A Comparative Study of Three Models for Animal Cell Growth Simulation Based on Biomics Technology

Hong Xiaoming

MID-LINK Technology Testing Co..LTD, Tianjin, 300457, China

Keywords: Biological technology, Animals, Cell growth simulation

Abstract: Different methods were used to establish cell in situ animal models. The biological characteristics of cell in situ animal models established by different methods were compared and studied. Effective and stable methods of cell in situ animal models were screened, and the effects of different methods on establishing cell in situ animal models were discussed. Therefore, based on the three models of biomics technology, the comparative study of animal cell growth simulation was carried out. The Monod equation, the Logistic equation and a simple structural model were used to simulate the growth of batch cultured animal cells. The results show that neither the Monod equation nor the Logistic equation fits well the growth of cells in the lag phase, and the structural model can describe the growth process of cells from the delayed phase to the stationary phase.

1. Introduction

Batch culture of cells is one of the most widely used culture methods. Cell concentration, substrate concentration, and product concentration in the culture system vary with time [1]. Only by studying at the molecular level can the mechanism of interaction between biological materials and the body be explained. Metabolomics focuses on all small molecule metabolites in the metabolic process and takes a non-discriminatory analysis of all substances in the process [2]. So far, no technology platform can fully achieve this goal [3]. At present, researchers have developed a variety of techniques that can print cell materials into three-dimensional structures [4]. Cell growth kinetics curves are generally divided into five stages, including delayed, exponential growth, deceleration, quiescent and decay stages. With the development of modern molecular biology technology, the evaluation of biocompatibility of biomaterials has gone from animal level and cell level to molecular level. Nowadays, metabolomics uses different analytical methods for different actual samples and different types of metabolites [5]. Therefore, the improvement of metabolomics methodology is also a hotspot nowadays. It is hoped to establish a method with high throughput, high sensitivity and detection of as much metabolite information as possible. However, how to detect the signal changes of tissue-like systems in real time, high throughput and non-invasive way is an urgent problem for high throughput drug screening [6].

Metabonomics is the separation and purification of metabolites and the detection of metabolite components by mass spectrometry, chromatography and NMR for samples of body fluids, cells and organs. Then the obtained data are analyzed and processed by means of bioinformatics, and useful information is obtained to obtain one or a group of molecular markers [7]. In the field of drug screening, the existing animal screening models have some shortcomings, such as species differences and long cycle, while the high throughput screening technology is quite different from the in vivo environment. The result is that the screening accuracy is low [8]. Cell 3D printing provides the possibility to construct a complex multi-tissue system drug screening model with human cells in vitro. Compared with the model of subcutaneous transplantation, the model of orthotopic lung transplantation with H460SM cells through chest wall puncture can form intrathoracic metastasis, but it is not easy to form distant metastasis [9]. However, the traditional biomolecular methods focus on the study of single or partial gene protein changes, and can not carry out high-throughput, large-scale research in the whole genome and proteome range, so it is impossible to fully and systematically understand the biological materials at the molecular level. The delay period of the body's influence refers to an adaptive process in which the cells suddenly

  DOI: 10.25236/isafb.2019.045

change after the access to the new culture system, causing changes in the physiological activities of the cells and temporarily stopping the proliferation, showing an adaptive process [10]. The molecular biocompatibility study of biomaterials can only clarify the interrelationship between individual gene proteins and understand their interactions in order to elucidate the mechanism of the different effects of biomaterials on tissues and cells.

