



***Candida Albicans* Biofilms on Catheters: Persistence, Dispersal, Drug Resistance and Host Response**

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Candida albicans can form a high-density-community of cells called biofilms on indwelling medical devices, which are shielded from host immune cells and antifungal drugs, alike. Host immune response to biofilms is poorly understood, thus contributing immensely to our failure in controlling catheter-related candidiasis. We used immunocompetent mice to demonstrate that subcutaneously (subQ) inserted catheters pre-infected with *C. albicans*, displayed consistently high levels of infection for over 10-14 days, while subQ infection without catheters resolved quickly within 5 days. Retention of catheters resulted in dissemination to kidney with fungal burden 2 logs higher than subQ infected mice. Blocking biofilm dispersal by downregulating *C. albicans PES1* *in vivo* significantly reduced biofilm dissemination. A novel repurposed compound alexidine dihydrochloride could block biofilm growth *in vitro* and *in vivo*, serving as a potential anti-biofilm drug. Host response in tissues surrounding catheter-biofilms *versus* subQ infection was studied by RNAseq, four days after catheter placement (or subQ infection). Gene expression data demonstrated largely a balanced pro- (Th-1) and anti-inflammatory (Th-10) immune response with neutrophil degranulation being the most upregulated group ($p=1.1e-16$) in tissues surrounding biofilms. Interestingly, the category that predominantly stood out was Interferon- α/β signaling upregulated >3 fold. These genes encode for Guanylate Binding Proteins 2, 3 and 5 (*GBP2*, *GBP3* and *GBP5*) - GTPases shown to be specifically upregulated by IFN- $\alpha/\beta/\gamma$ and markedly protective against bacteria and protozoan infections. The role of some of these newly discovered genes in anti-*Candida*/anti-biofilm activity, and identifying the *C. albicans* proteins that activate these host genes, are the subject of our ongoing investigation.