



Media-release

2016-05-27

Fungi – a promising source of chemical diversity

Moulds and plants share similar ways in alkaloid biosynthesis

Jena. The fungus *Aspergillus fumigatus* produces a group of previously unknown natural products. With reference to plant isoquinoline alkaloids, these substances have been named fumisoquins. Researchers from Jena discovered the novel substances together with their American colleagues while studying the fungal genome. The family of isoquinoline alkaloids contains many pharmacologically active molecules. This study, which has just been published in *Nature Chemical Biology*, shows that fungi and plants developed biosynthetic pathways for these complex molecules independently of each other. These findings make *Aspergillus* an interesting target for the discovery of novel drugs and their biotechnological production.

A large number of drugs used today originate from nature. Most of these molecules, which can be found with or without synthetic modifications and exert their beneficial effect on human health, are derived from microorganisms or plants. Thus, it is of great interest to discover novel active compounds in nature and use them for the treatment of diseases.

One well-known group of plant metabolites are the isoquinoline alkaloids. Today more than 2,500 different types are known and they are mainly found in poppy and barberry plants. Famous examples include the painkiller morphine or the cough remedy codein.

Together with colleagues from the US, scientists in the labs of Dirk Hoffmeister and Axel Brakhage at the Friedrich Schiller University in Jena found out that fungi synthesize certain natural products in a very similar way to plants. They analyzed the genome of the common mold *Aspergillus* and discovered a small cluster of genes whose function was previously unknown. Comparing these genetic sequences with known data implied that they might be responsible for the synthesis of novel natural products.

By manipulating the genetic sequences, characterizing the resulting metabolites and using radioactive labeling experiments it was possible to elucidate the structure of the novel molecules and to unravel the detailed biosynthetic pathways. The researchers discovered a new linkage mechanism for carbon atoms which had never been seen before in fungi. The whole fumisoquin biosynthetic pathway appears to be a combination of plant biosynthetic principles and the non-ribosomal peptide synthetases commonly found in fungi.

Axel Brakhage, university professor and head of the Leibniz Institute for Natural Product Research and Infection Biology, explains: "Fungi and plants diverged early on during evolution. The newly discovered fumisoquin synthesis pathway shows that there was a parallel development for the production of isoquinoline alkaloid compounds in both groups of organisms. This opens up new roads for combinatorial biotechnology in order to advance the search for novel active compounds and thus to develop urgently needed new drugs."

Dirk Hoffmeister, professor at the Institute for Pharmacy at Friedrich Schiller University, is pleased with the joint efforts: "The published study is a great example of the tight collaboration between the university and the Leibniz Institute for Natural Product Research and Infection Biology – Hans Knöll Institute – and our American partners. Good research does not know any borders."

The international scientific association "Faculty of 1000" included this publication in their hit list of seminal research results.

Figures and legends

16-09_Bild_1_Papaver.jpg

Breadseed poppies *Papaver somniferum* as well as many other poppy and barberry plants produce many Isochinoline alkaloids.

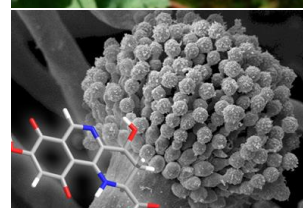
Copyright: FSU/Dirk Hoffmeister



16-09_Bild_2_Aspergillus_fumigatus_Konidiophor.jpg

The fungus *Aspergillus fumigatus* produces Fumisoquine in a way similar to plants.

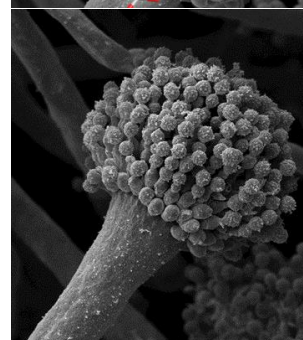
Copyright: HKI/ Schmalder-Ripcke, Kloss, Yu



16-09_Bild_3_Aspergillus_fumigatus_Konidiophor.jpg

A conidiophore of the fungus *Aspergillus fumigatus*. The fungus produces Fumisoquine in a way similar to plants.

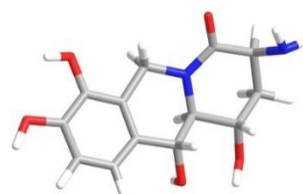
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16-09_Bild_4_Fumisoquin_A.jpg

Fumisoquin A, one of the novel Isochinoline alkaloids produced by *Aspergillus fumigatus*.

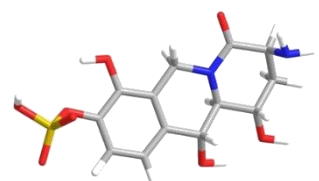
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16-09_Bild_5_Fumisoquin_B.jpg

Fumisoquin B, one of the novel Isochinoline alkaloids produced by *Aspergillus fumigatus*.

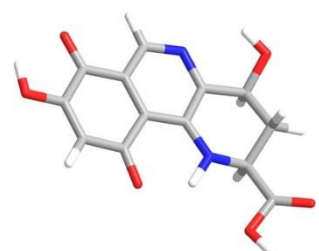
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16-09_Bild_6_Fumisoquin_C.jpg

Fumisoquin C, one of the novel Isochinoline alkaloids produced by *Aspergillus fumigatus*.

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Original publication

Baccile JA, Spraker JE, Le HH, Brandenburger E, Gomez C, Bok JW, Macheleidt J, Brakhage AA, Hoffmeister D, Keller NP, Schroeder FC (2016) Plant-like biosynthesis of isoquinoline alkaloids in *Aspergillus fumigatus*. *Nature Chemical Biology* 12(6), 419-424. doi: 10.1038/nchembio.2061.

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