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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的专一性机制中的应用研究

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Introduction

There is the original 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. The relevant discussion is presented correspondingly. In addition to the genetics of host body, the 'memory' of host cells, which allows host cells to fastly 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:

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;

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).

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

4. The host cells with apparent antibiotics 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;

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 as background samples and after-invasion samples), as well as in invasive bacteria samples (Please note: 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 a 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.

6. By the comparison between pre-invasion host cell samples (background samples) and after-invasion host cell samples with apparent antibiotics, the isozyme families, involved in the synthesis of antibiotics, are identified consequently (named as antibiotic 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 and host cells without antibiotics, 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.

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

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

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 = $\left|Xin\right|$ (i = 1, 2, ...I; n= 1, 2, ... N). Then the sum of Xe is conducted:

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

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. 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.

7.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 isozyme zymograms react differently and specifically in host cells with apparent antibiotics. 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, 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, discussed in next chapter, for exchange transfusion). 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-antibiotcs of trained cells.

Discussion:
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.

Conclusion of Metabolomics and Application on the Vaccine Production/新陈代谢组学结论与在疫苗生产中的应用

Recently, I have read the biochemical characteristics in some News reports about new drugs, and presented the following academic viewpoints: in the previous academic paper of metabolomics, it is proposed that the selection of isozymes as the indicative biochemical molecules for pathological analysis leads to better correlation with its phenotype characteristics, which is more stable and less environmental sensitive in the long-term as compared with other biochemical indicators. If medicines research chooses mRNA or tRNA as biochemical indicator, it is not expected to show a long-term stable and positive correlation to the eventual phenotype of antibody against virus, which is susceptible to environmental condition changes (such as diet and physiological work-rest timetable may significantly influence the results of bio-tests on mRNA), and this is especially important for the analysis of immunology generated by vaccine inoculation. The vaccine produced on the basis of the later indicator is similar to biochemical medicines only, which plays the role in remedy in the short term.译文：最近看了一些关于新药的新闻报道的特征描述，提出以下学术观点：本文在之前学术论文《新陈代谢组学》中一直提出使用同工酶最为指示性生化指标对病理进行分析才保证其长期稳定、可靠的表现型特征，不容易受制于环境条件的影响。如果是选用 mRNA 或是 tRNA 作为指示性生化分子，在此基础上对最终表现出来的抗体是否呈现阳性进行相关性分析，不会有长期稳定的正相关特性，而且容易受制于环境条件的影响（比如测试前期的饮食、生理作息时间等也可能会对 mRNA 测试结果产生显著影响）。这对于疫苗抗体的有效性分析尤其重要。因此这类疫苗抗体仅仅类似于西药，产生短期治疗效果。

Please note: This is the revised materials in book "Proceedings for Degree of Postgraduate Diploma in Environmental Science (3rd Edition)." Firstly Published on 26/08/2015. The 'chapter' content mentioned in this article is in previous book. Revised on 05/01/2021. Secondly Revised on 28/01/2021. Thirdly revised on 21/12/2021.This journal article is previously published as: Liu Huan. (2021). Article 8. Metabolomics and Application on The Specificity of Host-Invasion Interaction. Journal of Environment and Health Science (ISSN 2314-1628), 2021(02)., which is converted into Journal of Biological Sciences (ISSN 2958-4035). Both Journals belong to the same publisher, Liu Huan. The previous journal article is closed to the public, but the previous reference is still valid. Latest revised on 23/04/2023;25/04/2023; 29/05/2023.

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