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BACTERIAL PATHOGENESIS

What makes some *E. coli* efficient bladder colonizers?

Many women suffer from recurrent urinary tract infections (UTIs), most of which are caused by uropathogenic *Escherichia coli* (UPEC). Although putative urovirulence factors (PUFs) have previously been defined, for many PUFs the mechanism of uropathogenesis has not been established. In a detailed study of a large panel of human *E. coli* isolates, Hultgren and colleagues now find that differences in the transcriptional regulation of bacterial core functions, but not the presence of PUFs, are predictive of bladder colonization.

The authors collected 43 isolates from women who had recurrent UTIs and, as the isolates were collected both during symptomatic and asymptomatic episodes, they called them urine-associated *E. coli* (UAEC). In a comparison with *E. coli* strains isolated from other sites, PUF carriage was related to phylogenetic clade rather than the ability of a strain to colonize the bladder. As most UPEC strains belong to the B2 clade, which showed high levels of PUF carriage, previous PUF analyses might have been biased. To further clarify the role of PUFs, the authors inoculated mouse bladders with 21 representative UAEC strains. Neither the ability to colonize the bladder nor the bacterial loads correlated with PUF carriage. In fact, in competition experiments, some strains that had few PUFs were able to outcompete isolates that had more PUFs. Together, these results indicate that PUF carriage does not explain the potential of *E. coli* to cause UTIs.

To identify other factors that contribute to uropathogenesis, the authors compared the gene expression of efficient and deficient bladder colonizers after *in vitro* growth. A notable difference between the two UAEC groups was found in the expression of chaperone–usher pathway pili. Furthermore, RNA-seq data showed that transcripts that encode six core functions, including motility, chemotaxis and transport of carbohydrates, were differentially abundant just prior to infection. These results suggest that changes in the expression of conserved functions can affect the ability of UAEC to colonize the bladder.

As uropathogenesis seemed to be a dynamic process that was dependent on the differential regulation of core bacterial functions, the authors tested whether host factors also affect colonization efficiency. Therefore, they infected a second mouse strain with the same set of UAEC strains. Most strains showed similar levels of bladder colonization in both mouse models. However, two isolates colonized bladders less efficiently in the second mouse model, which indicates that varying interactions between pathogen and host determine uropathogenesis. Importantly, the ability of UAEC strains to colonize mouse bladders correlated with the inflammatory response in patients. At the time of a UTI, women who were infected with strains that efficiently colonized mice had higher levels of leukocytes in their urine, which is a sign of more severe disease.

Thus, the work by Hultgren and colleagues highlights that uropathogenesis is a complex, dynamic process that cannot be predicted simply by carriage of specific virulence factors.

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> “uropathogenesis seemed to be a dynamic process that was dependent on the differential regulation of core bacterial functions”

ORIGINAL ARTICLE Schreiber, H. L. *et al.* Bacterial virulence phenotypes of *Escherichia coli* and host susceptibility determine risk for urinary tract infections. *Sci. Transl. Med.* **9**, eaaf1283 (2017)
FURTHER READING Flores-Mireles, A. L. *et al.* Urinary tract infections: epidemiology, mechanisms of infection and treatment options. *Nat. Rev. Microbiol.* **13**, 269–284 (2015)