

## Making molecules that matter: Fighting mycetoma in the undergraduate laboratory

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The Breaking Good Project (<a href="www.breakinggoodproject.com">www.breakinggoodproject.com</a>) has been working with high school and undergraduate students from around the world, involving them in crowdsourced citizen science projects where they *make molecules that matter*. In this presentation, we will share the latest achievements of undergraduate students from The University of Sydney and their contributions to the Open Source Mycetoma project, MycetOS.

Mycetoma was first recognised by the World Health Organization as a neglected tropical disease in 2016. It is endemic to tropical and subtropical areas though the true burden of the condition is unknown. Currently, actinomycetoma (bacterial infection) can be effectively treated with a course of antibiotics at a 90% curative rate. Eumycetoma (fungal infection) treatment options, consisting of a combination of antifungal therapy and surgery, on the other hand are less effective with curative rates between 25-35%. MycetOS (<a href="https://github.com/OpenSourceMycetoma">https://github.com/OpenSourceMycetoma</a>) is an open source drug discovery collaboration searching for a viable treatment for eumycetoma.

In 2021, first year students at The University of Sydney focused on the synthesis of compounds in the 2-aminothiazole family (series 2), a hit identified from screening of the MMV Stasis Box against *Madurella mycetomatis*. Working as open scientists, the team synthesised and characterised 12 novel compounds. In all bar one instance, final products were obtained in >99% purity (HPLC) and in 25-84% yields. Biological evaluation of the compounds against *Madurella mycetomatis* provided evidence of a key structural 2-pyridine that is required for potent activity.

## Series 2 hit compound SAR Exploration 2021 MYOS\_00176\_00\_01 (MMV006357) MIC = 0.25 uM In vivo 28.6% larvae survival rate

## References

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- 3. W. Lim *et al*, "Addressing the most neglected diseases through an open research model: The discovery of fenarimols as novel drug candidates for eumycetoma" PLOS Negl Trop Dis, **12**(4), e0006437 (2018). DOI 10.1371/journal.pntd.0006437