

The orotomides were discovered by screening a 370,000 compound small molecule library for antifungal activity against *Aspergillus fumigatus*. The series was developed by standard SAR-driven iterative medicinal chemistry and antifungal susceptibility screening. Initially unknown, the mechanism of action was investigated in various ways:

1. Genetic screen ±An *A. nidulans* genomic library carried on the AMA1 plasmid  
(2)