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# 膵がんの進行を早める真菌

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近年の微生物叢（microbiome）研究では、細菌の dysbiosis が癌をはじめ、様々な疾患に影響していることが明らかとなってきた。しかし、研究の中心は細菌であり、真菌叢（mycobiome）と疾患との関連性については未解明な部分も多い。

ニューヨーク大学の Miller らは一部の真菌が腸管腔から膵臓に移動し、膵管腺がん（PDA）の発症に関係することを報告している。本研究では膵臓がん発症過程で真菌叢の変化が変化すること、そして一部の真菌が膵がんの増殖に関わることを明らかにしている。

## 紹介論文

## The fungal mycobiome promotes pancreatic oncogenesis via activation of MBL

Berk Aykut, Smruti Pushalkar, Ruonan Chen, Deepak Saxena, George Miller, *et al*.

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**Abstract**

Bacterial dysbiosis accompanies carcinogenesis in malignancies such as colon and liver cancer, and has recently been implicated in the pathogenesis of pancreatic ductal adenocarcinoma (PDA)1. However, the mycobiome has not been clearly implicated in tumorigenesis. Here we show that fungi migrate from the gut lumen to the pancreas, and that this is implicated in the pathogenesis of PDA. PDA tumours in humans and mouse models of this cancer displayed an increase in fungi of about 3,000-fold compared to normal pancreatic tissue. The composition of the mycobiome of PDA tumours was distinct from that of the gut or normal pancreas on the basis of alpha- and beta-diversity indices. Specifically, the fungal community that infiltrated PDA tumours was markedly enriched for *Malassezia* spp. in both mice and humans. Ablation of the mycobiome was protective against tumour growth in slowly progressive and invasive models of PDA, and repopulation with a *Malassezia* species—but not species in the genera *Candida*, *Saccharomyces* or *Aspergillus*—accelerated oncogenesis. We also discovered that ligation of mannose-binding lectin (MBL), which binds to glycans of the fungal wall to activate the complement cascade, was required for oncogenic progression, whereas deletion of MBL or C3 in the extratumoral compartment—or knockdown of C3aR in tumour cells—were both protective against tumour growth. In addition, reprogramming of the mycobiome did not alter the progression of PDA in *Mbl-* (also known as *Mbl2*) or *C3*-deficient mice. Collectively, our work shows that pathogenic fungi promote PDA by driving the complement cascade through the activation of MBL.