Salmonella enterica Serovar Typhimurium and _C. elegans_: An ideal host pathogen interaction model for microbial adaptation

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Salmonella infection and its host range always has raised concern over worldwide disease manifestation, mortality and morbidity. The emergence of drug resistant bacteria further increases the risk factor and shows the need to develop an efficient strategies against Salmonella infection and associated consequences. Currently in my laboratory, we are trying to address the microbial evolutionary adaptability aspect using *Caenorhabditis elegans* (*C. elegans*) as model organism and also we are studying the infection mediated developmental defects in worm. Evolutionary adaptations has been considered and reported also as an important survival strategy of all living organism including microorganism. We have observed that Salmonella have adapted better when they we repeatedly exposed to same host environment in *C. elegans* for many generation and in LB or F media as well. The emerged Salmonella strain shows hypermobility, increased biofilm formation, size etc., which may help them in increased virulence and better survivability in host. The bug was able to invade better in epithelial cells than its unpassaged counterpart, but to our surprise fold proliferation was comparable, in phagocytic cell (U937) they are better survivor and proliferate better which indicate that microbe has adapted themselves to survive better in host environment. Salmonella infection mediated neonatal mortality and fetal loss during pregnancy is known. Hence in another study using nematode model *(C. elegans)* of Salmonella infection, we found that Salmonella infection in able to cause certain developmental defect in worm, like increased egg retention, delayed hatching, and 8-10% reduction in egg hatching etc. These study further increase the concern over what will be the outcome on developmental stages of host if we have adapted/emerged bacterial infection? So the current study shows that Salmonella infection in host can be ground for pathogen's evolution and can further increase the infection associated risk including mortality, morbidity and even various developmental defect. With time such microbe will be more infectious and we need to develop combat strategies by targeting the responsible gene of such pathogenic phenotype.

Key words: Salmonella, Developmental defects, Adaptation, Virulence

"Please consider for short talk"

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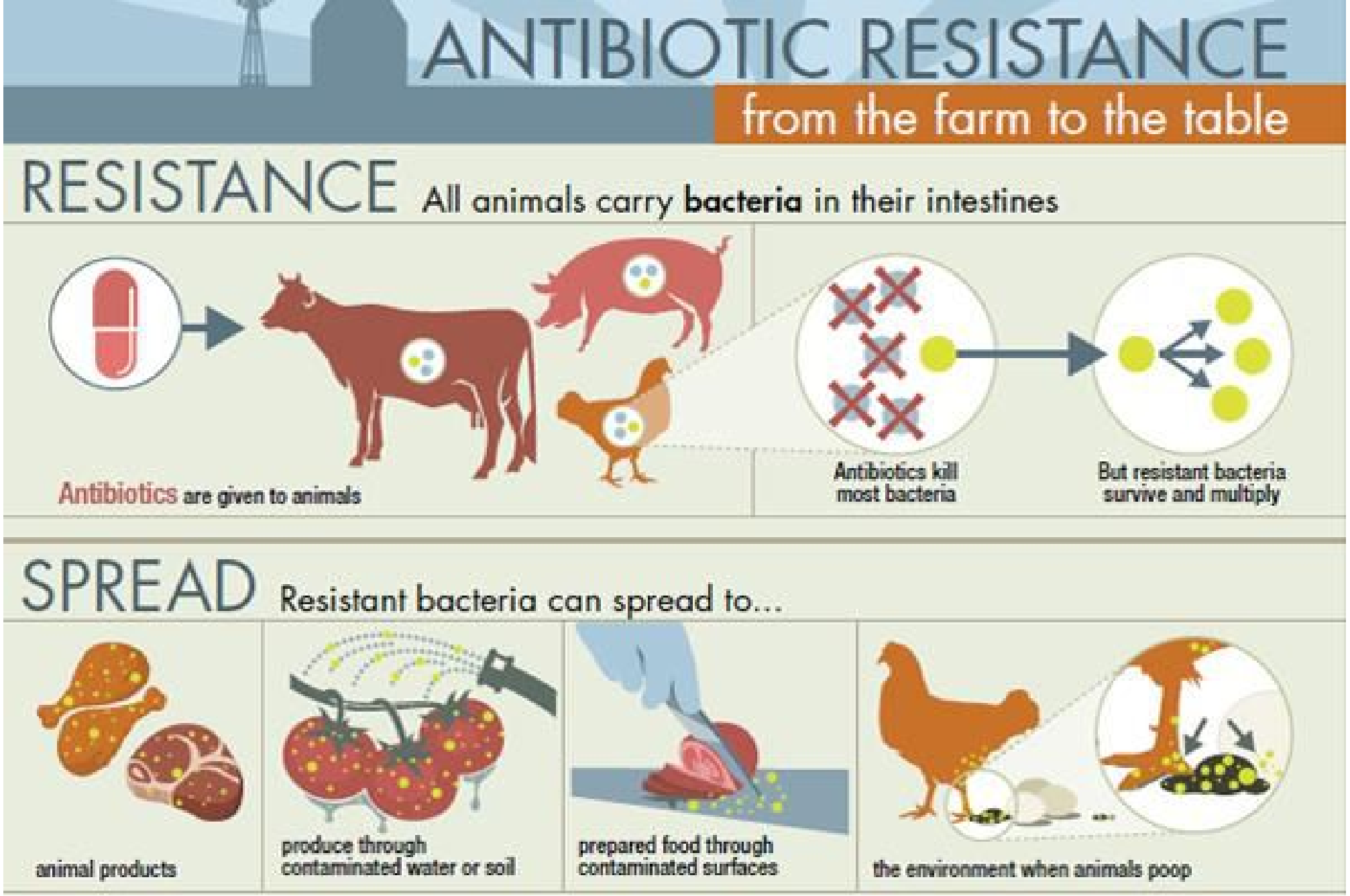

