Stem Cell Differentiation Base on Acoustic Wave Sensor

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ABSTRACT

This project was based on immobilizing bio-material. We used a new application for protein array and studied a new acoustic wave sensor which is based on silicon. We used the MEMS fabrication and the property of bio-material to build a high integration, surface solid and peculiar to sensing area. In this paper, we used the physical and chemical methods to modify the surface of area to form chemical linker for capture the target protein and detect the special transcription factor or signal which is presented in stem cell by the principle of Protein-protein interaction. And then, there is physical parameter such as frequency、phase and so on. Fortunately, the signal is presented from cell which is only observed by traditional molecular biotechnology as western blot、IF and so on. And now we could present the same data by physical information.

1 INTRODUCTION

In studying biochip, most of technology is based on mature optical selecting way. Although the optical way is already mature, it is limited by detecting circulation and can't make easily, conveniently and fast. Beside the property of fluorescent substrate is slowly decayed with time, and we can't control on the resolution and it isn't conveniently for taking machine. Our study is focusing on the principle of foot printing and Protein-Protein interaction to understand the progenitor cell is differentiated to which lineage. In general, the methods were three steps:

1. Extract from peripheral blood,
2. Culture and observe the phenomenon,
3. Remark the special marker and understand which stage is.

It is CFU-GEMM, CFU-GM and BFU-E, respectly, in Fig.2.

2 HYPOSTHESIS

In biology, the protein is real to perform the function. Therefore the gene presented is only in gene level but we don't know the really function in protein level, in Fig.1. So we proposed the project about an acoustic wave sensor, SAW (Surface acoustic wave). Therefore, there are a number of probes as small oligos、cDNA and chromosome which is the disease DNA sequence. Then we detect the sample via hybrid sequence in order to understand the sample with the disease sequence but it is still on gene level. Here we adopt the special binding between DNA Promoter (koza sequence) and transcription factor to know the interaction about protein and this is our creation in this project. In Fig.3, the factor as follow:

1. Using the interaction between TF and DNA Promoter or Protein-Protein interaction and this is core technology.
2. SAW, acoustic wave sensor is based on some weight change to cause wave、frequency and phase differentiation. And based on this information, we could suppose the target protein in sample.
3. On the other hand, we could modify the surface of chip via chemical and collocate different pattern array via MEMS process to integrity the common chip and make it useful.

By the way, the sensor platform could be made from a metal or silicon material and collocated the array. Then we immobilized the bio-material via chemical linker onto the surface of area.

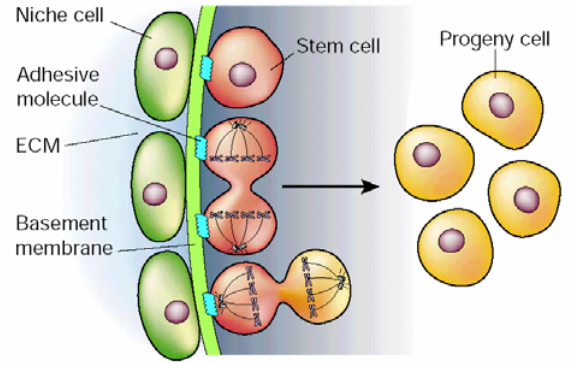

Figure 1: Stem cell life cycle and Niche structure.

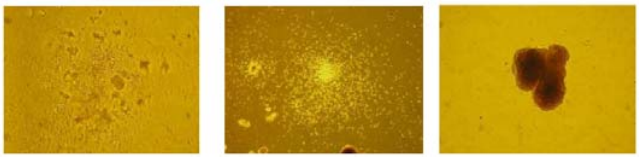

Figure 2: Primary culture from Peripheral blood.

