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Abstract (oral session)

Rapid detection of azole-resistance in Aspergillus fumigatus by isothermal microcalorimetry

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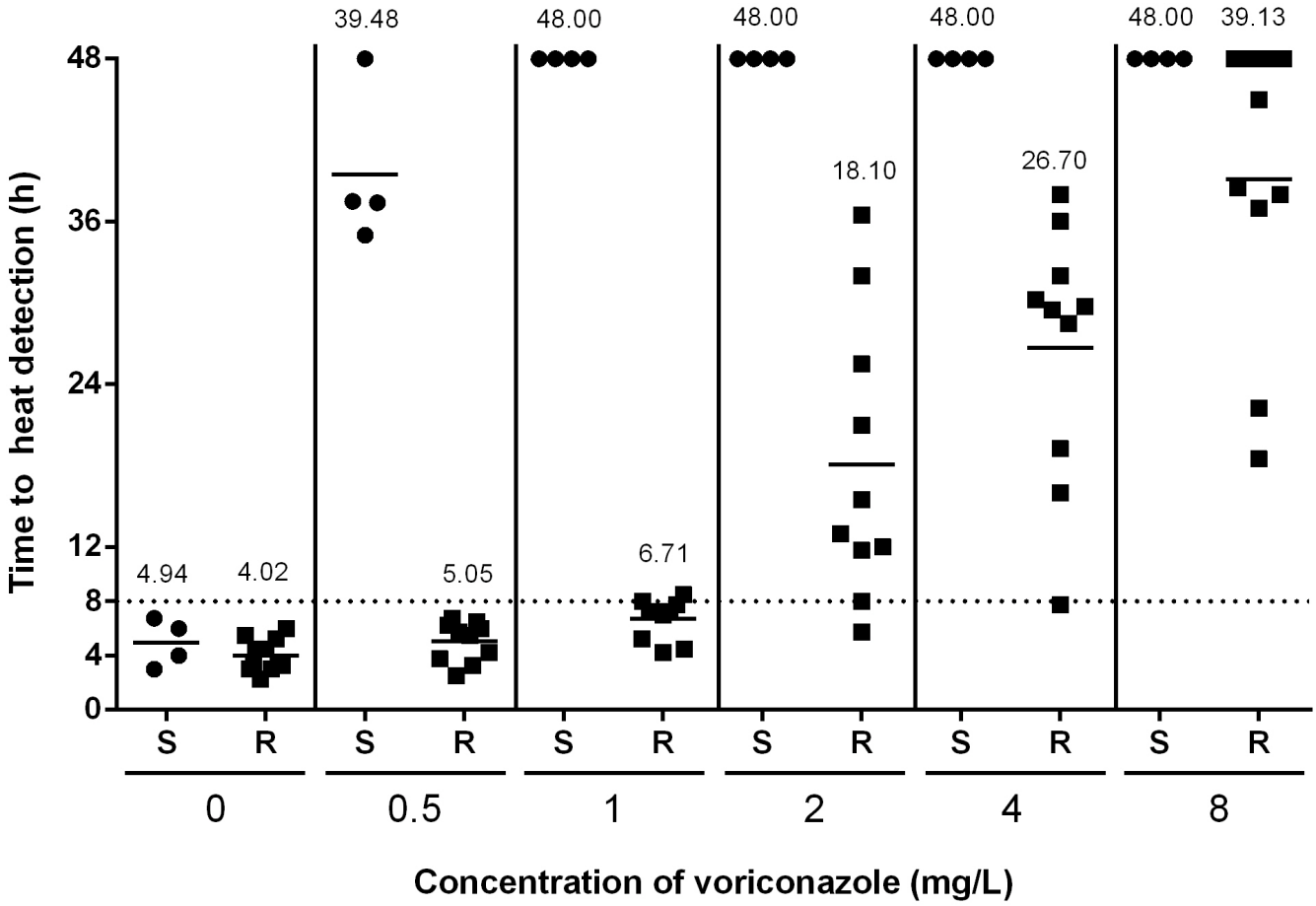
Objective: Azole resistance in A. fumigatus is an emerging problem. Due to an often rapid disease progression, early detection of resistance is crucial for an immediate start of optimal antifungal therapy. We evaluated isothermal microcalorimetry as a new method for rapid and accurate detection of voriconazole-resistance in genetically characterized azole-resistant A. fumigatus strains harboring mutations in the cyp51 gene. Methods: 11 resistant (MIC >2mg/L) and 4 susceptible (MIC <= 1 mg/L) A. fumigatus strains were tested. A. fumigatus ATCC 204305 was included for quality control. Isothermal microcalorimetry was performed at 37°C by inoculation of 10^5 conidia in 3 mL Sabouraud dextrose broth (SDB) containing serial dilutions of voriconazole. SDB only was used for growth control. Heat produced by fungal growth was measured for 48 h. Detection time was defined as heat flow exceeding 20 µ W. Results: Figure shows the time to heat detection (mean) of susceptible (S) and resistant (R) A. fumigatus strains in the presence of voriconazole at increasing concentrations. In absence of voriconazole the detection time for susceptible and resistant strains was 4.94 ± 1.7 h and 4.02 ± 1.2 h, respectively. In the presence of voriconazole at 0.5 mg/L, the detection time increased to 39.48 ± 5.8 h (p = 0.03) for susceptible strains, whereas growth related heat of resistant strains were detected within 8 h (indicated by the horizontal line) with a mean detection time of 5.05 ± 1.5 h. Growth of all susceptible strains was inhibited for at a concentration of 1 mg/L, whereas growth of resistant strains was detected in 6.7 ± 1.5 h. At concentrations of 4 and 8 mg/L, the detection time was 26.70 ± 9.5 h and 39.13 ± 10.9 h, respectively, for resistant strains. Conclusion: This proof-of-concept study demonstrates the potential of microcalorimetry as a useful tool for rapid detection of azole-resistant in A. fumigatus. Resistant strains could be distinguished from susceptible strains within 8 h in the presence of voriconazole at 0.5 mg/L. For further validation of the assay, additional resistant and susceptible A. fumigatus strains will be tested.


Time to heat detection (h)
48
36
24
12
8
4
0
4.94
4.02
39.48
5.05
48.00
6.71
48.00
18.10
48.00
26.70
48.00
39.13
S
R
0
0.5
1
2
4
8
Concentration of voriconazole (mg/L)