Comparative genomics of four Aspergillus species with focus on identification of specific secondary metabolite gene clusters

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Comparative genomics of four *Aspergillus* species with focus on identification of specific secondary metabolite gene clusters.

In order to examine the genetic diversity of the Aspergillus genus, and to establish new reference genomes for our ongoing project of sequencing all +300 species of the Aspergillus genus, a set of four diverse Aspergillus species (*A. campestris*, *A. novofumigatus*, *A. ochraceoroseus* and *A. steynii*) have been whole genome sequenced. Using comparative genomics, the selected species have been compared to a group of eight Aspergillus species with sequenced genomes to determine the level of genetic diversity. In examining the unique genes for each species, we have found that the most common function for these unique genes was involved in regulation. Another common function for the unique genes is often associated with secondary metabolism. These results show that parts of regulation and secondary metabolism is very species specific and important for the differentiation between species. We also hypothesize that these traits are particularly transferable from other organisms. Here, we have also demonstrated that comparative analysis of whole genome sequences can be used to identify and couple specific secondary metabolites to their respective gene clusters. In order to make the coupling, biological and chemical knowledge has to be combined with the genome sequences and prediction algorithms. Depending on the knowledge of the metabolite and the biosynthesis various approaches can be used. We have developed four strategies for this purpose and using these strategies it was possible to identify putative secondary metabolite clusters for aflatoxin, chlorflavonin, novofumigatoton and ochrindol in *A. ochraceoroseus*, *A. campestris*, *A. novofumigatus* and *A. steynii* respectively. Lastly, *A. novofumigatus* has been compared to a close relative, the pathogenic species *A. fumigatus*, to get a better understanding of the mechanisms of pathogenicity and virulence. The *A. fumigatus* genes known to be involved in pathogenicity/virulence were located in *A. novofumigatus* and orthologs identified. The genome sequences presented here illustrate the large diversity found in the Aspergillus genus and highlights the potential for discovery of new and beneficial secondary metabolites. It also shows how biological, biochemical and sequence information can be combined to identify genes involved in specific functions, thereby aiding the future experimental design involved in further investigations.

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