ISOLATION OF FUNGI FROM SABAH THAT PRODUCE BIOACTIVE COMPOUNDS WHICH EFFECT SIGNAL TRANSDUCTION

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ABSTRACT

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Filamentous micro-fungal strains were isolated from various environments in Sabah especially from the soil of the rain forest. Sabah with its unique natural resources provides the means for the discovery of new micro-fungal strains with the potential to produce novel bioactive secondary metabolite compounds which affect signal transduction. This is the main focus of this research. A total of 364 fungal strains were isolated. Extracts from the aerobic liquid fermentation of these fungal strains were screened for inhibitory effect on signal transduction of both yeast and bacterial strains. In the course of this research, soil samples have been collected in the expeditions that were carried out by this university to remote locations of Sabah. These expeditions include the primary forest of the Imbak Valley, limestone hill forest of Tabin Wildlife Reserve, the the lower montane heath forest forest of Maliau Basin Conservation Area and the montane forest of Mount Trus Madi. The soil samples were mostly collected from leaf litter under trees and other plants that were identified to species or genus level. A number for fungal strains were also isolated from explants and from fungal airborne spores of plates and in around the laboratory. The characteristics of the micro-fungi strains on the PDA agar were observed and this includes colour of the aerial and substrate mycelia, difussed pigmentation and growth rate on the PDA plates. Microscopic identification was done on the strains which showed activity on screening tests performed. All the micro-fungal strains isolated were grown in aerobic condition in liquid fermentation. It was these extracts that were used for the screening for specific molecular targets involve in signal transduction such as serine/threonine phosphatase, MAPK Kinase, MAP Kinase phosphatase, Ras/Raf protein interaction, and serine/threonine kinase. All the screening systems mention are base on the eukaryotic signalling pathways of yeast except for the serine/threonine kinase screen which is base on the prokaryotic signalling pathway of *Streptomyces griseus* which shares high similarity with eukaryotic signalling pathway. In this research, there were fungal strains which showed inhibitory effect to the serine/threonine phosphatase type 1 homolog, Glc7p especially the strains H9318 and H9307 from Maliau Basin. These two strains were latter found to inhibit dephosphorylation of phosphorylase catalyse by the mammalian serine/theronine phosphatase, Protein Phosphatase type 1 gama (PP1γ) as well. The effect on PP1γ as well as Glc7p is not supprising as both these protein shares more than 75% homology in its catalytic domain. Three strains which showed positive activity in the MAPK Kinase screening system are H9013, H9014 and H9019. No fungal strains were found to be affecting the MAP Kinase Phosphatase (MSG 5) and the Ras/Raf protein interaction which would indicate a positive result. There were numerous extracts from fungal strains which inhibit the growth of *Streptomyces griseus* and two strains which showed potential to be inhibitors of serine/threonine kinase (AfsK) of *Streptomyces griseus*. These two strains were H9016 and H9123. There were also two fungal strains H9341 and H9346 which showed toxicity in all the screens performed except for the serine/theronine kinase test of *S.griseus*. This would indicate these strains are toxic to at least *Scharomycetes cerevisiae* cells. The fungal strains isolated from soil and from other environment showed some specificity in the types of strains isolated and the secondary metabolites produced. The microfungi from Sabah proved to be prolific producers of diverse secondary metabolites which effect signal transduction and growth of cell.