Applied Systems and Synthetic Biology in Micro-Fluidic Biochips

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ABSTRACT

The design of bio-molecular systems within cells, it is a recently achievement of synthetic biology and systems biotechnology. Due to the structurity laws of synthetic biosystems theory: 1).structure integration, coordinative organization of genes network in genome; 2).function adaptation, duplication (amplify) and specific expression of genome involved in cell signalling; 3).construct stratification, multiple stratum of genome constructed by transpose, recombination and amplification. We developed the techniques of the Sequence Tagged Fragments Display (STFD) for analysis of genes differential expression between cell types, and the design of cell signal transduction and gene regulatory network within cell. By applied the methods of systems genetics and synthetic biology for biosystems analytics and artificial biosystems, it is very benefit for the technology integration of micro-fluidic biochips used for the design of cellular nano-factory and nano-computer of bio-molecules systems.

Keywords: Sequence Tagged Fragments Display (STFD), Cell Communication, Micro-fluidic Chips, Systems Biology, Synthetic Biology

1. SYNTHETIC BIOSYSTEMS – STRUCTURE THEORY

The structurity - pan-evolution theory of biosystems, derived from the integrated systems analysis of the structural evolution, functional development involved in psychological biology, chemical physics and genetic bionics etc. The structure evolution, the shape adaptation and the integrative function, involve bidirectional interactive process of adaptation and transformation environment, heredity and behavior regulation and so on. The structure theory of the structure integration, stable adaptation and constructive stratification of synthetic biological systems, it is the foundation of systems and synthetic biology [1-2].

The structurity theory [1] of synthetic biosystems includes the aspects of: 1).structure integration, cordinative organization of genes network in genome; 2).function adaptation, duplication (amplify) and specific expression of genome involved in cell signaling; 3).construct stratification, multiple stratum of genome constructed by transpose, recombination and amplification etc.

Systems genetics [3], developmental biology and pathogenesis of the genotype - phenotype of complex systems of cells dynamics, complex biological molecules involved in cells communication, genes interaction and control system of information, and new techniques of bioinformatics, computer-aided design of cell signaling, gene regulated expression network etc.

In the 1990s, it begins the development of bio-chip high-throughput bio-technology, integrated micro-fluidic chip technology systems and synthetic biology, the engineering design method of cell communication system, the molecular nanotechnology of building blocks within cells.

2. EVOLUTION AND DEVELOPMENT OF CELLS - CYTOGENESIS

The biosystems are constructed of cell units, and morphogenesis in biological evolution and topological systems, there are limitations of previous studies of biological systems in the black box between the state of the whole unit of material, energy and information input and output and feedback control analysis, including the artificial neurons and cellular automata, etc.

The progress of molecular cell biology and the success of genome projects, the study of biological systems start to deep investigation of the molecular network and genomic information system analysis of cells evolution and development. Cells in the central control of information is the chromosome genetic system, gene mutation pattern, gene structure and organization constitute the control levels of genetic information systems.

Evolution of genome structures and morphological development of organisms, the neurons in the self-organization of intelligent behavior are determined by the molecular systems of intracellular communication module and functional activities.

The cell structure is constructed of the membrane system, functional proteins, gene systems and matrix systems, etc., and which system includes various types of metabolic reaction matrix molecules, ions and so on. The evolution is from single cell species of prokaryotic, eukaryotic organisms to the multi-cellular eukaryotic organisms.

Different types of prokaryotic, eukaryotic cells are different species of organisms.

Eukaryotic cells in multi-cellular organisms, at first the ES cells differentiate into somatic cells and sex differentiation of cells, and then the somatic stem cells differentiate into various types of functional cells. The mutation pattern of cell chromosome or genes, it leads to genetic variation of organisms. The genetic mutations of somatic cells, it induces the formation of developmental variation abnormalities, including the formation of somatic tumor genetic variation. The fate of cells in the body, involved in cell regeneration, differentiation, apoptosis, migration and adhesion, etc., the different forms or statues of gene expression in different cells, which constitute the cells in different space-time of spatial and temporal expression of genes, the differences of gene expression level mapped in the groups of cells within organism's structure.

The genes expression with ES cell Σg0-> differentiation of cells C1, C1.1 ... the expression differences of genes Σg1 g1.1 ..., the C1 differentiate into cells C2, C2.1 ... level; therefore Σ (g0 g1-> n) is expressed functional genes of cells during the development (Figure 1.) of all the genes necessary.

