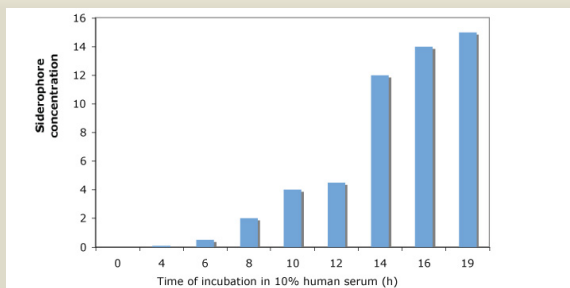


## Diagnostic Test and Drug Screening for Invasive Aspergillosis

An early detection test (ELISA TEST) is under development for markers of the fungus *Aspergillus fumigatus* in the blood of patients with invasive aspergillosis.

The test method detects a siderophore, called triacetylfulvarinine C (TAF), produced in large amounts (90% of total siderophores secreted) by *A. fumigatus* within hours after spore germination<sup>1</sup>. TAF is an iron chelator required for *A. fumigatus* virulence.<sup>2,3,4</sup>



**Figure 1.** Siderophore production (micromolar) by *A. fumigatus* when grown in serum-containing medium. Spores were inoculated at time 0 and grown at 37°C and 150 rpm.<sup>1</sup>

### The Problem

Inhalation of *A. fumigatus* spores by immuno-suppressed patients, e.g. patients who are receiving cytotoxic cancer chemotherapy, and bone marrow and solid organ transplant recipients, can result in the development of invasive pulmonary aspergillosis (IA)<sup>5</sup>. IA is now a leading cause of death in these patients, with mortality rates as high as 60% even with drug treatment<sup>5</sup>.

### The Alternative

The current test (BioRad Platelia) measures circulating galactomannan, a carbohydrate shed from the fungal cell wall during hyphal growth<sup>6</sup>. However, the sensitivity is variable (29-100%)<sup>6</sup> and false positive rates in children are high (83%)<sup>7</sup>. To improve patient survival, there is a need for earlier detection with high sensitivity.

A test is being developed for the detection of TAF circulating in the blood as a result of fungal infection<sup>8</sup>. This diagnostic test based on the TAF siderophore is superior to the galactomannan assay (BioRad) because:

- TAF is stable in human serum<sup>1</sup>
- Large amounts are secreted in serum early in the fungus life cycle<sup>1</sup>
- Anti-peptide antibodies have a high affinity compared to anti-carbohydrate antibodies
- Standard diagnostic sample extraction developed.

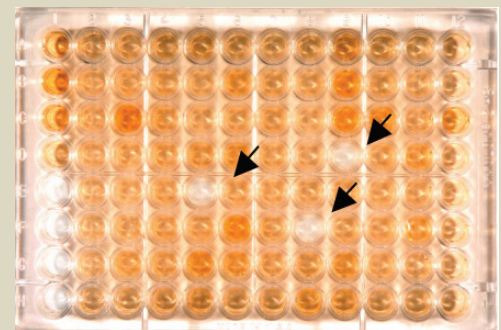
### The Benefits

An early detection test for aspergillosis will save lives by appropriate use of therapeutic agents which will:

Reduce unnecessary use of

- antifungal drugs;
- Decrease resistance to such agents;
- Reduce extensive hospitalization.

The overall aim is to save costs and resources in any healthcare system. Another benefit is to provide the pharmaceutical industry with a tool to screen new drug candidates.



**Figure 2.** Siderophore production by *A. fumigatus* in a 96-well plate assay. Inhibition of siderophore production is easily detected by a lack of colour development (arrows).

### Partnering Opportunity

Looking for partners to use the technology:

- Research collaboration
  - To screen a large library of samples
  - To develop a diagnostic kit for market
- Development strategy
- To ascertain market and regional size
- Licensing opportunity

### References

- <sup>1</sup> Hissen et al, 2004 Infect. Immun 72: 1402
- <sup>2</sup> Gifford et al, 2002 Infect Immun 70: 19-26
- <sup>3</sup> Hissen and Moore, 2005a J Biol Inorg Chem 10:211
- <sup>4</sup> Hissen et al, 2005b infect Immun 73: 5493
- <sup>5</sup> Latgé, JP 1999 Clin Microbiol Rev. 12:310
- <sup>6</sup> Menninck-Kersten et al. 2004 Lancet Infect Dis 4: 439
- <sup>7</sup> Menninck-Kersten MA et al 2005 J Clin Microbiol. 43:3925

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