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Mechanisms of Signal Transduction in Cells Facts and Hypotheses

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INTRODUCTION:

The life and functional activity of all eukariotic cells are ensured by the main vital activity programs: apoptosis, proliferation, differentiation. At the same time, apoptosis (genetically determined cell death), the basic program, is activated by the variety of internal and external factors, the realization of other programs is only possible when it is blocked. Modern achievements in biochemistry, molecular biology and molecular genetics have made it possible to define the basic stages of each of these programs, molecules responsible for the induction and propagation of a signal, but also factors transcriptional, ensuring the expression of certain genes and the link between matrix DNA and RNA polymerase. Internal cellular proteins, expressed by genes as a result of such a cascade of signals, are crucial for the performance of either cell program and determine the future fate of the cell. The cell itself plays a decisive role in the choice and execution of the vital functions program. This is related to the fact that the means of activation of signal molecules in a cell are of several types, depend on the presence and activity of certain intracellular signal molecules and transcription factors, and also, apparently, on the particular character of the signal received. In addition, there are certain cross links between the different ways of reporting, the way of choosing which is not clear until the end. For the perception of external signals, initiating these pathways, the cell uses its receiving device. What is common to all programs is the fact that the inclusion of signal pathways when the receptor is activated takes place by means of phosphorylation with highly specialized intracellular enzyme phosphokinases. However, the mechanism of binding of the ligand molecule with the receptor, as well as the mechanism of attraction and activation of intracellular phosphokinases, remain unclear until the end. Many well-known phenomena in biology and medicine also have no explanation from the classic position of modern biochemistry and molecular biology. We will provide several examples from biology. The salmon determines the direction of the odor spawning movement at a distance of 100 km from the place of birth, even if it is released at a place above the spawning ground. Male Saturn butterflies can find a female up to 11 km away. It has been established that a cubic meter of air at such a distance contains 1 molecule of female sexual attractant. It is well known that the dose-response effect of drugs does not always follow a linear relationship in the range of therapeutic doses. For example, small doses of caffeine and adrenaline cause a stimulating effect while large doses have a depressive effect. The same pattern is seen in many other drugs. Signal molecules, their pathways of interaction and the mechanisms of their movement inside cells (using elements of the cytoskeleton and protein transporters) have been studied extensively by modern types of biochemical analysis and molecular-genetic with several types of intravital visualization techniques. The critical importance of signal molecules is confirmed by the fact that a large fraction of the human genome (approximately 40% of the known genes of 26,383) is devoted to signal transduction (signal molecules, receptors, kinases, proto-oncogenes and ion channels). During this time, many mechanisms of initiation and transduction of intracellular signals do not lend themselves to interpretation from the point of view of molecular biology. This becomes obvious from a few figures: from 10 to 100,000 molecular receptors can be expressed on the cell surface; 4,000 protein molecules participate in signal transduction; signal molecules must cover a large distance during their movement inside a cell (the diameter of the molecule is approximately 2 to 10 nm while the diameter of the cell is approximately 10,000 nm).

Following questions arise:

1. How do signal molecules find their targets?
2. How their movement is directed?

In 2013, the Nobel Prize in Physiology and Medicine was awarded to Randy Shekman, James Rothman and Thomas Sudhof for their work on deciphering the mechanism of transporting and introducing signal molecules into target cells. However, these works did not provide an answer to the abovementioned questions. A different paradigm is required. The purpose of this article is to present a concept according to which the formation of signal pathways, the search for the target and the strength of ultimate effect on it obeys the physical laws of biophoton emission of signal molecules.

RESULTS OF OUR PILOT STUDY

We conducted pilot studies of dependence of the nature and magnitude of cell-mediated response on the concentration of inducing substances in in-vitro experiments. The following assumptions were made: the response strength depends on the quantity of target cells involved in the reaction; the concentration of inducer substance reflects the number of molecules involved in the process. Three cellular models were applied:

- Colony-formation in the soft agar of granulocyte-macrophage precursors (CFU-GM) under the effect of various concentrations of granulocyte colony-stimulating factor (G-CSF);
- Colony formation in the methyl cellulose of erythroid precursors (CFU-E) under the effect of various concentrations of erythropoietin (EPO);
- Apoptosis of murine melanoma cells (cell line B16) under the effect of various concentrations of vincristine.

The effect of G-CSF on CFU-GM in soft agar A factor stimulating the colonies of granulocytes (G-CSF) was used - Granocyte (Aventis) at dilutions of 2 μg / ml; 0.2 μg / ml; 0.02 μg / ml and 0.002 μg / ml (G-CSFf). In order to obtain ultra-low concentrations of Granocyte (G-CSFp), a potentiation of the homeopathic dilution technique was applied (Boiron laboratory, Paris). The homeopathic drug potentiated by Granocyte was obtained at concentrations of 2 x 10-12 to 2 x 10-60 (6CH and 30CH, respectively, according to the homeopathic nomenclature). The effect of various concentrations of this drug

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on the proliferation program has been studied in cell culture. Precursor cells extracted from the cord blood of neonates at 35-36 weeks gestation were used as target cells. The culture was carried out in the “agar medium drop by drop” system. The culture method, the course of the experiment and the results have been described previously. Three indicators were considered when analyzing the results: cloning efficiency (CE) - the sum of colonies and clusters for 105 explanted cells; proliferation potential (PP) - the ratio of the number of colonies to clusters; % of large colonies.