2. Current status and progress in research

2.1. Research on cell growth

As the body pathological changes, its metabolites will also produce corresponding changes. The lag phase of animal cell growth is often due to the lack of certain growth factors in the cells. The technology can perform high-throughput parallel analysis on the expression of genes in tissues or cells, and provides a means for large-scale research on gene regulation and its mechanism, and reveals the life processes of multi-gene synergy at different levels. The orthotopic transplantation model of human non-small cell lung cancer was successfully constructed. The animal models constructed by the two methods can be used for the study of the mechanism and treatment of human non-small cell lung cancer. The data collection and analysis of these metabolite changes, looking for biomarkers of the disease, contribute to the clinical diagnosis and classification of the disease. Although metabolomics was applied late in clinical disease diagnosis. However, compared with traditional diagnostic methods, it has shown its strong advantages and developed rapidly in recent years. Our laboratory research also proves that cell 3D printing technology can be used to construct more accurate drug screening model. The serum added to animal cell culture contains a lot of growth stimulating factors. In addition, the cells themselves need to synthesize specific growth factors to grow. Some people call it endogenous growth factors. The application of genomics and proteomics technology in the field of biomaterials is more and more extensive.

2.2. Development of genomics, proteomics and other biomics

With the development of genomics, proteomics and other biomics technologies, life science has developed from the isolation of individual gene proteins to the high throughput research of whole gene proteins. At the same time, it provides a powerful technology and method for evaluating the molecular biocompatibility and mechanism of biomaterials. Only when these growth factors accumulate to a certain concentration, the cells will grow. Therefore, the application of metabonomics in clinical and animal models of diseases is very broad. Moreover, the combination of the two technologies can better obtain changes in metabolites related to diseases and metabolic pathways. Cell 3D printing technology has been able to construct complex tissues and organs in vitro, which has expanded new theoretical and technological possibilities for many fields of life science. After the delay period, the cells enter the exponential growth phase. At this time, the cells were considered to have no repressive growth, and the cell concentration increased exponentially with time. With the basic completion of the Human Genome Project, the study of the expression patterns and functional patterns of proteins encoded and translated by functional genes has become an urgent need and a new task for life science research. . The basis of aging of the whole body is cell aging, that is, the loss of the inherent functions of cells associated with age (such as division, transportation, and information exchange), and finally the senescent cells die or are cleared by other cells.

3. Cell chip design and manufacturing

An electric cell-substrate impedance sensor (ECIS) is a type of electrical resistance change and membrane capacitance change that can simultaneously measure multiple groups of different cells. Cellular sensors for cell physiology and pathology studies of spatial changes in the cell layer-basal membrane. Complete metabolomics processes include: sample preparation, data collection, and analysis and interpretation of data. The development of proteomics and related technologies is accomplishing this goal. Gene expression profiling chip technology is an effective means of

genomics research, and is a kind of gene chip with relatively mature technology and the most widely used technology. Proteomics is a study of all proteins. By analyzing the dynamic changes in protein composition, expression levels and modification states, we understand the interactions and relationships between proteins. Study the science of protein composition and regulation of activity at the overall level. Compared with the model of orthotopic lung transplantation through chest wall puncture, the model of orthotopic lung transplantation with H460SM cells through bronchus can form distant metastasis. Its metastasis model simulates the progress of clinical lung cancer patients to the greatest extent, and is more suitable for the study of the mechanism and treatment of human non-small cell lung cancer. Thereafter, the conditions in the system gradually did not adapt to the growth of cells. Cells went through deceleration, quiescent and decay stages in turn, and the whole culture process was completed.

As shown in Fig. 1, the weight growth rate of experimental animals was significantly higher than that of the control group. When the time changed, the weight growth rate of the two groups was similar, and after further study, the weight growth rate of the experimental group was significantly higher than that of the control group.

