Linking secondary metabolites to gene clusters through genome sequencing of six diverse Aspergillus species

The fungal genus of Aspergillus is highly interesting, containing everything from industrial cell factories, model organisms, and human pathogens. In particular, this group has a prolific production of bioactive secondary metabolites (SMs). In this work, four diverse Aspergillus species (A. campestris, A. novofumigatus, A. ochraceoroseus, and A. steynii) have been whole-genome PacBio sequenced to provide genetic references in three Aspergillus sections. A. taichungensis and A. candidus also were sequenced for SM elucidation. Thirteen Aspergillus genomes were analyzed with comparative genomics to determine phylogeny and genetic diversity, showing that each presented genome contains 15–27% genes not found in other sequenced Aspergilli. In particular, A. novofumigatus was compared with the pathogenic species A. fumigatus. This suggests that A. novofumigatus can produce most of the same allergens, virulence, and pathogenicity factors as A. fumigatus, suggesting that A. novofumigatus could be as pathogenic as A. fumigatus. Furthermore, SMs were linked to gene clusters based on biological and chemical knowledge and analysis, genome sequences, and predictive algorithms. We thus identify putative SM clusters for aflatoxin, chlorflavonin, and ochrindol in A. ochraceoroseus, A. campestris, and A. steynii, respectively, and novofumigatoin, ent-cycloechinulin, and epiaszonalenins in A. novofumigatus. Our study delivers six fungal genomes, showing the large diversity found in the Aspergillus genus; highlights the potential for discovery of beneficial or harmful SMs; and supports reports of A. novofumigatus pathogenicity. It also shows how biological, biochemical, and genomic information can be combined to identify genes involved in the biosynthesis of specific SMs.

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Corresponding author: Andersen, M. R.
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Friends and foes - comparative genomics of 23 Aspergillus Flavi species

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Number of pages: 1
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Electronic versions:
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Flavi is a highly diverse section in genus Aspergillus encompassing species used in food fermentation and enzyme production (A. oryzae and A. sojae) as well as toxigenic and foodspoilers (A. parasiticus and A. flavus) in addition to many less studied species. Here we have whole genome sequenced 19 Flavi species and used comparative genomic tools to investigate the section. We have examined similarities and differences of this section with a special focus on the carbohydrate active enzymes (CAZy) and secondary metabolites to get an understanding of what is unique features for section Flavi. In addition we have studied selected secondary metabolite gene clusters (SMGC) found widely across the section to get an understanding of cluster evolution and development.

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Organisations: Section for Synthetic Biology, Network Engineering of Eukaryotic Cell factories, Department of Biotechnology and Biomedicine, New Bioactive Compounds, Novo Nordisk Foundation Center for Biosustainability, Section for Microbial and Chemical Ecology, Fungal Chemodiversity, Eukaryotic Molecular Cell Biology, Natural Product Discovery, Kikkoman Corporation, Aix-Marseille University, Joint Genome Institute, Aix-Marseille Université, Pacific Northwest National Laboratory
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Research output: Contribution to conference › Poster – Annual report year: 2018 › Research › peer-review
Investigation of inter- and intraspecies variation through genome sequencing of Aspergillus section Nigri

Aspergillus section Nigri comprises filamentous fungi relevant to biomedicine, bioenergy, health, and biotechnology. To learn more about what genetically sets these species apart, as well as about potential applications in biotechnology and biomedicine, we sequenced 23 genomes de novo, forming a full genome compendium for the section (26 species), as well as 6 Aspergillus niger isolates. This allowed us to quantify both inter- and intraspecies genomic variation. We further predicted 17,903 carbohydrate-active enzymes and 2,717 secondary metabolite gene clusters, which we condensed into 455 distinct families corresponding to compound classes, 49% of which are only found in single species. We performed metabolomics and genetic engineering to correlate genotypes to phenotypes, as demonstrated for the metabolite aurasperone, and by heterologous transfer of citrate production to Aspergillus nidulans. Experimental and computational analyses showed that both secondary metabolism and regulation are key factors that are significant in the delineation of Aspergillus species.

