World Academy of Science, Engineering and Technology
International Journal of Mathematical and Computational Sciences
Vol:14, No:12, 2020

LaeA/1-Velvet Interplay in Aspergillus and Trichoderma: Regulation of Secondary Metabolites and Cellulases

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Abstract : Filamentous fungi are of considerable economic and social significance for human health, nutrition and in white biotechnology. These organisms are dominant producers of a range of primary metabolites such as citric acid, microbial lipids (biodiesel) and higher unsaturated fatty acids (HUFAs). In particular, they produce also important but structurally complex secondary metabolites with enormous therapeutic applications in pharmaceutical industry, for example: cephalosporin, penicillin, taxol, zeranol and ergot alkaloids. Several fungal secondary metabolites, which are significantly relevant to human health do not only include antibiotics, but also e.g. lovastatin, a well-known antihypercholesterolemic agent produced by Aspergillus. terreus, or aflatoxin, a carcinogen produced by A. flavus. In addition to their roles for human health and agriculture, some fungi are industrially and commercially important: Species of the ascomycete genus Hypocrea spp. (teleomorph of Trichoderma) have been demonstrated as efficient producer of highly active cellulolytic enzymes. This trait makes them effective in disrupting and depolymerization of lignocellulosic materials and thus applicable tools in number of biotechnological areas as diverse as clothes-washing detergent, animal feed, and pulp and fuel productions. Fungal LaeA/LAE1 (Loss of aflR Expression A) homologs their gene products act at the interphase between secondary metabolisms, cellulase production and development. Lack of the corresponding genes results in significant physiological changes including loss of secondary metabolite and lignocellulose degrading enzymes production. At the molecular level, the encoded proteins are presumably methyltransferases or demethylases which act directly or indirectly at heterochromatin and interact with velvet domain proteins. Velvet proteins bind to DNA and affect expression of secondary metabolites (SMs) genes and cellulases. The dynamic interplay between LaeA/LAE1, velvet proteins and additional interaction partners is the key for an understanding of the coordination of metabolic and morphological functions of fungi and is required for a biotechnological control of the formation of desired bioactive products. Aspergilli and Trichoderma represent different biotechnologically significant species with significant differences in the LaeA/LAE1-Velvet protein machinery and their target proteins. We, therefore, performed a comparative study of the interaction partners of this machinery and the dynamics of the various protein-protein interactions using our robust proteomic and mass spectrometry techniques. This enhances our knowledge about the fungal coordination of secondary metabolism, cellulase production and development and thereby will certainly improve recombinant fungal strain construction for the production of industrial secondary metabolite or lignocellulose hydrolytic enzymes.

Keywords : cellulases, LaeA/1, proteomics, secondary metabolites
Conference Title : ICSRD 2020 : International Conference on Scientific Research and Development
Conference Location : Chicago, United States
Conference Dates : December 12-13, 2020