WHAT MAKES AN ORGANISM PATHOGENIC?

**Uropathogenic Escherichia coli – an opportunistic pathogen and model system**

Approximately 50% of women will suffer a urinary tract infection (UTI) at some point in their life, and 20-30% of these women will suffer a recurrent UTI within three to four months. The rates of UTI increase in the immunosuppressed, including the elderly and children, and may result in significant complications, including renal scarring, septicemia, and pyelonephritis.

Nearly 80% of community acquired UTIs are caused by uropathogenic *E. coli* (UPEC), a Gram-negative gammaproteobacteria. UPEC has been linked to several outbreaks in recent years, and, of particular concern, antibiotic resistance within UPEC has begun to spread intercontinentally, resulting in increased morbidity and mortality. This spread of multi-drug resistant, highly virulent strains of UPEC, as well as the rate of infection in the U.S. necessitate an understanding of the underlying population dynamics of this pathogen.

In addition to being clinically important, UPEC is also an excellent model system to study the evolution of virulence in opportunistic pathogens. UPEC have been used to study biofilm formation, pili expression, epithelial cell invasion, toxin production, and population bottlenecks, in addition to its obvious use as a model for uropathogenicity. UPEC offer a number of unique advantages as a model system, including the range of laboratory tools available specific to *E. coli*, the tractability of genetic modification, and the wealth of genomic data available for the pathogen. Despite these benefits, and in contrast to other forms of pathogenic *E. coli*, the genome dynamics and population structure of UPEC remain largely unexplored. Additionally, although there has been attention paid to the global phylogenetic structure of UPEC, relatively few investigations have sought to describe the within-host distribution of the UPEC populations or elucidate the changes in population structure that occur within patients with recurrent UTIs. However, new technologies and bioinformatic tools now enable high-resolution descriptions of bacterial population structures using genomic analyses, enabling research into these unexplored areas. These analyses into population structure will facilitate a better understanding of how virulence has evolved in *E. coli* by describing the selection pressures faced by UPEC in their host habitats.

**The population structure of UPEC – a tale of two homes**

*Escherichia coli* are associated with a number clinical conditions, each caused by different strains of *E. coli* harboring different repertoires of gene sets and virulence factors, and, as such, have been categorized according to their pathology and genomic content. *E. coli* that cause disease in the gastrointestinal tract are grouped together and include enteropathogenic *E. coli* (EPEC), capable of causing adherent and effacing lesions in the gastrointestinal tract, enterohaemorrhagic *E. coli* (EHEC) that elaborate Shiga toxin and cause haemolytic uremic syndrome, Enteroaggregative *E. coli* (EAEC) and diffuse-adherent *E. col*i (DAEC) which differ in the organization during attachment to the epithelium, enteroinvasive *E. coli* (EIEC) which are capable of invading the gut epithelium, and adherent invasive *E. coli* (AIEC) which are associated with Crohn's Disease{Nataro:1998uo, DarfeuilleMichaud:2002dx, Kaper:2004bm}. A separate group consists of extra-intestinal pathogenic *E. coli* (ExPEC) and includes strains capable of causing neonatal meningitis (NMEC) and uropathogenic *E. coli* (UPEC) capable of causing urinary tract infections (UTIs) {Russo:2000vr}. In addition to phenotype, these categories of *E. coli* are delimited by differences in the genomic content of the strains, which differ markedly between pathotypes{Rasko:2008bx, Touchon:2009kw}.

Delineation of ExPEC, and consequently UPEC, strains from non-pathogenic strains of *E. coli* is difficult given the presence of ExPEC virulence factors in non-pathogenic strains {Kohler:2011cn}.

Currently, the most widely used method of grouping strains into a phylogenetic structure relies on Multi-Locus Sequence Typing (MLST), which has been used to categorize a collection of strains that vary in geographical position,

*UPEC are found predominantly in clade B2, which is overrepresented in gut and bladder populations*

*Impact of UTI on strain richness in the gut and bladder*

*Transmission and recurrence*

**UPEC virulence factors – multi-purpose tools**

*UPEC genotypes are varied, but structured*

*Virulence factors, phylogeny, and phenotype.*

*Urovirulence factors: swords or plowshares?*

**Future plans directions and unanswered questions**