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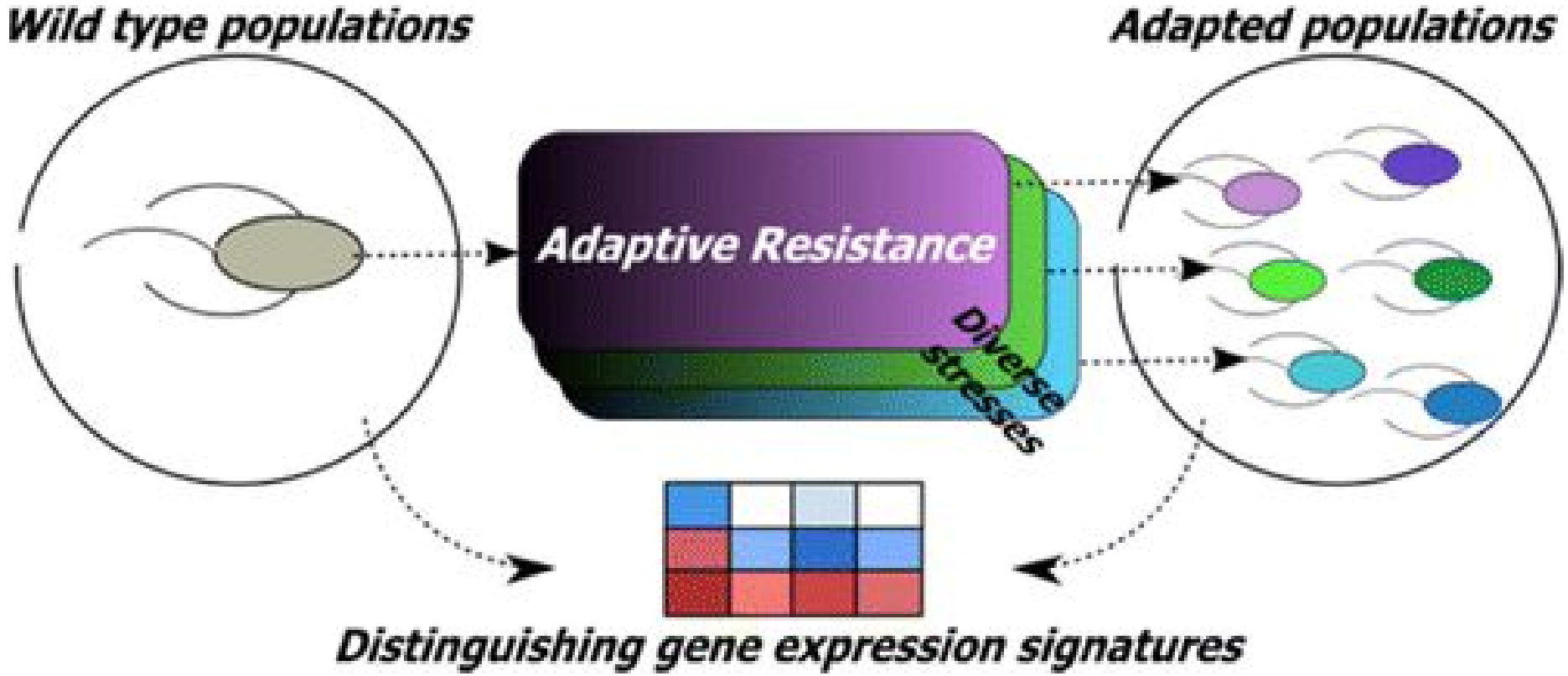

