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Normally the urinary tract is a sterile environment that is kept free of bacteria by the rinsing flow of urine and by antibacterial factors and immune cells. Despite these host defense mechanisms, urinary tract infection (UTI) is one of the most common infections in humans. About 50% of all women will have at least one UTI during their lifetime, and of those around 25% will have one or more recurrent UTI. The majority of all UTIs are caused by uropathogenic Escherichia coli (UPEC). UPEC strains have acquired successful strategies to subvert the host defense and antibiotics to persist in the urinary tract. Multidrug-resistant UPEC isolates are increasing around the globe and pose a risk to public health. Knowledge about their virulence properties and host activating mechanisms is important for identifying alternative treatment strategies to cope with the growing threat. Thus, the studies presented in this thesis focus on the host defense mechanisms during a UPEC infection.