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Corresponding author: Andersen, M. R.
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Publication date: 2018
Peer-reviewed: Yes

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BFI (2018): BFI-level 3
Scopus rating (2018): CiteScore 19.88 SJR 21.508 SNIP 5.477
Web of Science (2018): Impact factor 25.455
Web of Science (2018): Indexed yes
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10.1038/s41588-018-0246-1
Source: FindIt
Source ID: 2440590492
Research output: Contribution to journal › Journal article – Annual report year: 2018 › Research › peer-review

The Aspmine - Comparative genomics analysis of 6 new species of Aspergillus section Sparsi, ochraceorosei, Tanneri and Robusti

Background: Sequencing genomes of filamentous fungi will reveal the genetic mechanisms that lead to a high diversity and frequency of bioactive compounds.
Conclusions: Sequencing of new species identifies thousands of new proteins and gene clusters involved in metabolite production.

General information
Publication status: Published
Organisations: Section for Synthetic Biology, Network Engineering of Eukaryotic Cell factories, Department of Biotechnology and Biomedicine, New Bioactive Compounds, Novo Nordisk Foundation Center for Biosustainability, Section for Microbial and Chemical Ecology, Fungal Chemodiversity, Joint Genome Institute, Westerdijk Fungal Biodiversity Institute, Joint Bioenergy Institute, Aix-Marseille University
Number of pages: 1
Genetic diversity of 100+ Aspergillus species: The aspMine analysis resource

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Organisations: Section for Synthetic Biology, Network Engineering of Eukaryotic Cell factories, Department of Biotechnology and Biomedicine, New Bioactive Compounds, Novo Nordisk Foundation Center for Biosustainability, Section for Microbial and Chemical Ecology, Fungal Chemodiversity, Eukaryotic Molecular Cell Biology, Joint Genome Institute, Utrecht University
Publication date: 2017
Peer-reviewed: Yes
Event: Poster session presented at Comparative genomics of eukaryotic microbes: Dissecting sources of evolutionary diversity.
Electronic versions:
poster_asilomar.pdf
Research output: Contribution to conference › Poster – Annual report year: 2018 › Research › peer-review

The Aspergillus Mine - publishing bioinformatics.
Genome analysis is no longer a field reserved for specialists and experimental laboratories are doing groundbreaking research using genome sequencing and analysis. In this new era, it is essential that data, analysis and results are shared between scientists. But this can be a challenge, even more so with no computational specialist. Here we present a setup for analysis and publication of genome data of 70 species of Aspergillus fungi. The platform is based on R, Python and uses the RShiny framework to create interactive web-applications. It allows all participants to create interactive analysis which can be shared with the team and in connection with publications. We present analysis for investigation of genetic diversity, secondary and primary metabolism and general data overview. The platform, the Aspergillus Mine, is a collection of analysis tools based on data from collaboration with the Joint Genome Institute. The Aspergillus Mine is not intended as a genomic data sharing service but instead focuses on creating an environment where the results of bioinformatic analysis is made available for inspection. The data and code is public upon request and figures can be obtained directly from the web-app. This resource will be of great benefit to the Aspergillus community which is in a rapid development in regards to genome sequencing and analysis. At the moment, the service includes analysis of more than 70 genomes, and is expected to double in the next 6 months, with the final goal of the project is the analysis of 300 Aspergillus species.

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Organisations: Department of Systems Biology, Network Engineering of Eukaryotic Cell Factories, Fungal Chemodiversity, Metabolomics Platform, Eucaryotic Molecular Cell Biology, CBS-KNAW Fungal Biodiversity Centre, Joint Genome Institute, Joint Bioenergy Institute
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Source ID: 127424549
Research output: Contribution to conference › Poster – Annual report year: 2016 › Research › peer-review
Diversity of carbohydrate metabolism in species of Aspergillus

The filamentous fungus Aspergillus niger and its close relatives in Aspergillus section Nigri are of broad interest to the scientific community including applied, medical and basic research. The fungi are prolific producers of native and heterologous proteins, organic acids (in particular citrate), and secondary metabolites (including bioactives and toxins such as ochratoxin A). Because of these abilities they represent a substantial economic interests in bioenergy applications. In a project collaboration with the US Joint Genome Institute and JBEI we are sequencing 300 different species of Aspergillus and establishing an online analysis platform for the scientific community, aspMine300.