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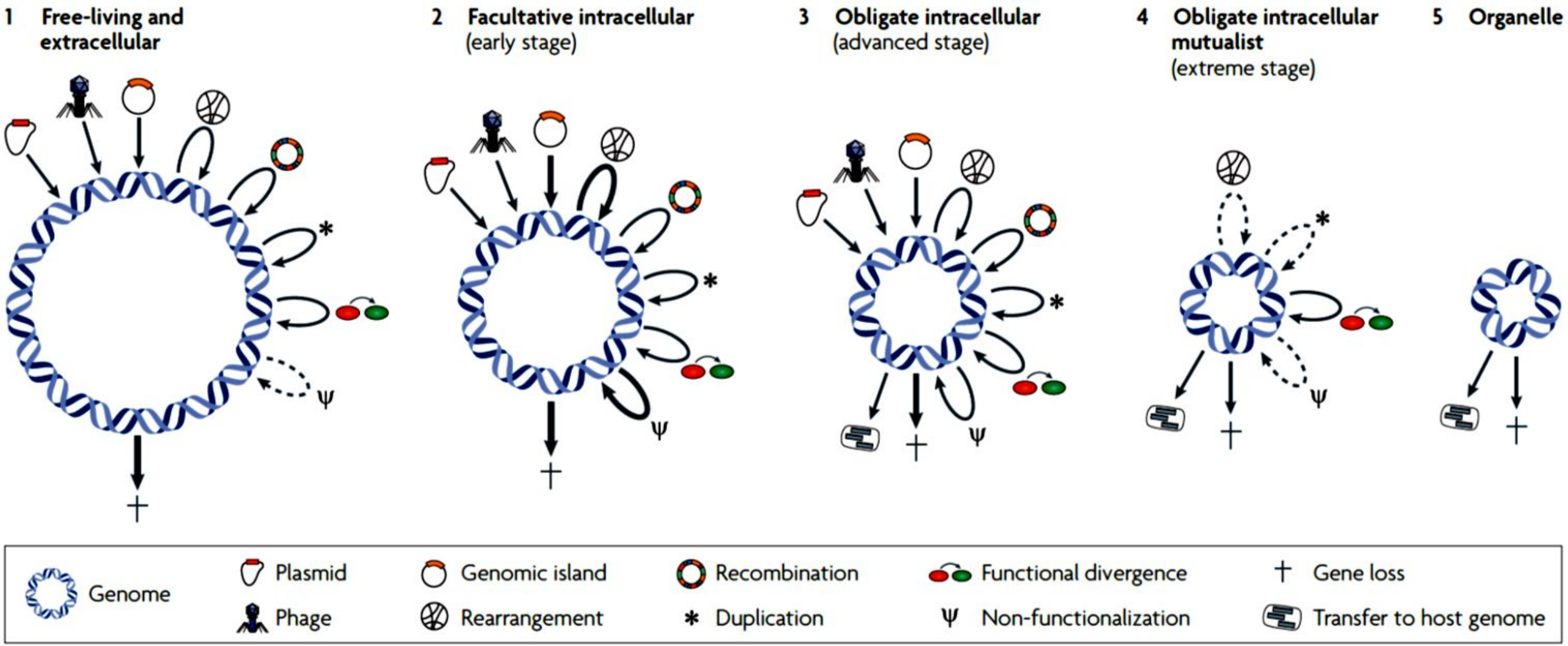
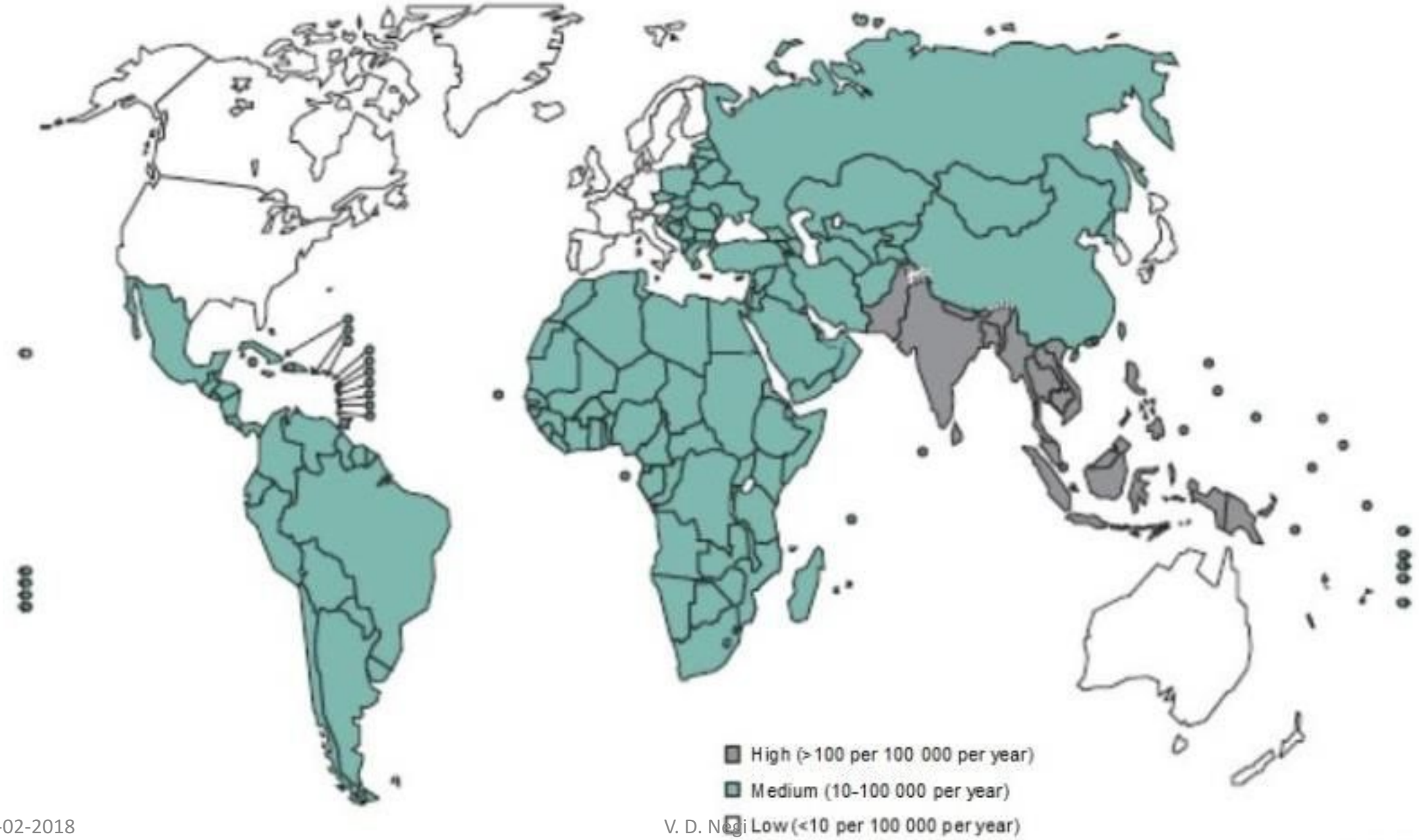


