Al-Anbar University

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GENOMICS AND BACTERIAL PATHOGENICITY

Bacteria are haploid and limit genetic interactionsthat might change their chromosomes and potentiallydisrupt their adaptation and survival in specific environmentalniches.

The Clonal Nature of Bacterial Pathogens

One important result of the conservation of chromosomalgenes in bacteria is that the organisms are **clonal**. For mostpathogens, there are only one or a few clonal types that arespread in the world during a period of time. For example,epidemic **serogroupA meningococcal meningitis** occurs inAsia, the Middle East, and Africa and occasionally spreadsinto Northern Europe and the Americas. On several occasions,over a period of decades, single clonal types of serogroupA ***Neisseria meningitidis***have been observed to appearin one geographic area and subsequently spread to otherswith resultant epidemic disease.

There are many types of***Haemophilusinfluenzae***, but only clonal *H.influenzae*type Bis commonly associated with disease. There are two clonaltypes of ***Bordetella pertussis***, both associated with disease.Similarly, ***Salmonella*** **serotype Typhi** (typhoid fever) frompatients is of two clonal types. There are, however, mechanismsthat bacteria use, or have used a long time in the past,to transmit **virulence genes** from one to another.

Mobile Genetic Elements

Primary mechanisms for exchange of genetic informationbetween bacteria include **natural transformation** and **transmissiblemobile genetic elements** such as **plasmids**, **transposons**,and **bacteriophages** (often referred to as “phages”).Transformation occurs when DNA from one organism isreleased into the environment and is taken up by a differentorganism that is capable of recognizing and binding DNA.

In other cases, the genes that **encode** many bacterial virulencefactors are carried on plasmids, transposons, or phages.**Plasmids are extrachromosomal pieces of DNA and are capableof replicating**. **Transposons are highly mobile segmentsof DNA that can move from one part of the DNA to another**.This can result in **recombination** between extrachromosomalDNA and the chromosome. If this recombination occurs, thegenes coding for virulence factors may become chromosomal.Finally, **bacterial viruses** or **phages** are another mechanismby which **DNA can be moved from one organism to another**.Transfer of these mobile genetic elements between membersof one species or, less commonly, between species can resultin transfer of virulence factors, including **antimicrobial resistancegenes**. A few examples of plasmid- and phage-encodedvirulence factors are given in Table 1.

Table 1: Examples of Virulence Factors Encoded by Genes onMobileGeneticElements

Genus and Species	Virulence Factor and Disease
Plasmid encoded	
Escherichia coli	Heat-labile and heat-stable enterotoxins that cause diarrhea
Escherichia coli	Hemolysin (cytotoxin) of invasive disease and urinary tract infections
Escherichia coli and *Shigella*species	Adherence factors and gene products involved in mucosal invasion
Bacillus anthracis	Capsule essential for virulence (on one plasmid)
	Edema factor, lethal factor, and protective antigen are all essential for virulence (on other plasmids)
Phage encoded	
Clostridium botulinum	Botulinum toxin that causes paralysis
Corynebacteriumdiphtheriae	Diphtheria toxin that inhibits human protein synthesis
Vibrio cholerae	Cholera toxin that can cause a severe watery diarrhea

Pathogenicity Islands

Large groups of genes that are associated with pathogenicityand are located on the bacterial chromosome are termed **pathogenicity islands** (**PAIs**). **They are large organized groups of genes, usually 10-200 kb in size. The major properties of PAIs are as follows: they have one or more virulence genes ; they are present in the genome of pathogenic members of a species but absent in the nonpathogenic members; they are large; they typically have a different guanine plus cytosine(G + C) content than the rest of the bacterial genome; they are commonly associated with tRNA genes; they are often found with parts of the genome associated with mobile genetic elements; they often have genetic instability; and they often represent mosaic structures with components acquired at different times. Collectively, the properties of PAIs suggest that they originate from gene transfer from foreign species.** A few examples of PAI virulence factors are provided in Table 2.

