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Cell signaling in yeast: A mini review

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ABSTRACT

Background

Understanding cellular mechanism of communication is the main goal of systems biology. Unicellular yeasts are effective model to understand the molecular interactions that generate cell polarity induced by external inputs. The mechanisms of many extracellular stimuli are induced by complexes of cell surface receptors, G proteins. The mechanisms of many extracellular stimuli are induced by complexes of cell surface receptors, G proteins and mitogen activated protein (MAP) kinase complexes. Many components, their interrelationships, and their regulators of these mechanisms were initially identified in yeast. A complex web of sensing mechanisms and cooperation among signaling networks such as a cyclic adenosine monophosphate dependent protein kinase, mitogen-activated protein kinase cascade and 5-adenosine monophosphate activated protein kinase induce various changes in physiology, cell polarity, cell cycle progression and gene expression to achieve differentiation. Ras-cAMP pathway explained in yeast model with signalling function of the oncogenic mammalian Ras protein. So studies on yeast cells may enlighten some underlying mechanism which will be beneficial to understand the mechanisms of disease.

Keywords

Copper, iron, magnesium, malaria, micronutrients, zinc

Introduction

Understanding how various cells make use of small common range of circuit components to communicate with each other or other cells in order to achieve diverse functions is the main goal of systems biology [1]. Signaling of cell to cell is a must for the development of multicellular organisms such as plants and animals, but this prerequisite has also evolved in groups that are not necessarily multicellular, such as bacteria and unicellular fungi [2]. As such, the evolution of complex signaling systems increases with complexity of the organisms, from yeasts, to nematode worms, fruit flies and humans [3].

A cell that secretes and senses the same molecule is said to be communicating with itself and this is referred to as "self-communication" [1, 4, 5]. Conversely, a cell that communicates with its neighbouring cells and not with itself undergoes "neighbour communication" [1, 5]. However, the secreting and sensing cell may communicate with both itself and with its neighbours [4]. According to Youk et al., (2014) various parameters are the key to the secrete and sense circuits that allow cells to undergo diverse classes of behaviours. This means that the secrete and sense circuits have functional flexibility, explaining its recurrence throughout nature [1, 6].

Various cases have been studied with great detail such as: insulin secreted and sensed by human pancreatic B cells or human Tells [7, 8], that secrete and sense the cytokine interleukin-2 (IL-2) to regulate their growth; bacteria cells that secrete and sense autoinducers in a process called quorum sensing [6, 9- 11]; and the vulva precursor cells in Caenorhabditiselegans secrete and sense the diffusible Delta, just to name a few [1].

The mechanisms of many extracellular stimuli are induced by complexes of cell surface receptors, G proteins [12], and mitogen activated protein (MAP) kinase complexes [13]. Many components, their interrelationships [10, 14], and their regulators of these mechanisms were initially identified in yeast [13]. It was through the analysis of haploid yeast cells and their response to peptide mating pheromones that lead to the understanding of G protein and MAP kinase signaling mechanisms [13, 15]. With the aid of new and powerful genomic, proteomic and computational approaches, the analysis of the pheromone response pathway among other mechanisms may reveal other principles that are applicable to more complex organisms [13].

Another important aspect of signaling is interspecies signalling which occurs especially in bacteria [11], yeast, general insects and even in vertebrates [16]. Signaling molecules used by multicellular organisms are usually called pheromones [15], which function in warnings against danger, helping in reproduction and even indicating the source of food. However, in unicellular organisms signaling can be used in morphology changes such as from dormant to vegetative state as seen in yeast defense against bacteriophages or enhancing virulence in their hosts [17-19].

Cells have capacity for sensing and discrimination of extracellular stimuli; means that all cells undergo cell signaling and signal transduction. One common mechanism for detecting and transmitting extracellular signals uses cell surface receptors coupled to intracellular heterotrimeric guanine nucleotide–binding proteins (G proteins) [13, 20]. It is important to note that although usually stated as separate entities, extracellular and intracellular sensing may be interdependent [5, 21].

Conrad et al. stated that the glucose repression pathway in the yeast Saccharomyces cerevisiae raised a lot of interest due to its involvement in various cascades of nitrogen catabolite repression, general amino acid control (GAAC), phosphate regulation, and regulation controlling ethanol fermentation. This is of fundamental value asa characteristic to this species, which also has great industrial importance [21, 22]. Eventually, other nutrient regulation pathways like sulphate, metal ions, and vitamin were investigated [21].