Christina Toft & Siv G. E. Andersson: *Nature Reviews Genetics* **volume 11**, pages 465–475 (2010)

Salmonella enterica serotypes Typhi, Paratyphi A and Paratyphi B
Each year, there are an estimated 22 million cases and 600,000 related deaths worldwide due to *Salmonella typhi*



Bull World Health Organ 2004;82(5):346-53

- **Rational:** To target the bug responsible for causing world wide infection and death (neonatal, infant, elderly person and immunocompromised)
- **Novelty:** Targeting the gene responsible for emergence of hyper virulent Salmonella during frequent infection/endemic

Evolutionary adaptation

- Evolutionary adaptation of virulence as in malarial parasite *Plasmodium falciparum* for generation to generation (*Borst, P., et al, 1995, Roberts, D.J., et al , 1992, Scherf, A., et al, 1988.)*
- With repeated in vitro passaging of *Staphylococcus aureus,* the change in physiology in term of reduced aconitase activity and regulator, the accessory gene regulator (agr) alteration was reported *(Somerville, G.A., et al., 2002)*
- The emergence of multidrug resistant pathogenic strain and adaptation of microbes toward antibiotics and associated genotypic changes has been reported *(Nikaido, H., 2009 , Perron, G.G., et al., 2012)*
- *Pseudomonas aeruginosa* has adapted the commensalism and lost virulence when passed through *C. elegans. (Hinrich Schulenburg et al 2015)*

➢Salmonella and evolution

➢In vivo passaging of *Salmonella* also shown to **increased growth rate** and increased intracellular survival than in vitro, But the **phenotype is lost** when cultured in vitro *(Mastroeni, P., et al., 2011)*

➢ It has been also reported that *Salmonella* strains are considerably more virulent after murine passage relative to other isolates (**100-fold decreased LD50**) *(Heithoff D.M., et al., 2012)*

➢ Host adaptation observed in *Salmonella* Enteritidis in immuno-compromised host, leading to mutation in the mismatch repair gene (***mutS***) *(Elizabeth J.K,et al.,2016)*

➢Evolutionary Remodeling of Bacterial Motility Checkpoint Control help in better motility under selection pressure in *E.coli (Victor Sourjik et al 2017)*

Conclusions:

- Passaging through different environment have helped bug to adapt and evolve to become more virulent
- In intracellular environment they are surviving better that unpassged counterpart
- Bacterial size and flagellar number have increased and may be helping in virulence
- Various genes associated with virulence are upregulated (not shown)
- Biofilm and flagellar expression was enhanced

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