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Microbiology

Finding Dracula's silver bullet: the fight against a bloodthirsty fungus

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ABSTRACT

That's correct, the darkness loving, light fearing, blood sucking prince of darkness, Count Dracula was a fungus. In our recent research, we describe that just like Dracula, the fungus Aspergillus fumigatus "wants your blood."

Bela Lugosi in Dracula (1931) - Image credits: Public domain

That's correct, the darkness loving, light fearing, blood sucking prince of darkness, Count Dracula was a fungus. In our recent research, we describe that just like Dracula, the fungus *Aspergillus fumigatus* "wants your blood." The parallels are uncanny, both prefer dark places (Dracula: a coffin, *Aspergillus*: a compost pile), both are very difficult to kill, both are opportunistic predators (Dracula stalking unwitting victims and *Aspergillus* invading immune suppressed persons) and both are driven by a bloodthirsty need.

For those of you unfamiliar with *Aspergillus fumigatus*, you shouldn't be, as you have likely inhaled thousands of *Aspergillus* spores today. *Aspergillus fumigatus* is a common mold (a type of fungus) that grows in decaying organic material (does it sound like a thing Dracula would do?), releasing airborne spores that cause a variety of lung diseases in millions of persons worldwide. In some people *Aspergillus* lies dormant, colonizing their lungs and causing conditions such as severe asthma. But in others it rises from its dormant state and invades its victims, resulting in often-fatal fungal pneumonias. Previously, the reason behind this switch in the mold's behavior was unknown. People that undergo lung transplantation are particularly vulnerable to *Aspergillus*-related pulmonary diseases, which occur in one third of the patients. Most would attribute an increased risk of invasive infections to the medications that suppress the immune system used after the transplant. However, one fact puzzled us: lung transplant recipients develop diseases related to fungal colonization that is with the fungus living inside the host without

directly harming host tissue; and those pulmonary diseases classified as invasive, when the mold spreads into host tissues causing damage. So, if it is not immune suppression driving invasive fungal infections (as all lung transplant patients are immunosuppressed) then, what could it be? The plot thickens.

We performed mini-transplants. Removing a *REALLY* small piece of trachea from one mouse and implanting it into a recipient mouse. This simulated a lung transplant. We found that rejection of the transplant created "blood lakes" in the donor tissue that had been transplanted. The appearance of these blood lakes predicted a change in behavior of the fungus from colonization to invasion. We found that *Aspergillus* liked blood, but what it really wanted was the iron in it, and the more iron it got, the deeper the invasion became, its hunger was insatiable.

A passage from Bram Stoker's Dracula, describing the sea voyage of Dracula to London
"On the 2nd of August, another crew member disappears. At midnight…the remaining deck hand disappears and the captain and the mate are the only remaining men aboard."

Iron is one of the primary components of blood, allowing hemoglobin to transport oxygen from the lungs to our cells. Iron is essential for nearly all living organisms including harmful bacteria and fungi. Thus, the competition for iron is a critical battleground between the infected host and the infecting pathogen. We found that in our mini-transplants the blood became large iron deposits, like fertilizer for a plant. To make sure that we were not just describing a phenomenon in tiny mouse transplants, we obtained biopsies from persons after lung transplant. These tissues also had increased iron levels. So, we concluded that when the iron balance is shifted in the lungs it increases the risk of infection by vampire-like pathogens.

All hope is not lost. Dracula has garlic and sunlight, *Aspergillus fumigatus* has iron chelators. Chelators are chemicals that bind metals, lowering the amount available for the fungus. When we treated transplanted mice with iron-binding chelators the fungus was not invasive. The ramifications of this are potentially important as a treatment for these infections and others. Remember that iron is a fundamental need. Thus, pathogens are less likely to develop resistance. (Sigh of relief)

So, by now you are likely convinced that indeed Count Dracula is a fungus, but in case there remains doubt, consider this:

A passage from Bram Stoker's Dracula describing the contents on the ship.
The only cargo on board the ship was "a ballast of silver sand, with only a small amount of cargo-a number of great wooden boxes filled with mold."

Here the 'mold' represents Transylvanian earth, lairs that Dracula rests in, in order to replenish his strength. Just like a fungus.