Gene cluster dynamics throughout the Aspergillus genus

In the era of high-throughput sequencing, comparative genomics can be applied for evaluating species diversity. In this project we aim to compare the genomes of 300 species of filamentous fungi from the Aspergillus genus, a complex task. To be able to define species, clade and core features, this project uses BLAST on all proteins of all genomes. With a potential of 300 Aspergillus species each having ~12,000 annotated genes, traditional clustering will demand supercomputing. Instead, our approach reduces the research space by identifying isoform families within each genome, creating intragenomic protein families (iPFs), and then connecting iPFs across all genomes. The initial findings in a set of 31 species show that ~48% of the annotated genes are core genes (genes shared between all species) and 2-24% of the genes are defining the individual species.

Genome mining of the genetic diversity in the Aspergillus genus - from a collection of more than 30 Aspergillus species

In this project we aim to compare the genomes of 300 species of filamentous fungi from the Aspergillus genus, a complex task. To define species, clade and core features, this project uses BLAST on all proteins of all genomes. With a potential of 300 Aspergillus species each having ~12,000 annotated genes, traditional clustering will demand supercomputing. Instead, our approach reduces the research space by identifying isoform families within each genome, creating intragenomic protein families (iPFs), and then connecting iPFs across all genomes. The initial findings in a set of 31 species show that ~48% of the annotated genes are core genes (genes shared between all species) and 2-24% of the genes are defining the individual species. The methods presented here will allow for detailed investigation into mapping of genotypetype phenotypes across a very large set of genotypes without losing information.

General information

Publication status: Published
Organisations: Department of Systems Biology, Network Engineering of Eukaryotic Cell Factories, Fungal Chemodiversity, Metabolomics Platform, Eucaryotic Molecular Cell Biology, Joint Genome Institute, Joint Bioenergy Institute, CBS-KNAW Fungal Biodiversity Centre
Number of pages: 1
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Event: Abstract from Exploring the genomic complexity and diversity of eukaryotes, Sant Feliu de Guixols, Spain.
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Source ID: 124072321
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General information

Publication status: Published
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Publication date: 2015
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Formation of Sclerotia and Production of Indoloterpenes by Aspergillus niger and Other Species in Section Nigri

Several species in Aspergillus section Nigri have been reported to produce sclerotia on well-known growth media, such as Czapek yeast autolysate (CYA) agar, with sclerotia considered to be an important prerequisite for sexual development. However Aspergillus niger sensu stricto has not been reported to produce sclerotia, and is thought to be a purely asexual organism. Here we report, for the first time, the production of sclerotia by certain strains of Aspergillus niger when grown on CYA agar with raisins, or on other fruits or on rice. Up to 11 apolar indoloterpenes of the aflavinine type were detected by liquid chromatography and diode array and mass spectrometric detection where sclerotia were formed, including 10,23-dihydro-24,25-dehydroaflavinine. Sclerotium induction can thus be a way of inducing the production of new secondary metabolites from previously silent gene clusters. Cultivation of other species of the black aspergilli showed that raisins induced sclerotium formation by A. brasiliensis, A. floridensis A. ibericus, A. luchuensis, A. neoniger, A. trinidadensis and A. saccharolyticus for the first time.

