Regulation of cell metabolism by cell cycle machinery.

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Introduction

In human cells, the cell cycle control machinery is composed of about 20 cyclin-dependent kinases (CDKs), 29 cyclins and several inhibitors and activators of these complexes. It has been described that only CDK1 is essential for the proper control of cell cycle progression [1]. Therefore, the emerging question is what is the purpose of the other CDKs? The answer can be found in physiological functions yet to be discovered in certain cell types or specific environmental situations. In fact, evidences about coordination between the cell metabolism machinery and the machinery of control of the cell cycle are increasing [2-6]. A clear example is found in adipocytes (a typical non-proliferative cell type). The critical role of some of these CDKs in the differentiation of adipocytes or in the functionality of the mature adipocyte is demonstrated [2,3,5,6]. The malfunction of these CDKs and other cell cycle regulators may lead to physiopathological processes such as obesity or cancer. These findings open a field of investigation to decipher the metabolic implications of the cell cycle machinery, as well as, in an opposing manner, the regulation of cell cycle progression by metabolic genes, in some organs and tissues.

As opposed to single-cell eukaryotes, cells of multicellular creatures as a usually have a unlimited access to nutrients. Be that as it may, they are not cell-autonomous for supplement take-up but rather rely upon proliferation-regulating pathways. Mitogen-intervened initiation of signaling routes triggers nutrients take-up and represents the rate-limiting cue for cell cycle passage [7]. As an outcome, development factor-fortified cells start cell division in a manner similar to that of yeast presented to a supplement rich medium [8]. Appropriately, without mitogens, even in a supplement rich condition, cells won't enter the cell cycle. Then again, even within the sight of promitogenic cues, glucose deprivation will keep cells from proliferating, which is a generally utilized technique for synchronizing mammalian cells. The way that signaling pathways planning cell cycle movement control, and are controlled by, changes in cell metabolism [9], demonstrates that, additionally in multicellular organisms, there must be a crosstalk between these pathways, cell cycle and metabolism. However, the molecular premise that interfaces supplement accessibility, biosynthetic intermediates and energetic balance profoundly cell cycle machinery remains incompletely understood. Here, we will give a overview of how the cell cycle machinery and metabolism are interconnected.

Cell Cycle Regulation of Metabolism

Evidence is rising in help of the coordinated temporal regulation of metabolism directly by the cell cycle modulators. A first sign for this originated from the perception that in yeast, metabolites of nucleotide, protein and lipid synthesis are cyclically fluctuating, as a component of cell cycle progression [10]. Indeed, it has been demonstrated thusly that the glycolysis-promoting enzyme 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 3 (PFKFB3) is subjected to cell cycle dependent temporal regulation by members from the ubiquitin proteasome system [11]. From that point forward, various mechanisms have been revealed that couple the cellular metabolic state to the cell cycle.

Most physical cells are separated and quiet, that is, they live in the G0 phase of the cell cycle. Following mitogenic stimulation, cells commonly re-enter the cell cycle and continue through the G1 stage, in which the stage is set for DNA replication. Upon section through the G1/S limitation point, cells enter S phase in which they double their DNA content, proceed onward into the G2 phase and the last mitotic (M) phase, in which cellular contents are separated more than 2 daughter cells. Key proteins for the tight regulation of the cell cycle are cyclin-dependent kinases (CDKs), which connect with one of various cyclins over the cell cycle to ensure accurate cell cycle movement [12]. The kinase movement of cyclin-CDK complexes is tightly regulated by a plethora of CDK inhibitors (CKIs), which stop cell cycle movement in ominous conditions.

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