

## Lecture consigliate da Anna Prigitano (gennaio 2019)

Il biofilm è formato da cellule, adese a superfici naturali (mucose) o artificiali (cateteri, protesi, ecc), incorporate in una matrice extracellulare (ECM), composta da polisaccaridi, proteine, acidi nucleici e altri componenti prodotti dalle cellule stesse. La complessità strutturale, la presenza di una matrice extracellulare, l'eterogeneità metabolica e l'up-regulation dei geni della pompa di efflusso sono alcuni dei fattori che determinano la maggior difficoltà nel trattare le cellule in forma sessile rispetto a quelle in forma planctonica. I microrganismi organizzati in biofilm sono infatti più resistenti ai farmaci antifungini rispetto alle cellule planctoniche. Molti funghi importanti dal punto di vista clinico producono biofilm; tra questi: *Candida*, *Aspergillus*, *Cryptococcus*, *Trichosporon*, *Coccidioides* e *Pneumocystis*.

Alcuni articoli per conoscere ed approfondire questo argomento possono essere:

[Fungal biofilms](#). Fanning S, Mitchell AP. PLoS Pathog. 2012;8(4):e1002585. doi: 10.1371/journal.ppat.1002585. Epub 2012 Apr 5

Fungal biofilms, drug resistance, and recurrent infection. [Desai JV<sup>1</sup>](#), [Mitchell AP<sup>1</sup>](#), [Andes DR<sup>2</sup>](#).

[Cold Spring Harb Perspect Med](#). 2014 Oct 1;4(10). pii: a019729. doi: 10.1101/cshperspect.a019729.

A biofilm is a surface-associated microbial community. Diverse fungi are capable of biofilm growth. The significance of this growth form for infection biology is that biofilm formation on implanted devices is a major cause of recurrent infection. Biofilms also have limited drug susceptibility, making device-associated infection extremely difficult to treat. Biofilm-like growth can occur during many kinds of infection, even when an implanted device is not present. Here we summarize the current understanding of fungal biofilm formation, its genetic control, and the basis for biofilm drug resistance.

[Fungal Biofilms: Update on Resistance](#). Borghi E, Borgo F, Morace G. Adv Exp Med Biol. 2016;931:37-47. doi: 10.1007/5584\_2016\_7

Over the past decade, the emergence of biofilm-related invasive fungal diseases has been the subject of numerous studies focused on antifungal resistance and its impact on antifungal therapy in severely ill patients. The majority of the studies investigated the molecular mechanisms involved in antifungal resistance and pathogenicity of biofilm production by *Candida albicans* and *Aspergillus fumigatus*, the most common etiologic agents of yeast and mold invasive infections. The main mechanism characterizing biofilm-related antifungal resistance is the production of extracellular matrix, a physical barrier preventing the drugs from entering and expressing their activity. However, over-expression of efflux pumps, genetic changes of drug targets, persister cells, biofilm-host immune system interaction, proteins leading to filamentation, all together contribute to the onset of biofilm antifungal resistance. Some of these mechanisms are shared with planktonic cells and are often related to developmental phases of biofilm formation. All physical and genetic factors leading to biofilm-related antifungal resistance have been briefly discussed.