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Metabolic adaptation triggers *Candida albicans* biofilm phenotype

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Background & Aims

Candida albicans biofilm formation is highly variable amongst clinical isolates¹. The ability to form biofilms can impact clinical outcomes in certain patient groups². We have shown that amino acid metabolism plays an important role in constitutively driving high biofilm phenotypes³, though we have also observed strains with a low biofilm phenotype capable of forming biofilms under certain conditions, suggesting a degree of adaptability^{1,3}. We hypothesised that the biofilm phenotype is inducible in those organisms, therefore, we aimed to use a multi-omics approach to investigate metabolic adaptation in these strains.

Methods

C. albicans (CA) clinical isolates categorised as High or Low Biofilm Forming (HBF and LBF)²

Biofilm Formation: RPMi ± 20% FCS
10⁶ CFU/mL at 37°C

Microscopic Analysis (SEM)

Biofilm Biomass (Crystal Violet)

Transcriptomics (HiSeq 50bp Sequencing)

Extracellular Metabolomics (LC/MS)

Bioinformatics

RNA-Seq reads quality control (FastQC, Trimmalore)

Polyomics Metabolomics Pipeline (PIMP)

Transcript Abundance (Kallisto)

Differential Expression (DESeq2)

KEGG Pathways (ClusterProfiler, KEGGREST)

Identified Peaks = retention time and mass
Annotated Peaks = mass only

Pathway Visualisation (MetExplore, Pathview)

References

- Kean *et al.* 2018. Gaining Insights from *Candida* Biofilm Heterogeneity: One Size Does Not Fit All. *J Fungi* (Basel). 15:4(1). pii: E12. doi: 10.3390/jof4010012. Review.
- Rajendran *et al.* 2016. Biofilm formation is a risk factor for mortality in patients with *Candida albicans* bloodstream infection-Scotland, 2012-2013. *Clin Microbiol Infect.* 22(1):87-93. doi: 10.1016/j.cmi.2015.09.018. Epub 2015 Sep 30.
- Rajendran *et al.* 2016. Integrating *Candida albicans* metabolism with biofilm heterogeneity by transcriptome mapping. *Sci Rep.* 6:35436. doi: 10.1038/srep35436.

Results

Figure 1. Serum induced biofilm formation

Figure 3. Secretome of LBF *C. albicans* strains in FCS & RPMi

Figure 2. RNA-Seq of serum induced LBF *C. albicans*

A: Differential expression in RPMi and FCS

B: Deregulated functional categories in RPMi vs +FCS

C: FCS deregulated pathways in LBF at 24h

ID	Score	Symbol	Genes
ca00260	950.70	Glycine, serine and threonine metabolism	CH42, SHM1, SHM2, GCV1, GCV2
ca00670	850.75	One carbon pool by folate	SHM1, SHM2, GCV1, ADE3
ca00260	858.07	Valine, leucine and isoleucine biosynthesis	CH42, Cae7_0053, ILV2
ca00270	434.07	Cysteine and methionine metabolism	CH42
ca00930	319.16	Glyoxylate and dicarboxylate metabolism	SHM1, SHM2
ca00960	319.16	Methane metabolism	SHM1, SHM2
ca00940	319.16	Cyanosulfate acid metabolism	SHM1, SHM2
ca00960	125.04	C5-Branched dibasic acid metabolism	CaP7_0053, ILV2
ca00960	40.70	Biotin metabolism	ILV2
ca00770	40.70	Pantoic acid and CoA biosynthesis	ILV2

D: Metabolic pathways: 24h serum exposure

Figure 4. Matched over-represented pathways

Figure 5. Serine metabolism is an important pathway