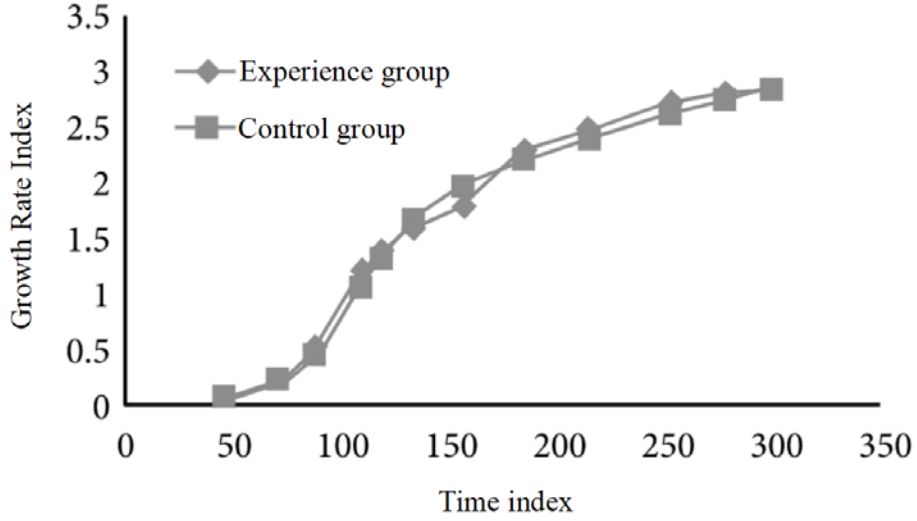

Figure 1 Experimental data of two groups of experimental animals

Sample preparation means that the enzyme activity is immediately blocked by liquid nitrogen cooling method under in vitro conditions, so that the metabolic state stops quickly, and then extracted with water or organic matter separately. The interaction between extracellular matrix (ECM) and cell proliferation can be quantitatively studied in real time and continuously by micro-ampere current measurement, and the morphological changes of adherent cells during migration can be measured. In collaboration with Cell Chip Company, our lab has adopted cell chips integrated with eight sets of IDEs arrays, each of which is a unit. The two units are independent of each other, and each group of IDEs can print different cells. It can monitor the growth, reproduction, toxicity, adhesion and morphological changes of cells in real time. Due to its good stability, optical effects and special bioaffinity effects, gold nanoparticles have developed rapidly in in vivo applications such as drug carriers, carrier frameworks for materials, and tumor-targeted therapies. Control models have been successfully used to describe the growth of microorganisms, especially secondary growth phenomena. Cellular senescence can be divided into replicative and non-replicating. The former refers to the proliferative disorder caused by the DNA damage reaction caused by the replication stress, and the permanent division stops. The latter refers to the loss of function after differentiation due to damage to important membrane structures such as organelles due to production, processing, transportation, and internal environmental stability pressure.

As can be seen from Fig. 2, as the culture time prolonged, HO-8910 cells adhered, stretched and proliferated on the chip, and the impedance value monitored by the chip continued to increase.