Ras-cAMP pathway explained in yeast model with signaling function of the oncogenic mammalian Ras protein [23]. Parallel research focused on glucose regulation of storage carbohydrate levels through the cAMP-PKA pathway. Whereby the findings on glucose transporter gene cloned in yeast led to the discovery that the protein that was unable to transport acted as a glucose sensor for glucose induced upregulation of regular glucose transporters [21]. These findings lead to the discovery of a similar amino acid sensor in addition to the establishment of the concept of transporter like proteins being used as sensors for the nutrient they likely once transported previously in evolution [24].

Many fungi undergo multiple growth patterns depending on environmental conditions [25]. A typical example is yeast and filamentous forms [26]. According to Lorenz et al, filamentous growth may enable immobile organisms to seek suitable environmental conditions. Take conjugation of compatible cell types in the maize pathogen Ustilagomaydis for example, which results in the formation of a filamentous heterokaryon which is responsible for host infection [25, 27, 28].

Polymorphism between yeast, hyphal and pseudohyphal forms in Candida albicans (opportunistic human pathogen [29] has been proposed to be a mode for tissue invasion and dissemination during infection [25]. In the same manner, the human pathogen Cryptococcus neoformans has a filamentous growth form accompanied by spore formation or haploid fruiting which has only been observed in cells of the mating type, which are more virulent [30]. In the budding yeast Saccharomyces cerevisiae however, severe nitrogen starvation induces diploid cells to differentiate into a filamentous, pseudohyphal growth form. This pathway of developmentis said to be a scavenging mechanism under which a particular nutrient is the limiting factor [25].

Glucose-sensitive yeasts like Saccharomyces cerevisiae and *Schizosaccharomyces pombe* prefer fermentation over respiration. In these yeasts, synthesis of key enzymes of respiratory sugar dissimilation is repressed by the presence of rapidly fermentable sugars, such as glucose or fructose. This enables these yeasts to compete effectively for survival, because the ethanol produced during fermentation inhibits growth of competing microorganisms. This ethanol can subsequently aerobically be used as a non-fermentable carbon source resulting in a complete use of all available carbon [31, 22].

Therefore, different environmental stimuli usually employ the same set of signaling molecules to achieve different developmental outcomes among other responses [32]. A complex web of sensing mechanisms and cooperation among signaling networks such as a cyclic adenosine monophosphate dependent protein kinase, mitogen-activated protein kinase cascade and 5-adenosine monophosphate activated protein kinase induce various changes in physiology, cell polarity, cell cycle progression and gene expression to achieve differentiation [33]. Fortunately, the mating pheromone response pathway of the yeast Saccharomyces cerevisiae. Saccharomyces cerevisiae has long been used as a model organism for basic biological research. It is easy to manipulate, copes with a wide range of environmental conditions and regulates provides an advantageous model system for exploring these signaling pathways [34].

This budding yeast has proven necessary in explaining the mechanisms of mitogen-activated protein (MAP) kinase [35, 36] and G protein signaling. A combination of genetic, biochemical and molecular biological analysis of the response of haploid yeast cells to their peptide mating pheromones has established basic principles of G protein signaling and regulation [13, 34]. Budding yeast cells can thus communicate by releasing a signaling molecule called the mating factor [3, 5, 13]. Other intracellular processes may include: protein synthesis, mitochondrial biogenesis, retrograde response to mitochondrial dysfunction, proteasome machinery, and even programmed cell death. As opposed to *Saccharomyces cerevisiae* which is a budding yeast, *Schizosaccaromyces pombe* is fission yeast that has gained popularity with respect to studying cell growth and division [26]. Fission yeast chromosomes share a couple of important features with human chromosomes, making it a very useful model in human genetics. Studying signalling proteins in yeast has advanced our understanding of brain and nervous system development

Conclusion

Unicellular yeasts are effective model to understand the molecular interactions that generate cell polarity induced by external inputs. Both the Saccharomyces cerevisiae and *Schizosaccaromyces pombe* yeast genomes have just over 12 million base pairs, with Saccharomyces cerevisiae having around 6,000 genes while *Schizosaccaromyces pombe* having just over 5,000. And it has been estimated that about 20 per cent of human genes plays a key role functionally resembles to Yeast. There is no unambiguity that human diseases result from the disruption of very basic cellular processes, such as DNA repair, cell division, gene expression and genetic interaction and the environment. So, studies on yeast cells may enlighten some underlying mechanism which will be beneficial to understand the mechanisms of disease.

Abbreviations

General amino acid control (GAAC), guanine nucleotide–binding proteins (G proteins), interleukin (IL), mitogen activated protein (MAP)

Authors' contribution

All authors contributed equally.

Competing interests

The authors declare no conflicts of interest.

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