gylori uses its type IV secretion system (T455) (the so-called cag system) in the colorization of gastric epithelial cells. The secreted effector CagA has a dramatic effect on host cells, including major changes in cellular morphology, and contributes to chronic gastric inflammation and possibly also the formation of gastric servinoms.

Bartonella

Bartonole spp. require two different T488s for pathogenicity. The Two system, where extensive gene duplication creates variant pilus subunits, is necessary for optimization of envitwopytes. The VHS system and its secreted Bartonels effector proteins (Bops) are belowed to be responsible for most of the cellular effects of the interaction of Bartonels with host endothelial cellu: action memorypements, resulting in investome formation, activation of a pro-inflammatory response and initibilition of apoptosis. Together with a T485-independent mitogenio stimulus, these effects result in endothelial cell survival and profilension, and the formation of vasoprofilensitive furnows.

Legionella pneumophila

L procemphile can replicate within macrophages by interflering with the normal pathway of endocytaxis. The functions of two effectors translocated by the Doktors T450 aystam have been identified. RelF is a guarine nucleotide exchange factor that excuts ACP ribosytation factor (ARF) poteins to the Legionellacontaining vacuals. Lick is believed to be involved in maintaining the integrity of the Legionella cell. A pool of other translocated effectors (Dick; substate of loss/Dot transporter) were identified and their functions remain to be explored. It has been shown recently that activation of cespace 3 to dependent on the Doktom T455. Caspase 3 to dependent on the Doktom T455. Caspase 3 to be phagesomal membrane and inhibiting endowite facion.

Agrobacterium tumefaciens

The VMDD4 system in the plant pathogen A sumelacients is the postolypical T495. A sumelacients transitionales oncogenic single-stranded DHA (T4DHA) into a variety of dicetyledonous plants, causing tumoum known as drown galls. The T-DNA is translocated as a nucleoprotein complex with VinD0, which, along with VMD2, ensures that the T-DNA is translocated to the nucleus. Other secreted effectors include the F-box pacter Vinf; the instancializer target of which remains unknown, and VHD2, which is also of unknown function.

Bordetella pertussis

The Pti T458 found in 8, pertussis, the causative agent of whooping cough, differs from the other systems shown in this poster as it ascettes its effector protein the pertussis toxin (PTX) — into the extended future mileu. The downstream effects of PTX include ADP riboxylation of the inhibitory G posters (G), which increases the intracellular levels of oAMP and modulates intracellular signaling pothways, leading to cell death.

PURTHER READING

Rows, D. 1, Specific services of participant transmiss Core Open Ministrie & 20130 IEEE Concerning, F. & Charles, M. 1, The executive case in section in approximate matter in sections 4. I. I. 1999 - All 1998, P. A. Herning, A. & Schwanz, M. 2014, S. 1999, S. 1999, Instanting Specific securities and the first Ministria of Ministria II (1999). Security Sciences and Ministria participants for concerning the Ministria Ministria (1999). Security Sciences and Ministria participants for concerning the Ministria (1999). Security Sciences and Ministria participants for concerning the Ministria (1998). Security Sciences and Ministria Sciences II (1999). Security Sciences and Ministria (1999). Security Sciences and Ministria participants for concerning the Ministria (1998). Security Sciences and Ministria Sciences II. 1999, Security Sciences and Ministria (1998). Security Sciences and Ministria Sciences II. 1999, Security Sciences and Ministria (1998). Security Sciences and Ministria Sciences II. 1999, Security Sciences and Ministria (1998). Security Sciences and Ministria Sciences II. 1999, Security Sciences and Ministria (1998). Security Sciences and Ministria Sciences II. 1999, Security Sciences and Ministria (1998). Security Sciences and Ministria Sciences II. 1999, Security Sciences and Ministria (1998). Security Sciences and Ministria Sciences II. 1999, Security Sciences and Ministria (1998). Security Sciences and Ministria Sciences II. 1999, Security Sciences and Ministria (1998). Securit

Designed by Brinsh Rewords, Billing Bradlagh Chalanne, A. Branne, R. Braggad ang A. Change and an Mill, Chang & A. Va Figuretine L, Will Diemer, Ang Will Diemer, Ang Will Diemer, Ang



What happens once bacteria are in?



Listeria cytoskeleton



DNA cytoskeleton pathogen vacuole

Damage caused by bacteria

- **Direct** from bacteria action
- Indirect from host response



Cytolysin

AB toxins



Viruses





HIV capsid





Beta-hairpin can adopt alternate conformations that differ by up to 15 Å.





HIV-1 reverse transcription is inhibited by blockade of the capsid pore



CA_{hexamer} crystal structure in complex with hexacarboxybenzene, which is co-ordinated by R18

Current approach to AIDS treatment

- Nucleoside Reverse Transcriptase Inhibitors
- Protease Inhibitors
- Fusion Inhibitors
- Highly Active Antiretroviral Therapy
- Non-Nucleoside Reverse Transcriptase Inhibitors



Blocking assembly: protease inhibitors



HIV protease

Homo-dimeric aspartyl protease

Encoded by pol gene

Peptide mimics of cleavage sites are inhibitors

Cleaves polyprotein to produce capsid components





