DETERMINATION OF THE METABOLITE PROFILES OF *KLEBSIELLA PNEUMONIAE* INFECTED SPLEEN ORGAN BY LC/MS-QTOF

RESEARCH DISSERTATION

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ABSTRACT

Spleen of *Rattus norvegicus* was used in order to identify the metabolite profile of the normal and the infected rats with *Klebsiella pneumoniae*. During the infection, many metabolite pathways may be involved in the pathogenesis of *Klebsiella pneumoniae* infection. This study was conducted using the advanced technologies of chromatography, LC/MS-QTOF. Six samples of normal and infected rats were prepared. For the extraction, the organs were grounded, then mixed with extraction solvent which is water: methanol: chloroform with ratio 2:4:4 respectively. The mixtures were then centrifuged and dried using concentrator. After that, the samples were injected into the LC/MS-QTOF. Using the Agilent Metabolomic Discovery software, analysis was done by transferring the data from the LC/MS-QTOF into the software. The result showed that there are significant metabolites and pathways involved in the pathogenesis of *Klebsiella pneumoniae* infection. In the 2D and 3D PCA, different metabolites were expressed by the control and infected groups. The up and down regulation of the metabolites in the normal and infected condition were further analysed. The significant pathway involved in the study are retinol and tryptophan pathways. Retinol are essential for growth and cell differentiation, particularly of epithelial tissue and tryptophan metabolism under pathological conditions is a powerful mediator of responses in both the innate and adaptive immune systems. Therefore, by knowing the pathways involved using pathway analysis, it provides clues to the researchers to strategize approaches to prevent and treat hosts or patients with spleen infected with *Klebsiella pneumoniae*.

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CHAPTER 1

INTRODUCTION

1.1 Background of study

In this study, the metabolism of the normal and spleen organ infected by *Klebsiella pneumoniae* was investigated using advanced technologies of chromatography. Then, the differential metabolite profiles were used to identify the pathways pertubated during a diseased condition. The study is initiated with extraction process of normal and infected spleen with extraction solvent (water: methanol: chloroform). The uses of extraction solvent is to separate the polar compound, non-polar compound and the protein of spleen organ resulted from centrifuged process. Then, by using the LC/MS-QTOF, the metabolites which were extracted were identified and interpretation of the data and pathway analysis was performed. High Throughput (HT) machine like LC/MS-QTOF permit the identification of biomarkers of infected organs. Hence it is able to recognize specific metabolic pathways which are associated with the disease. Some biological networks of metabolomics will be detected by computation system (Zhang et al., 2008). The data from LC/MS-QTOF was transferred for further analyses using Agilent Metabolomic Discovery which is the software that is available in the iPROMISE. By knowing the pathway involves in certain disease, modern drug formulation can be modified to inhibit the pathway involved so that the disease can be cured.