3. NETWORK OF CELL COMMUNICATIONS - CELLULAR DYNAMICS

Neuro-endocrine, immune regulation and cell signal transduction, gene expression regulation, constitute a psychosomatic medicine, systems medicine [4] model of biological systems, the system genetics of complex trait, pathogenesis of genotype - phenotype of the cells convert the information system dynamics (dynamics of cytogenesis) mechanism.

Cell lineages mapping and morphogenesis of cells (Figure 2.), are involving cell proliferation, differentiation, apoptosis and migrant, the occurrence of movement dynamics of cytogenesis and the evolution of biological forms of topology.

The research and application of the cell proliferation, differentiation and apoptosis cells (cytogenesis) and the nervous, endocrine and immune cells such as two-way communication, which involved in the module, structure and dynamic evolution of systems of signal transduction and gene regulatory network. Neurons and neural networks, gene expression, axon growth and neural feedback form neural development.

Transcriptional regulation of gene, transcription factors involved in complex systems, the interaction between transcription factors, transcription factors constitute the self-feedback regulation of gene expression such as operation, gene regulation and process time rhythm (figure 3.) [5] of signal transduction etc.

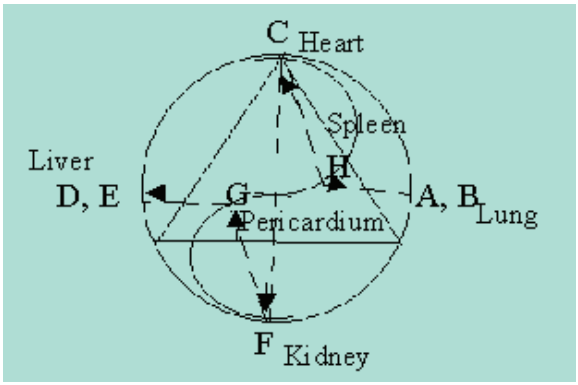

Figure 3: Stable Oscillator (Molecule, Cell & Organ).

Biological metabolism of cell is the energy dissipation manifested cells, biological substances or periodic system replacement parts, so as to maintain steady-state structure [5] and function of organisms.

By using of the methods of experiments, computation, engineering and biosystems theory for the research of biosystem analytics and artificial biosystem, development of micro-fluidic chips to become the laboratory key technologies. The artificial design and the genetic engineering of cell molecular systems such as signal conduction and gene expression network, as well as signals transmission and feedback regulation between cells communication. To develop micro-fluidic chips and nano-biotechnology of cells communication, will be useful in the applications of drug discovery, gene clone and transgene expression and so on.

4. DESIGN AND SYNTHESIS OF ARTIFICIAL CELLS - ENGINEERING

The gene is a concept of genetic information, the genome is the programmed control system of information, the design of cell signal conduction, gene regulation network and the model of cell dynamics are useful in the studies of transgenic oviduct bioreactor [3], metabolism engineering, cell computer [6-7] and drug discovery of medical screens etc.

E. coli, yeast cells, animal and plant cells are commonly used cells in the development of genetic engineering and biotechnology, a single gene expression vector is a traditional genetic engineering techniques. The feedback loop design of stimulation and inhibition of gene regulated expression is the first achievement of synthetic biology technology.

Synthetic biology is developed for designing, synthesis technology [8] of molecular system modules, genes structure and artificial cell system.

In the 20th century, intelligence computer, the development of nano-bio-molecular devices, biotechnology has developed into the cells research and development of complex molecular systems, cell bionic engineering and

synthetic biology of artificial cell design of complex molecular systems.

As a highly integrated technology system to re-design of molecular machines, the signal transduction and gene regulation system such as in the model [7] of molecular cell computer in 2002. By using of signal transduction, gene regulation principles of cell communication, cell sensor computer models can be applied to the development of synthetic biology drug screening and other bio-chip technology.

Systems biology, analysis of biological systems regulation models of gene expression, cell structure and dynamics of signal network to provide the theoretical basis and principles of synthetic biological design of artificial life system.