3 RESULT AND DISCUSSION

In Fig.4 and Fig.5, the study is based on the principle of Protein-Protein interaction and Gene expression and let the protein cascade which is only at present in cell differentiation and signal transduction quickly explicit the whole participate protein in cell. We went out of our way to do some hematopoiesis research such as PU-1、c-Myb and so on. The performance is :

1. We made an acoustic wave sensor fabrication by MEMS process.
2. Coating metal, Au and then modify the chemical NH_3 group.
3. And then coat a dehydroxy layer in order to remove some nonspecial chemical substrate which adsorbed onto the surface that is increased the noise on sensor.
4. The midfield acoustic wave sensor fabrication with bio-material and matches the circuit and tests the function.
5. Matching the thermal control to let the all fabrication with feedback control. It make the consistent temperature to stable the three-dimension of protein structure.
6. At the same time, we could culture the simple cell line, U937, or earlier precursor cell and stimulate the cell differentiation by drug.
7. After cell lysis, we extract the protein from cell to do assay.

As a follow, we could understand the developing of disease or precursor differentiation and prevent the disease. It could reduce the breadth time of studying. We want to make the bio-platform matching acoustic wave sensor system、array system developing、optimal design and set up the immobilization technology.

- Set up an immobilization technology about bio-material and bio micro-fabrication.
- Set up a disease and stem cell research to reduce risk of mistake and go up the developing the medical.
- Develop the bio micro fabrication package and spread the new application area.

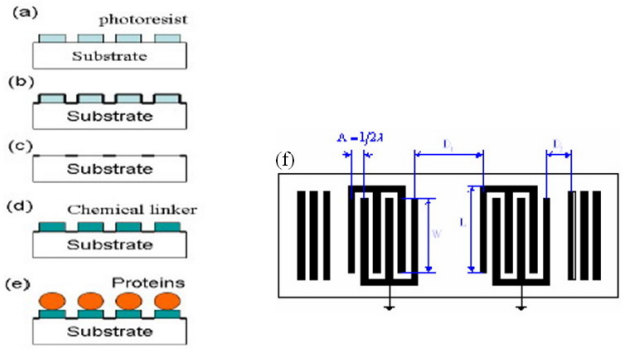

Figure 3: Fabrication process and SAW sensor structure.

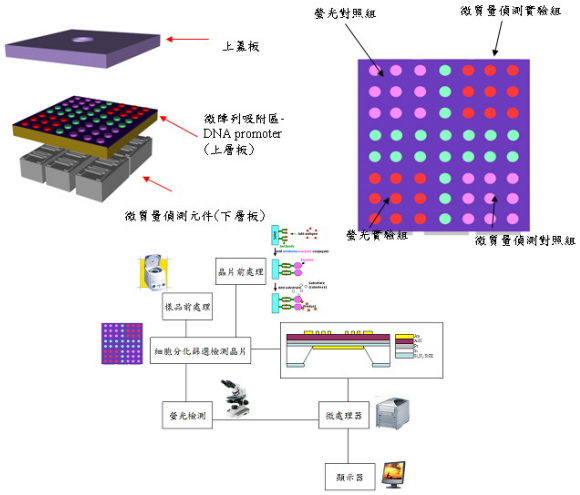

Figure 4: Acoustic wave sensor module and testing method sketch map.

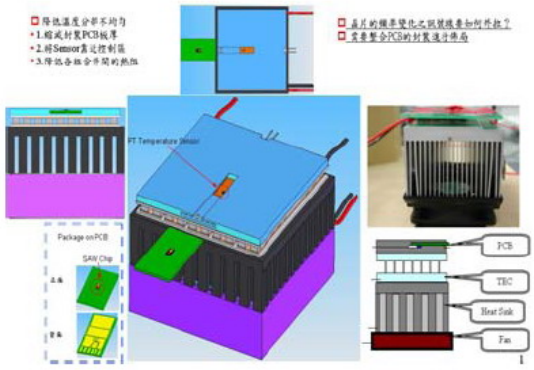

Figure 5: The design for thermometer.

REFERENCES

[1] Chen JJW, Wu R, Yang PC, Huang JY, Sher YP, Han MH, Kao WC. 1999. "Profiling expression patterns & isolating differentially expressed genes by cDNA microarray system with colorimetry detection." *Genomics* 51:313-324.

[2] MacBeath G, and Schreiber SL : Printing proteins as microarrays for high-throughput function determination. *Science* 2891760-1763, 2000.

[3] Alan B Cantor and Stuart H Orkin. (2001) "Hematopoietic development: a balancing act" *Current Opinion in Genetic & Development* 11:513-519