General information
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Organisations: Department of Systems Biology, Natural Product Chemistry
Contributors: Frisvad, J. C., Petersen, L. M., Lyhne, E. K., Larsen, T. O.
Number of pages: 11
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Original language: English
Keywords: fruit, sclerotia formation, Fungi Plantae (Fungi, Microorganisms, Nonvascular Plants, Plants) - Fungi Imperfecti or Deuteromycetes [15500] Nigri section Aspergillus brasiliensis species Aspergillus ibericus species Aspergillus luchuensis species Penicillium rubens species Aspergillus saccharolyticus species Aspergillus niger species sensu stricto Aspergillus floridensis species Aspergillus neoniger species Aspergillus trinidadensis species Aspergillus aculeatus species strain-IBT 21030 Aspergillus welwitchiae species, Monocotyledones Angiospermae Spermatophyta Plantae (Angiosperms, Monocots, Plants, Spermaphytes, Vascular Plants) - Gramineae [25305] rice common, CYA agar, dihydro-24,25-dehydroaflavinine, gene cluster, raisin, 03502, Genetics - General, 03504, Genetics - Plant, Biochemistry and Molecular Biophysics, diode array detection laboratory techniques, liquid chromatography laboratory techniques, chromatographic techniques, mass spectrometry laboratory techniques, spectrum analysis techniques, Molecular Genetics, MULTIDISCIPLINARY, THAI COFFEE BEANS, SEXUAL REPRODUCTION, FUMONISIN B-2, ANTIINSECTAN METABOLITE, CRYPTIC SEXUALITY, TUBINGENSIN-A, OCHRATOXIN, MYCOTOXINS, GROWTH, FUNGI
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Dereplication Strategies for Discovery of Marine Microbial Natural Products

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Organisations: Center for Microbial Biotechnology, Department of Systems Biology, Section for Aquatic Microbiology and Seafood Hygiene, National Institute of Aquatic Resources
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Event: Abstract from Gordon Conference in Marine Natural Products, Ventura Beach, California, U.S.A.
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Research output: Contribution to conference › Conference abstract for conference – Annual report year: 2008 › Research

Four Psychrotolerant species with high chemical diversity consistently producing cycloaspeptide A, Penicillium jamesonlandense sp. nov., P. Ribium sp. nov., P. Soppii and P. Ianosum

General information
Publication status: Published
Organisations: Center for Microbial Biotechnology, Department of Systems Biology, Department of Biotechnology
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Publication information
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ISSN (Print): 1466-5026
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Web of Science (2006): Indexed yes
Original language: English
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Source: orbit
Source ID: 190372
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Four psychrotolerant species with high chemical diversity consistently producing cycloaspeptide A, P. jamesonlandense sp. nov., P. ribium sp. nov., P. soppil and P. Ianosum

General information
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Publication date: 2006
Peer-reviewed: Yes

Publication information
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Secondary metabolite and mycotoxin production by the Rhizopus microsporus group

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Organisations: Center for Microbial Biotechnology, Department of Systems Biology
Contributors: Jennesen, J., Nielsen, K. F., Haubraken, J., Lyhne, E. K., Schnurer, J., Frisvad, J. C., Samson, R.
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Publication date: 2005
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Publication information
Journal: Journal of Agriculture and Food Chemistry
Volume: 53
Original language: English
Source: orbit
Source ID: 184021
Research output: Contribution to journal › Journal article – Annual report year: 2005 › Research › peer-review

Projects:

Physiology, ecology and resistance of the mycoflora associated with different types of food, with emphasis on cheese and other dairy products
The influence of important combinations of intrinsic, extrinsic and processing factors on the germination, growth and production of secondary metabolites and volatiles by fungi associated with dairy products including starter cultures, will be investigated. Studies of atmosphere composition (O2 and CO2) and humidity will be emphasized. Interactions between fungi on fermented cheese are studied by in situ analysis of secondary metabolites production. The results will be used in design of mathematical models, which can be used in the quality management of especially cheese production.

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Ukendt: DKK12,125,057.00
01/09/1992 → 31/12/1996
Collaborators: Danish Dairy Research Foundation
Award relations: Physiology, ecology and resistance of the mycoflora associated with different types of food, with emphasis on cheese and other dairy products
Project: Research