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GENERAL INFORMATION

Cell signalling pathways interaction in cellular proliferation: Potential target for therapeutic interventionism☆

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Abstract Nowadays, cellular physiology is best understood by analysing their interacting molecular components. Proteins are the major components of the cells. Different proteins are organised in the form of functional clusters, pathways or networks. These molecules are ordered in clusters of receptor molecules of extracellular signals, transducers, sensors and biological response effectors. The identification of these intracellular signalling pathways in different cellular types has required a long journey of experimental work.

More than 300 intracellular signalling pathways have been identified in human cells. They participate in cell homeostasis processes for structural and functional maintenance. Some of them participate simultaneously or in a nearly consecutive progression to generate a cellular phenotypic change.

In this review, an analysis is performed on the main intracellular signalling pathways that take part in the cellular proliferation process, and the potential use of some components of these pathways as target for therapeutic interventionism are also underlined.

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PALABRAS CLAVE
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Interacción de las vías de señalización intracelulares participantes en la proliferación celular: potencial blanco de intervencionismo terapéutico

Resumen La fisiología celular es actualmente mejor entendida a partir de sus componentes moleculares interactuantes. Las proteínas son las principales biomoléculas que constituyen las células. Las diferentes proteínas se organizan en asociaciones formando conjuntos, vías, o redes funcionales. Estos conjuntos se encuentran organizados en moléculas receptoras de señales extracelulares, transductoras, sensoras y efectoras de respuestas biológicas. La identificación de las diferentes vías de señalización intracelulares en los diferentes tipos de células ha requerido largas jornadas de trabajo experimental.

Se han identificado más de 300 vías de señalización intracelular en las células humanas, las cuales participan en los procesos celulares básicos y especializados para mantener la homeostasis estructural y funcional. Varias de ellas participan de forma simultánea o cercanamente consecutiva en la generación de un cambio fenotípico celular.

En esta revisión analizamos las principales vías de señalización intracelular que participan en el proceso de proliferación celular y remarcamos la estrategia de utilizar algunos componentes de estas vías como blanco de un potencial intervencionismo terapéutico.

Background

The capacity of human beings to see, perceive and respond to environmental signals depends on the activation of intracellular signalling pathways of their different constituting cells. These signalling pathways provide mechanisms to organise molecular information through cells, as it occurs with the central nervous system when it conducts the transduction of environmental information and organises the comprehensive response of the different body organs. In this way, sense organs are sensitive to certain kinds of stimuli (for example, light, pressure or sound waves), given that cell surface receptors bind to specific ligands. One cell may have dozens of different receptors that simultaneously receive signals and transmit them to the inside of the cell at the same time. All cells use specific intracellular signalling pathways to record incoming information, to translate it, to make different molecules interact and to produce a biological response, thus generating a specific phenotypic pattern.[1]

Signalling pathways mainly consist of a protein chain where proteins interact with each other in a previous sequence that was established through evolution. Plants and animals share certain basic intracellular signalling mechanisms; however, some organisational components are predominant, while others are less frequent and certain pathways are unique to each kingdom.

Over the last decades, a large number of intracellular signalling pathways, each with countless molecular components, have been identified. This characterisation has been conducted in the context of different cellular processes of specific types of cells, in conditions of both health and disease. A general understanding has been reached in relation to how these groups of molecules work in terms of circuits and complex systems.

The normal development and functioning of multicellular prokaryotes and eukaryotes depend on a consecutive series of cellular interactions based on biochemical changes. The different cellular stages are mainly due to genetic transcription patterns that, upon translation, produce the interaction with other molecules and, finally, regulate different cellular functions.

Cloning and sequencing of DNA segments and purification and sequencing of proteins have led, for example, to understand how some oncogenes code for growth factors (such as v-Sis) and to recognise their receptors (such as ErbB) and signalling pathway proteins (such as v-Src). Likewise, it has been demonstrated that the transduction of signals occurs through both second messengers, and protein–protein interactions and protein–nucleic acid interactions, or how epigenetic cellular conditions modify the effector response due to extracellular signals.[2]

In this article, the general principles of intracellular signalling pathway functioning will be described, and the modular organisation of pathways participating in the cellular proliferation process will be analysed, as an example of a complex molecular model that cells use to conduct various cellular processes.

Proteins as participating biomolecules

Proteins are the most common and complex biomolecules within cells, and they constitute their structural and functional elements. Proteins are functional molecules of biological work. Based on their direct genetic coding in human cells, there would be 22,000 different proteins; however, this number is increased more than 10 times due to the different transcription combinations of genes and post-transductional changes that occur in the endoplasmic reticulum and Golgi apparatus. They are essentially composed of 20 types of amino acids in different proportions. There are small proteins (40–80 amino acids), medium and large (more than 10,000 amino acids), and