The design and engineering of artificial cell construction, the key is the design of protein structure and protein complex system, metabolic enzyme reaction is catalytic protein, the protein encoded by the gene and regulatory expression; therefore, the analysis, design and synthesis for biosystems are the design and synthesis of genes and genomic structure of the cell, that is the applications of systems genetics, and will be used in the development of systems biotechnology [6, 8] involved in pathology diagnosis, drug screening and bio-chips, bio-engineering data, software and other biosystems for the development of translational, personal systems medicine.

5. NANO-MICRON TECHNOLOGY – INTELLIGENT ROBOTS

Design and synthesis of artificial cellular signal transduction and gene regulatory networks, molecular computing as a biological computer system, compared to silicon computer is referred to as the concept of wet or cell computer. By using of computer aided design of artificial enzymes and metabolism in response to the development of bio-reaction chain optimization in transgenic bioreactor as the cell factory etc.

The genetic modified cell or bionic designed cell [6] is a bio-molecular nano-machine, which can be used as cell factory - bioreactor, or used as cell nano-computer. A kind of cell machine is a bio-molecular complexity, it is constructed of material system – molecules module, energy system – organelle and information system – genes, by design of signal transduction networks and synthesis gene regulatory structures of cells.

Self-reproduction and evolution of the machine, in theory: 1) to seek feedback on energy consumption and automatic import energy, 2) to operate the machine manufacturing factory production line, 3) to improve the process and engineering design blueprint of machines itself.

Synthesis of nano-biotechnology and micro-fluidic technology, breakthroughs in the cellular and molecular design of nano-bio-technological systems and cells communications in the future, will develop the cellular automata as a unit structure of the artificial intelligence robots.

The gene regulation, signal transduction and metabolism systems within cell, respectively, can be regarded as cell computer software systems, hardware systems and energy systems, but also as cell factory information system, control system and reaction systems and so on, according to different objectives carefully designed and engineered artificial cells that can develop solar energy, pharmaceutical factory and bionic robot technologies of artificial cells.

REFERENCES

[1] Zeng B.J. Structure theory of self-organization systems, Communications on Transgenic Animals, CAS, No. 8-10, 1996.

[2] Benner S., Biology from the bottom up. Nature 2008(452):692-4.

[3] (Bangzhe) Jie Zeng, Transgenic animal expression system – the goldegg plan, Communication on Transgenic Animals, CAS, Nov. 1994 (the term "system genetics" was coined).

[4] Zeng B.J. From positive to synthetic medical science, Communications on Transgenic Animals, CAS, Nov. 1995.

[5]Zeng B.J., The rhythems stability model of animal development, 94-Symposium for Yong Chinese Developmental Biologists, Beijing, Oct. 10-15, 1994.

[6] Zeng B.J. On the concept of systems biological engineering, Communications on Transgenic Animals, CAS, June, 1994.

[7] Zeng B.J. Automatic cell - the bio-computer, Genbrain biosystem network, the Associates for Biosystem science and Engineering (since Jan. 1999), June, 2002 edited[1].

[8] Gulati S., Rouilly V., Niu X., Chappell J.,Kitney R. I.et.al., Opportunities for microfluidic technologies in synthetic biology. J.R. Soc. Interface 6 Aug. 2009:6(Suppl.493-506).

[1] Author: Zeng Jie (Bangzhe), director of the Benjoe Institut of Systems Bio-Engineering. He was born in 1963, China, and studying in Israel, Germany and England since 1997 to 2006. He established the structurity theory – pan-evolution of biosystems, the concepts of systems medicine, systems genetics and systems bioengineering, and the oviduct bioreactor, genomic intelligence of cell computer during the 1991-1999 years. The term of system genetics was coined by him in 1994.

