therapy and surgery with low success rates, resulting often in amputation and social stigma. To improve the current therapeutic successes rates a novel drug is needed. Due to the lack of interest in the pharmaceutical industry, in-vivo open source drug discovery programs for mycoses was established called MycoDIS.

In total 1560 compounds were screened for in vitro activity against M. mycetomatis and many more are currently being screened. Compounds that were able to inhibit growth at 100 μM, 25 μM, and had an IC50 < 8 μM were selected for studying the in vivo efficacy in an M. mycetomatis model in the interdigital Galleria mellonella

One of the 1560 compounds screened against M. mycetomatis, 302 was able to aid patient growth at 100 μM, 25 μM of those most active to be screened in vivo. From these, 25, rate did protruding larval survival. These included 37 α-cyano tested, olefilin, fruridin, MMV016557, MMV422474, MMV71076, and MMV712837. Based on these results, 6 compound were selected for further studies. We included 3 compounds (active: 1), the astomammata (active: 5), the phenothiazines (active: 5), the phenoxazins (active: 5), and the ketones (active: 6). For all 1 in 18 total additional compounds were screened. By analyzing the in vitro activity and in vivo efficacy to relation to the chemical properties of the molecules it appears that the LogP value of a compound was important for penetrating into the mycosis grain.

In conclusion, using an open source drug discovery approach for mycoses we were able to identify novel lead compounds. Some of these compounds were highly active against M. mycetomatis (dinuclear, amphotericin, phagosacids, and ketones), while other compounds such as the lamellodermatae also active against other causative agents as well. Screening more analogs of identified compounds allowed us also to identify chemical properties which are favorable for grain penetration in vivo. This will allow us to chemically design more active compounds for this difficult to treat infection.

S6.5d Molecular identification of mycoses causative agents from patients in hospitals setting in Senegal

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S6.5d 1 Biofilms of improving the management of mycoses: working towards the 2030 goal, September 22, 2011, 2:45 PM

- 6:15 PM

Mycoses is a chronic granulomatous inflammatory disease that is caused either by bacteria or fungi. The diagnosis of species is important to guide the therapeutic management of patients particularly for white and yellow grains. However, the identification of the causative agents using mycological and histological techniques is a real problem in our countries. This study aims to identify etiological agents using molecular techniques in Senegal.

Methods: A retrospective study was carried out to compare mycological and histological techniques with molecular methods in patients admitted in the hospital setting. Blood specimens and/or grains obtained from those patients were examined by PCR targeting the ITS (fungal agent) and 16S (actinomycoses agents) genes. Sequencing with the Sanger method allowed us to identify the species.

Results: Preliminary results were obtained from 30 patients. The grains collected were black (18%), red (4.7%), white (47%), and yellow (9.3%). Discriminative PCR ITS vs 16S identified 7 actinomycoses agents including white and yellow grains and 5 fungal agent. The fungal agent was identified after sequencing in Microsporean languag.

Conclusions: The preliminary results of this study show the importance of discriminative PCR to guide the therapeutic choice of clinicians. Its widespread use could improve the detection and management of mycoses cases in Senegal.

S7.1d Reliability of bedside point-of-care tests for Candida neoformans , M. tuberculosis and S. pneumoniae in adults living with HIV presenting with suspected central nervous system infection (CNS) in low- and middle-income settings: Preliminary results from the DREAM study

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S7.1d 1 Update in management of fungal infection in adult hematology, September 25, 2012, 10:30 AM - 12:00 PM

Background: Bedside point-of-care (POC) testing, with parallel laboratory testing, offers a unique opportunity to improve and speed up the diagnostic workflow of people living with HIV with suspected CNS infection in resource-limited settings.

Objectives: To assess the agreement between POC tests for Cryptococcus neoformans, Mycobacterium tuberculosis, and Streptococcus pneumoniae performed at the bedside and in the routine laboratory, in African low- and middle-income countries (LMICs).

Methods: From January to March 2012, the following POC tests were performed in parallel at the bedside and in the routine laboratory: Cryptococcal antigen lateral flow assay (CrAg LFA,Immy) in blood and cerebrospinal fluid (CSF); tuberculosis lipoprotein immunomagnetic beads (TB-LAM, Alere) in urine, and, where indicated, pneumococcal antigen (Streptococcus pneumoniae OP, Bocon) in CSF.

Participants: HIV-infected adults (>18 years old) suspected of CNS infection.

Setting: The prospective multicenter DREAM study (Driving Research in Meno and Encephalitis Mortality) in five hospital sites in Cameroon, Malawi, and Tanzania.

Primary outcome: Cohen’s kappa statistic of agreement between the results of POC tests obtained at the bedside and the routine laboratory.

Results: The study included 516 consecutive participants (mean age 39.2 ± 10 years; 48.7% ART-experienced; 46.3% male, and 37% HIV-positive [75%]). In total, 14,653 (34.3%) participants had positive bedside CrAg in blood, 14,915 (35.4%) positive bedside CrAg in CSF, 4,474 (31.8%) positive bedside TB-LAM in urine, and 1,017 (5.1%) positive bedside SP in CSF. Kappa statistics evaluating agreement between bedside and laboratory test results were 0.89 (95% confidence interval [CI] 0.85-0.93; p < 0.01) for blood CrAg, 0.89 (95% CI 0.88-0.90; p = 0.001) for CSF CrAg, 0.92 (95% CI 0.87-0.96; p < 0.05) for urinary TB-LAM, and 0.68 (95% CI 0.60-0.76; p < 0.05) for CSF SP.

Conclusions: Bedside POC tests for Cryptococcus spp. are highly reliable and can be safely performed in parallel to laboratory testing to expedite targeted treatment in people living with HIV with suspected CNS infections in African LMICs. Other bedside POC tests need further evaluation before large-scale implementation.
Environmental surveillance of *Aspergillus fumigatus* in Dutch agricultural crops

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Conclusions: Our results suggest that not only azole-containing plant-waste material but also other agricultural crops can be hotspots for resistance selection in *A. fumigatus* and underscores the need to further investigate transmission routes.

**ST4a**

Vaccine-inducing lung resident CD4+ memory T cells are protective against *Cryptococcus gattii* infections

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Cryptococcus gattii is a highly virulent fungal pathogen that can cause cryptococcosis in previously healthy individuals. It is not fully understood how innate and acquired immune responses cooperatively suppress *C. gattii* infection. Here, we have reported the following findings, (1) Specific environment for exposure of dectin-1 and dectin-2 ligands in cryptococcal cells (PLOS ONE 2019, PMID 31398236), (2) C2013-mediated immune recognition for *C. gattii* and capsule dependent immune...