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Article 4. Metabolomics and Application on The Specificity of Host-Invasion Interaction/新陈代谢组学在宿主细胞与生物入侵关系专一性机制中的应用研究

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Abstract

This article designs a systematic matrix to analyze the overall isozyme zymogram, which is produced by the simulation of host-invasion interaction in Lab.

Key words: Host-Invasion Interaction, Metabolomics, Specificity, Isozyme Zymogram, Pathology.

Introduction

There is a new experiment method designed to examine and diagnose the immunology of host cells against microbial pathogens (including virus and bacteria), based on the metabolomics test designed in my previous article [3]. In addition to the genetics of host body, the 'memory' of host cells, which allows host cells to fast and accurately identify the bio-signals of specifically invasive pathogens so that the immunological reaction of host cells functions punctually, also plays a significant role in immunology. However, this 'memory' of host cells can be inherent, which is passed on from parental generation, or acquired skills which are cultivated through the past 'battle' against disease.

The isozyme families, associated with the pathology (or immunology), include the AST, CK, LDH, B-ALP and G6PD,... etc [1]. The examples of selecting other potential isozyme primers based on the past research have been illustrated in my previous article [3]. Specificity of host-invasion interaction examination:

Step 1. There are two different genetic strains of host cells (sample 1 and sample 2) in the same tissue (such as the blood samples abstracted from parallel rat samples) selected and cultivated in this research;

Step 2. Before bacteria invasion simulation, the samples of host cells are cultivated in

the same environmental conditions (named as pre-invasion samples). After this, bacteria invasion simulation is conducted in a proportion of host cell samples (However, the other environmental condition for cell cultivation is not changed during bacteria invasion simulation).

Step 3. The bacteria (or virus) invasion targeting the cells of host tissue is simulated in Lab by inoculation of pathogens.

Step 4. The host cells with apparent antibiotics (or antibody) specifically against a strain of invasive bacteria is identified and cultivated during bacteria invasion simulation (named as after-invasion samples), and the other host cells without apparent antibiotics are also cultivated during bacteria invasion simulation for comparison; Please note: it is important to ensure the uniform pathogenicity of a bacteria (or virus) strain for the invasion simulation;

Step 5. The systematic metabolomics test (both experiment and data analysis methods are listed by my previous articles of this journal[3]) is conducted after bacteria invasion process against host cells (in both pre-invasion samples (background samples) and after-invasion samples), as well as in invasive bacteria samples (the bacteria samples collected are cultivated during invasive simulation process); Please note: this metabolomics test is also applicable on virus classification in this research, after the virus is cultivated in host-invasion simulation process, and the cultivation and separation procedure of virus can be found in relevant references.

In this experiment data analysis, the 3-dimension (I× E × N) matrix X includes: I is the total amount of enzyme species within an isozyme family; E is the total amount of isozyme families; N is the total amount of zymograms among different bio-samples of host cells in this pathogen invasion simulation.

Step 6. By the comparison between pre-invasion host cell samples (background samples) and after-invasion host cell samples with apparent antibiotics/antibody, the isozyme families, involved in the synthesis of antibiotics/antibody, are identified consequently (named as antibiotic/antibody isozymes). A matrix Sn is designed to quantitatively analyze the isozyme families below; Further more, in these after-invasion samples, by comparison between host cells with apparent antibiotics/antibody and host cells without antibiotics/antibody, the specific isozyme zymograms of antibiotic host cells is diagnosed, with the specific active enzyme 'species i' involving in antibiotics synthesis identified in the zymogram; Finally, the Principal Components Analysis (PCA) is conducted on the basis of Matrix S designed in my previous article [3], then it is to deduce that which enzyme species play the major role in antibiotics synthesis by quantitative statistics analysis.

$$\text{Sn}=\begin{vmatrix} X11 & X12 & ..... & X1e \\ X21 & X22 & ..... & X2e \\ ..... & ..... & ..... & ..... \\ Xi1 & Xi2 & ..... & Xie \end{vmatrix} \quad (e = 1, 2, ... E)$$

$$\text{Matrix Sn}_{\text{sum}} = \sum_{n}^{1} Sn \, (n = 1, 2, ..., N)$$

Matrix Sn_{sum} is the I × E dimension matrix, and parameter N is the total amount of zymograms between pre-invasion host cell samples (background samples) and after-invasion host cell samples with apparent antibiotics. PCA is conducted by inputting the variables of isozyme families (e = 1, 2, ... E) to quantitatively analyze 'which isozyme families contribute to the most variations in this statistic matrix.'

In my previous article [3], the Matrix Xe is design, where Xe = │Xin│(i = 1, 2, ...I; n= 1, 2, ... N). Then the sum of Xe is conducted:

$$\text{Matrix } X_{\text{sum}} = \sum_{E}^{1} Xe \, (e = 1, 2, ..., E)$$

Based on the sum of Matrix Xe, the UPGMA (unweighted pair group method with arithmetic averages) analysis is conducted, which classifies the variables of different bio-samples (n=1, 2, ... N) according to the similarity of isozyme zymogram among them.

Hypothesis test in this experiment:

It is expected that the patterns of antibiotic isozyme zymograms in bio-samples of host cell with apparent antibiotics specifically correspond to the zymograms of a specific invasive bacteria strain, regardless of genetic difference between sample 1 and sample 2, which means that the bio-samples of host cells with apparent antibiotics in both sample 1 and sample 2 are classified into the same group by UPGMA analysis, regardless of genetic difference. Consequently, the effectiveness of gene expression patterns in host cells is mainly determined by the specific phenotype of a invasive bacteria or virus strain. This hypothesis may provide the theoretical indication for bio-medicine production.

The patterns of zymograms in host cells without apparent antibiotics vary. Similarly, for the other strains of invasive bacteria (or the other phenotypes of the bacteria or virus within the same genetic strain), the patterns of antibiotic/antibody isozyme zymograms react differently and specifically in host cells with apparent antibiotics.

Discussion:

This study does not only help to diagnose the pathology and invasive bacteria strain, but also provides the indicators of 'training' host cells in future, establishing the 'memory' of triggering the antibiotics/antibody, to improve the immunology by biophysical 'learning' in site. Then 'exchange transfusion' is applicable on the medical treatment (For example, if the cancerous blood cells of a rat is caused by virus, then blood cells from other healthy rats with better immunology can be trained by biophysics technology for exchange transfusion, which will be discussed in the next article of this journal). So far there is a number of case reports with regards to exchange transfusion such as Yu (2011) [2], and the recommended volume of bloods per exchange is no more than 10% of total bloods. However, the volume of 'trained' bloods per exchange should be less than this recommended value, due to the allo-antibody of trained cells.

Compared with the bio-signal of environmental gradient simulation, the bio-signal of biotic factor identified by cells is specific, whereas the bio-signals of abiotic factors show the patterns of 'environmental gradient' (the gene expression patterns vary gradually in response to the gradual change of environmental factors along the environmental gradient).

Please note: The characteristics of host cells with apparent antibiotics can be identified as: relatively active cell division rate; And constant and healthy ratio between erythrocyte and leukocyte cells. Usually the ratio between erythrocyte and leukocyte tends to be identical in the long term when cells are cultivated in the same environmental conditions of Lab, regardless of genetic variation. However, when enzyme activity is ignored and only variation in enzyme species is considered in this research, the difference in the ratio of erythrocyte to leukocyte between two different genetic strains can be ignored in UPGMA analysis too.

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