

Written responses to open questions of the webinar ‘Discovering and developing new treatments for fungal infections’ originally broadcast on 27 July 2021. See webinar recording here: <https://revive.gardp.org/discovering-and-developing-new-treatments-for-fungal-infections/>

Question asked	Response from the speakers
Is there any specific immunomodulating pathway specific for fungi to target? Discriminating them against bacteria and virus	I suggest to read the article: Immunomodulation for the Treatment of Fungal Infections: Opportunities and Challenges (Frontiers in Cellular and Infection Microbiology, 2020)
Was the FKS vaccine further optimized, or it was dropped out once the efficiency in humans was not observed?	I think the FKS vaccine has been dropped. Investigators are now focusing on different vaccine/strategies.
Are there any noted severe side effects of monoclonal antibodies (mABs)? How frequently do antigens of fungi mutate, making mABs inefficient?	<p>About the first question: I suggest the article: The safety and side effects of monoclonal antibodies (Nature Reviews Drug Discovery, 2010). It is an old review but a nice one.</p> <p>About the second question: Frequently. We also see this with Covid-19 (see Mapping mutations to the SARS-CoV-2 RBD that escape binding by different classes of antibodies (Nature Communications, 2021) for a recent article)</p>
For the acylhydrazone compounds, most of the substituents on the aromatic rings are chlorine and bromine. Were fluorine analogues synthesized and tested? If so, what are their efficacies?	Yes, the data are being prepared for publication.
For Tejas Bouklas - How easy was it to recruit students for these purposes? Also, what do students do, except for collecting soil samples or other activities? Do they get some sort of advanced mentoring in learning specific techniques, or you expect them to get that knowledge in regular lectures?	It was very easy to recruit students as they took the courses as either part of their required first-year course or as a requirement in their advanced years (if interested in health careers). Students spend only the first two weeks collecting soil samples, then advance to molecular biology and microbiology techniques that are standard to most biomedical science graduate degrees. They receive the theoretical background for these techniques in complimentary lecture courses that span the length of the labs.
For both speakers - Derivatives of cannabis are getting more and more popular nowadays. Are you aware of using medical cannabis as antimycotic treatment? What are your personal comments on the potential of cannabis as antimycotic?	Yes, cannabis have antimicrobial effect, including antifungals. I am not sure tough if this antifungal effect is achieved by a concentration of the cannabis not sufficient to induce a neurological effect.

Remaining audience questions from the webinar ‘Discovering and developing new treatments for fungal infections’, broadcast on 27 July 2021.

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Have you noticed any systematic absorption of D13 or other analogues?	Yes
Is there any research on white nose syndrome in bats?	Not with our compounds
What is your opinion of natural products as a source of novel antifungal agents?	<p>Natural products would address the issue of abundance, resistance-issues, and production issues. As evidenced by the crowd-sourcing of these products, this is not an easy task as there are several rediscoveries, and efforts will have to be widespread to address the growing drug resistance.</p> <p>There are wonderful natural antifungal compounds out there. We just need to develop them.</p>
For Tejas Bouklas - Does your institution have a recruiting placement program for your Sea Phages and Tiny Earth Students to place them in jobs in the biotech companies doing antimicrobial research?	Yes, we have a few statewide entities (CSTEP, STEP), a Health Professions advisory committee, and individual faculty advising. We also work closely with the career office.
What are the reasons for the long treatment requirement of existing antifungal therapies	Mostly, the lack of fungicidal effect of azoles.
For Maurizio Del Poeta - Since SB-AF-1002 is more active by iv route - is there any oral PK data available which can correlate to the lower efficacy by po dosing?	Yes, we do have these data and has been published.
For Maurizio Del Poeta - How worried should one be about "Mucormycosis" that is caused by covid-19 due to the use of steroids? What type of research is occurring in regards to Mucormycosis? What are the current treatments against this besides surgically removing it?	<p>This is indeed an important complication of Covid-19, mainly occurring in diabetic subject using steroids and frequent in India. Our drugs are efficacious against Mucor, at least in vitro and we are currently testing this in the animals. Current treatment are classic antifungals. We hope our study (see Group IIA secreted phospholipase A2 is associated with the pathobiology leading to COVID-19 mortality (Journal of Clinical Investigation, 2021)) will help in identifying severe Covid-19 before mucor will occur. Treating these patients with an anti-PLA2 should prevent covid severity and perhaps also its complications (Clinical trials are on-going).</p>

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Acylhydrazones are nonspecific warheads. Is that not a problem?	The compounds have been used for a variety of diseases. Fungal specificity is achieved by producing subclasses. As long as they are not toxic, we are fine with that.
For Tejas Bouklas - Just would like to say what amazing work you are doing. I am currently participating in Antiboitcs Undersea with University of Westminster in London, UK which is similar to tiny Earth/ SEA_PAGES. What advise could you gave to students such as me, who is in their final year of their biomedical science, to successfully take advantage of these programmes and tips to showcase the skills gained, and how to continuously develop these skills post-progamme/ after completing the programme.	As I am sure you are aware, your training is quite diversified and therefore marketable with the program you are completing. My general advice to showcase this is to consider communicating your progress via publications and presentations. Specifically, publications in teaching-focused or student-focused journals (e.g. JMBE) and presentations at national and international levels to establish post-graduate connections.
How can we enroll in tiny earth project?	Please click “join us” at https://tinyearth.wisc.edu . There are annual training sessions and symposiums; however, you do not necessarily have to attend those to enroll. After joining, you can receive access to all curriculum resources.