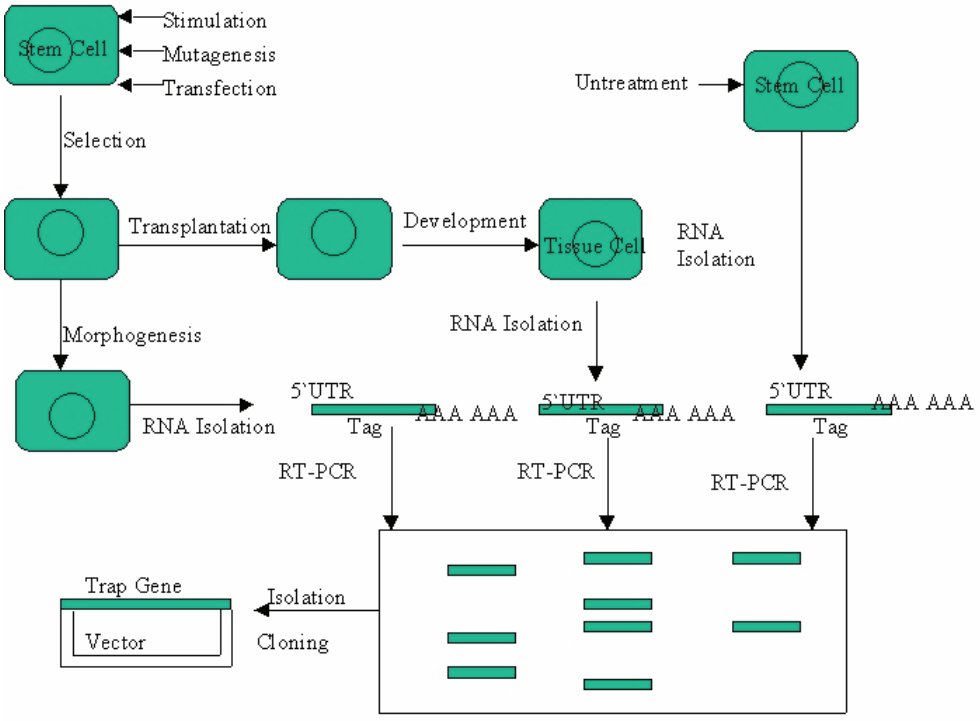

Figure 1: Sequence Tagged Fragment Display.

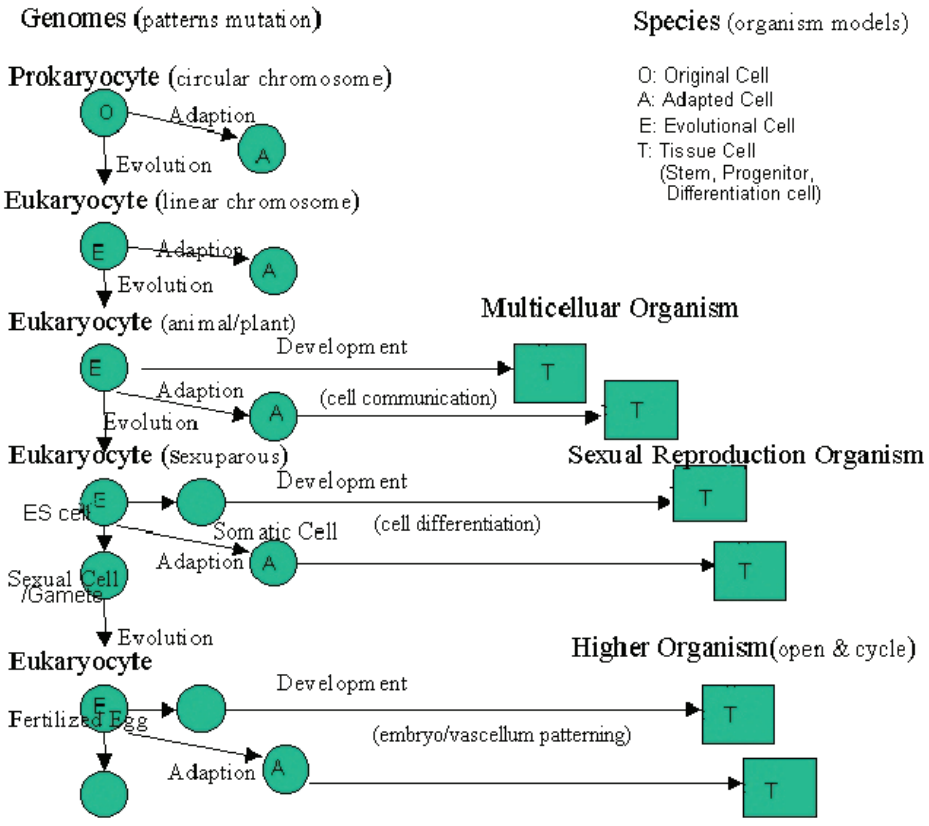

Figure 2: Evolution and Development of Cells.