1. What is uropathogenic E. coli
   1. UPEC causes disease and is an excellent model organism for the study of opportunistic pathogens
   2. What is a UTI and how is it defined?
      1. Symptoms of UTI?
      2. Incidence of UTI
      3. What is recurrent UTI?
      4. What bacteria are able to invade bladders and what bacteria cause disease
      5. Asymptomatic bacteria are also capable of existing in the bladder
   3. How is UPEC cleared from the host
      1. Natural clearance
      2. Antibiotic therapy
2. What is the population structure of UPEC
   1. Population structure of E. coli in general
      1. Describe four major clades of E. coli
      2. Where are E. coli found? Where are UPEC found?
      3. What is the function of E. coli and UPEC in their habitats?
   2. Global pop structure of UPEC and E. coli?
      1. Geographically distinct abundance of the different groups
   3. Transmission of UPEC
      1. Fecal-oral route of transmission
      2. Sex-partner
   4. Within host population structure of UPEC
      1. During UTI population structure in the bladder
         1. Figure
         2. IBCs
         3. QIRs
         4. Chronic
      2. Gut UPEC
         1. Moreno papers
         2. Other papers
3. Distribution of virulence factors in UPEC
   1. What virulence factors exist in UPEC
   2. Abundance of virulence factors
   3. Introduction of pan-genome
4. Questions that remain in the host
   1. What is the fine-grained population structure of UPEC?
   2. What strains cause recurrent UTI? Is it the same strain?
   3. Where do these strains come from?
      1. Proportion that are community acquired versus remittance in the host?
   4. Does the gut act as a reservoir for UPEC virulence factors?
      1. How many virulence factors are found in UPEC against other E. coli species?
   5. Does the population structure of UPEC change during recurrent UTI?
   6. How much recombination is involved in uropathogenesis and intra-host evolution?
      1. Note the 100 times greater chance of SNP change due to recombination than mutation from 2010 commensal E. coli paper
5. What studies of these questions will reveal
   1. Treatment plan – if you know that gut E. coli are part of the problem, then it must be addressed.
   2. Enable better understanding of how E. coli inhabit multiple environments
   3. Better understanding of how E. coli have evolved, and why they are pathogenic in the first place.
6. Experimental plan

Hypothesis: Virulence genes that increase fitness in the gut also increase fitness in the bladder and vise versa. ??

Aim 1: Identify abundance and allelic distribution of virulence factors in patients with recurrent UTI

Aim 2: Identify population structure of E. coli in gut and bladder

Aim 3: Determine competitive advantage of virulence genes.??

Questions I am trying to answer:

1. Are recurrent UTIs caused by the same strain?
2. Do genotypes that succeed in the bladder succeed in the gut?
3. Wholesale shifts occur in the gut and the bladder at the same time. Is this a recombination or strain replacement?
4. Is there a core UPEC genome? How different is the core UPEC genome compared to the core genome of E. coli?
   1. How variable is the UPEC accessory genome?
   2. Do virulence genes co-occur?
5. What is the competitive advantage of virulence genes? Do they offer fitness advantage in the gut?
   1. In patients with a secondary invasion of UPEC, could do subtraction between the genomes to identify regions that are different and ask if they are these virulence genes are responsible for the competitive advantage between isolates.

What is known:

UPEC exist in the gut