Table2: A Few Examples of the Very Large Number of Pathogenicity Islands of Human Pathogens

Genus and Species	PAI Name	Virulence Characteristics
Escherichia coli	PAI I536, II536	Alpha hemolysin, fimbriae, adhesions, in urinary tract infections
Escherichia coli	PAI IJ96	Alpha hemolysin, P-pilus in urinary tract infections
Escherichia coli (EHEC)	O157	Macrophage toxin of enterohemorrhagic*Escherichia coli*
Salmonella serotype Typhimurium	SPI-1	Invasion and damage of host cells; diarrhea
Yersinia pestis	HPI/pgm	Genes that enhance iron uptake
Vibrio cholerae El Tor O1	VPI-1	Neuraminidase, utilization of amino sugars
Staphylococcus aureus	SCC mec	Methicillin and other antibiotic resistance
Staphylococcus aureus	SaPI1	Toxic shock syndrome toxin-1, enterotoxin
Enterococcus faecalis	NPm	Cytolysin, biofilm formation

PAI, pathogenicity island

SPI, *Salmonella* pathogenicity island

HPI, high pathogenicity island

VPI, *Vibrio* pathogenicity island

SCC, staphylococcal cassette chromosome mec

SaPI, *Staphylococcus aureus*pathogenicity island

NP, non-protease

REGULATION OF BACTERIALVIRULENCE FACTORS

Pathogenic bacteria (and other pathogens) have adapted bothto saprophytic or free-living states, possibly environmentsoutside of the body, and to the human host. In the adaptiveprocess, pathogens husband their metabolic needs andproducts. They have evolved complex signal transductionsystems to regulate the genes important for virulence. Environmental signals often control the expression of thevirulence genes. Common signals include temperature, ironavailability, osmolality, growth phase, pH, and specific ions(eg, Ca^{2+}) or nutrient factors. A few examples are presented inthe following paragraphs.

The gene for diphtheria toxin from *Corynebacteriumdiphtheriae*is carried on temperate bacteriophages. Toxin isproduced only by strains lysogenized by the phages. Toxinproduction is greatly enhanced when *C.diphtheriae*is grownin a medium with low iron.

Expression of virulence genes of *Bordetella pertussis* is enhancedwhen the bacteria are grown at 37°C and suppressed whenthey are grown at lower temperatures or in the presence ofhigh concentrations of magnesium sulfate or nicotinic acid.

The virulence factors of *Vibriocholerae*are regulated on multiplelevels and by many environmental factors. Expressionof the cholera toxin is higher at a pH of 6.0 than at a pH

of8.5 and higher also at 30°C than at 37 °C.Osmolality and amino acid composition also are important.As many as 20 other genes of *V.cholerae*are similarlyregulated.

*Yersiniapestis*produces a series of virulence plasmid-encodedproteins. One of these is an antiphagocytic fraction 1 capsularprotein that results in antiphagocytic function. Thisprotein is expressed maximally at 35-37°C, the host temperature,and minimally at20-28 °C, the flea temperature atwhich antiphagocytic activity is not needed. The regulationof other virulence factors in *Yersinia* species also is influencedby environmental factors.

Motility of bacteria enables them to spread and multiplyin their environmental niches or in patients. *Yersinia enterocolitica*and *Listeria monocytogenes*are common in the environmentwhere motility is important to them. Presumably,motility is not important in the pathogenesis of the diseasescaused by these bacteria. *Y.enterocolitica*is motile when grownat 25°C but not when grown at 37°C. Similarly, *Listeria* is motilewhen grown at 25°C and not motile or minimally motile whengrown at 37 °C.

References:

(1) Indira T. Kudva, Nancy A. Cornick, Paul J. Plummer, Qijing Zhang, Tracy L. Nicholson, John P. Bannantine, Bryan H. Bellaire. (2016). **Virulence Mechanisms of Bacterial Pathogens, Fifth Edition.**

(2) FAIRBROTHER, R.W. (2013). **A Textbook of Bacteriology, FourthEdition.**