# MBG FOCUS TALK

hosted by Ditlev E. Brodersen, Structural Biology

MBG Focus Talks in Molecular Biology

**Tuesday 19 April 2016 at 10:15-11:00**

Dept. of Mathematics, Aud. D2 (1531-119)


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## One substrate, two enzymes and three products:– what gliotoxin self-protection mechanisms have taught us about fungal biochemistry


One of the key drivers for investigating microbial natural products has been their association with virulence against plant or animal hosts. Nowhere is this better exemplified than with the study of the fungal 'toxin', gliotoxin, produced by the opportunistic fungal pathogen Aspergillus fumigatus. However, I contend that exploration of gliotoxin biosynthesis and oxidoreductase GliT-mediated self-protection can also reveal, directly and indirectly, new aspects of fungal systems biology. Biosynthesis of, and self-protection against, the redox-active metabolite gliotoxin is encoded by the gli gene cluster in A. fumigatus. In addition, gliotoxin biosynthesis is influenced by a newly discovered bis-thiomethyltransferase GtmA which sequentially converts gliotoxin to a bisthiomethylated derivative, and the implications and significance of this hitherto unknown bioconversion will also be explored in the presentation. Further systems impacts of interfering with gliotoxin biosynthesis are only just emerging and, surprisingly, it appears that the biosynthesis of apparently unrelated natural products, like the antioxidant ergothioneine, is influenced either by gliotoxin, or specific reactions within its biosynthetic pathway. So, the activity of gliotoxin against fungi and animal cells, often mediated by interference with redox homeostasis, is revealing new metabolic interactions within eukaryotic systems. We've been lucky - nature has provided a most useful natural product with which to reveal some of its many molecular secrets.