Summary of: Recent advances in the genome mining of Aspergillus secondary metabolites (covering 2012,Äì2018)..pdf

Key Findings and Quantitative Results

Secondary Metabolites in Aspergillus Species: - **Genome Mining**: Advances in genome sequencing have revealed that fungi have the capacity to produce a far greater number of secondary metabolites than have been isolated, as many genes involved in SM biosynthesis are either silent or expressed at very low levels in standard laboratory conditions. - **Cluster Activation**: Scientists have activated silent clusters to link them to downstream products, facilitating drug discovery. - **Cluster Identification**: Aspergillus species have been identified as having the capacity to produce a variety of SMs, including terpenes, sterols, and more. - **Cluster Biosynthesis**: The biosynthetic pathways of these clusters have been elucidated, providing a foundation for further research.

Specific Advances in Genome Mining:

Aspergillus nidulans: - **Ent-Pimara-8** (ent-pimara-8) - Activated by PbcR, leading to high up-regulation of SM biosynthetic genes. - **Asperniduglene** - Proposed pathway by activating sdg cluster. - **Aspernidine** - Proposed pathway by activating pkf cluster. - **Microperfuranone** - Proposed pathway by activating NRPS-like genes.

Aspergillus fumigatus: - **Hexadehydroastechrome** - Proposed pathway by activating HasD cluster. - **Endocrocin** - Proposed pathway by activating ivoA and ivoC. - **Trypacidin** - Proposed pathway by activating tpc cluster.

Aspergillus niger: - **Kotanin** - Proposed pathway by activating KtnS. - **Azanigerones** - Proposed pathway by activating azA and azB. - **Yanuthone D** - Proposed pathway by activating yanA.

Aspergillus terreus: - **Aspterric acid** - Proposed pathway by activating AstA cluster. - **Phenguignardic acid** - Proposed pathway by activating pgnA. - **Asperphenamate** - Proposed pathway by activating pynA. - **Citreoviridin** - Proposed pathway by activating CtvE cluster.

Key Findings:

- **Silent Genes**: Many genes involved in SM biosynthesis are silent or expressed at very low levels, necessitating activation to produce SMs. - **Cluster Activation**: The activation of silent clusters has led to the identification of new SMs. - **Biosynthetic Pathways**: The proposed pathways provide a foundation for further research into SM biosynthesis. - **Drug Discovery**: The identification of SM clusters has facilitated the discovery of new drugs.

Quantitative Results:

- **Cluster Activation**: Over 66 predicted core synthase enzymes in A. nidulans have been linked to downstream SM products. - **Cluster Identification**: Over 40 predicted SM core synthase enzyme-encoding genes in A. fumigatus have been linked to downstream SM products. - **Cluster Biosynthesis**: The proposed pathways have facilitated the identification of new SMs. - **Drug Discovery**: The activation of silent clusters has led to the identification of new SMs, which have been linked to downstream products.

Example Quantitative Results:

- **Ent-Pimara-8** - 7 adjacent genes encoding a diterpene synthase, geranylgeranyl pyrophosphate synthase, HMG-CoA reductase, translation elongation factor, shortchain dehydrogenase, hypothetical protein with partial similarity to methyltransferase, cytochrome P450, and a cytochrome P450. - **Asperniduglene** - 14 genes encoding PKS, NRPS, and NR-PKS, leading to the identification of asperniduglene A1. - **Aspernidine** - 14 genes encoding PKS, NRPS, and NR-PKS, leading to the identification of aspernidine A. - **Microperfuranone** - 14 genes encoding PKS, NRPS, and NR-PKS, leading to the identification of microperfuranone.

Conclusion:

- **Genome Mining**: Advances in genome sequencing have enabled the identification of SM clusters. - **Drug Discovery**: The activation of silent clusters has facilitated the identification of new SMs. - **Biosynthetic Pathways**: Proposed pathways provide a foundation for further research into SM biosynthesis. - **Silent Genes**: Many genes involved in SM biosynthesis are silent or expressed at very low levels, necessitating activation.

References:

- **J. F. Sanchez et al.** (2012): Nat. Prod. Rep. - **J. F. Sanchez et al.** (2012): Nat. Prod. Rep. - **J. F. Sanchez et al.