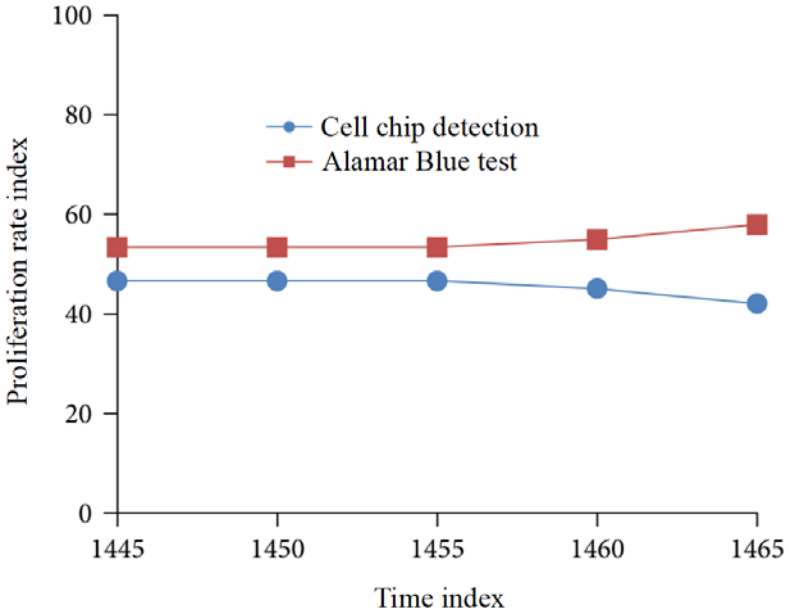

Figure 2 Chip surface proliferation curve obtained by two kinds of detection

4. Conclusion

Bio-omics technology has become an important technology in aging research. However, there are still some limitations in bio-omics technology, such as the introduction of errors in batch operations and false positives in some research results. From the simulation of the cell growth curves of the three models, the Mon-note equation can better fit the cell growth from the exponential growth phase to the stationary phase. The levels of lactic acid in plasma, urine and kidney extracts were significantly increased, which was related to abnormalities in glycolysis and gluconeogenesis. In this study, cell hydrogel materials were assembled to the surface of the chip by cell 3D printing technology, and impedance detection was performed on the cells in the stent. Mon (The equation cannot describe the growth of cells in the delayed phase, because in the initial stage of culture, S is the largest, so the spelling is also the largest. With the growth of cells, S decreases, spelling decreases gradually until 0. Due to the defect of leptin receptor gene, the metabolism of amino acids related to leptin receptor regulation is abnormal, such as the decrease of phenylalanine and tyrosine content. In a word, because of the defect of leptin receptor gene and the change of genotype, the metabolic phenotype of organism changes accordingly. Specific growth rate reflects the actual growth ability of cells, so the model can not only describe the growth curve of cells, but also describe the specific growth rate curve of cells, in order to fully describe the growth of cells.

References

[1] Shiba Y, Ohshima T, Sato M. Growth and morphology of anchorage-dependent animal cells in a liquid/liquid interface system. (2014) Biotechnology and bioengineering, 57(5), 583-589.

[2] Dodson M V, Allen R E, Du M, et al. INVITED REVIEW: Evolution of meat animal growth research during the past 50 years: Adipose and muscle stem cells. (2015) Journal of Animal Science, 93(2), 457-481.

[3] Rourou S, Ben Ayed Y, Trabelsi K, et al. An animal component free medium that promotes the growth of various animal cell lines for the production of viral vaccines. (2014) Vaccine, 32(24), 2767-2769.

[4] Wahrheit J, Nicolae A, Heinzle E. Dynamics of growth and metabolism controlled by glutamine availability in Chinese hamster ovary cells. (2014) Applied Microbiology and Biotechnology, 98(4), 1771-1783.

[5] Zhang H, Liu X, Gao Z, et al. Excessive retinoic acid inhibit mouse embryonic palate mesenchymal cell growth through involvement of Smad signaling. (2016) Animal Cells & Systems the Official Publication of the Zoological Society of Korea, 21(1), 1-6.

[6] Characterization of a growth-elevated cell line of human bone marrow-derived mesenchymal stem cells by SV40 T-antigen. (2015) Biotechnology and Bioprocess Engineering, 20(3), 498-505.

[7] Toman M, Cipin R, Vorel P. Thermal Calculation of Li-Ion Battery Pack. (2017) Journal of Fermentation & Bioengineering, 67(2), 138-140.

[8] Lígia S Nobre, Hélia F. Jeremias, Carlos C. Romão, et al. Examining the antimicrobial activity and toxicity to animal cells of different types of CO-releasing molecules. (2015)D alton Transactions, 45(4), 1455-1466.

[9] Chagnon A, Hudon C, Mcsween G, et al. Cytotoxicity and reduction of animal cell growth by Clostridium M-55 spores and their extracts. (2015) Cancer, 29(2), 431-434.

[10] Suzuki T. Surface instability of calcium phosphate ceramics in tissue culture medium and the effect on adhesion and growth of anchorage-dependent animal cells.. J. (2014) Biomed. Mat. Res. 34(4), 507-517.