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Metabolomics Conference 2017: APC as an entry point to study small molecule regulation of the cell cycle - Nubia Barbosa Eloy - Max Planck Institute

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The anaphase-promoting complex/cyclosome (APC/C) is a multi-subunit E3 ubiquitin ligase that plays a major role in the progression of the eukaryotic cell cycle. This unusual protein complex targets key cell-cycle regulators, such as mitotic cyclins and securins, for degradation via the 26S proteasome by ubiquitination, triggering the metaphase-to-anaphase transition and exit from mitosis. The identification of the complete set of genes encoding subunits of the APC in Arabidopsis suggests that the basic processes controlled by proteolysis mediated by ubiquitin in plants are similar to those of other organisms. However, results from several groups indicate that the APC has other specific functions in the regulation of plant development. The cell cycle, or cell-division cycle, is that the series of events that happen during a cell that cause it to divide into two daughter cells. These events include the duplication of its DNA (DNA replication) and a few of its organelles, and subsequently the partitioning of its cytoplasm and other components into two daughter cells during a process called cellular division. In cells with nuclei (eukaryotes), (i.e., animal, plant, fungal, and protist cells), the cell cycle is split into two main stages: interphase and therefore the mitotic (M) phase (including mitosis and cytokinesis). During interphase, the cell grows, accumulating nutrients needed for mitosis, and replicates its DNA and a few of its organelles. During the mitotic phase, the replicated chromosomes, organelles, and cytoplasm separate into two new daughter cells. To make sure the right Replication of cellular components and division, there are control mechanisms referred to as cell cycle checkpoints after each of the key steps of the cycle that determine if the cell can reach subsequent phase. In cells without nuclei (prokaryotes), (i.e., bacteria and archaea), the cell cycle is split into the B, C, and D periods. The B period extends from the top of cellular division to the start of DNA replication. DNA replication occurs during the C period. The D period refers to the stage between the top of DNA replication and therefore the splitting of the bacterial cell into two daughter cells. The cell-division cycle may be a vital process by which a single-celled embryo develops into a mature organism, also because the process by which hair, skin, blood cells, and a few internal organs are renewed. After cellular division, each of the daughter cells begin the interphase of a replacement cycle. Although the varied stages of interphase aren't usually morphologically distinguishable, each phase of the cell cycle features a distinct set of specialised biochemical processes that prepare the cell for initiation of the cellular division. The eukaryotic cell cycle consists of 4 distinct phases: G1 phase, S phase (synthesis), G2 phase (collectively referred to as interphase) and M phase (mitosis and cytokinesis). M phase is itself composed of two tightly coupled processes: mitosis, during which the cell's nucleus divides, and cytokinesis, during which the cell's cytoplasm divides forming two daughter cells. Activation of every phase depends on the right progression and completion of the previous one. Cells that have temporarily or reversibly stopped dividing are said Interphase proceeds in three stages, G1, S, and G2, followed by the cycle of mitosis and cytokinesis. The cell's nuclear DNA contents are duplicated during S phase. Mitosis is instantly followed by cytokinesis, which divides the nuclei, cytoplasm,

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organelles and cell wall into two cells containing roughly equal shares of those cellular components. Mitosis and cytokinesis together define the division of the cell into two daughter cells, genetically just like one another and to their parent cell. This accounts for about 10% of the cell cycle. Because cytokinesis usually occurs in conjunction with mitosis, "mitosis" is usually used interchangeably with "M phase". However, there are many cells where mitosis and cytokinesis occur separately, forming single cells with multiple nuclei during a process called endoreplication. This happens most notably among the fungi and slime molds, but is found in various groups. Even in animals, cytokinesis and mitosis may occur independently, as an example during certain stages of pomace fly embryonic development. Errors in mitosis may result in necrobiosis through apoptosis or cause mutations which will cause cancer. Regulation of the cell cycle involves processes crucial to the survival of a cell, including the detection and repair of genetic damage also because the prevention of uncontrolled cellular division. The molecular events that control the cell cycle are ordered and directional; that's, each process occurs during a sequential fashion and it's impossible to "reverse" the cycle. Two key classes of regulatory molecules, cyclins and cyclin-dependent kinases (CDKs), determine a cell's progress through the cell cycle. Leland H. Hartwell, R. Timothy Hunt, and Paul M. Nurse won the 2001 Nobel Prize in Physiology or Medicine for his or her discovery of those central molecules. Many of the genes encoding cyclins and CDKs are conserved among all eukaryotes, but generally more complex organisms have more elaborate cell cycle control systems that incorporate more individual components. Many of the relevant genes were first identified by studying yeast, especially baker's yeast. Genetic nomenclature in yeast dubs many of those genes cdc (for "cell division cycle") followed by an identifying number, e.g. cdc25 or cdc20. Cyclins form the regulatory subunits and CDKs the catalytic subunits of an activated heterodimer; cyclins haven't any catalytic activity and CDKs are inactive within the absence of a partner cyclin. When activated by a bound cyclin, CDKs perform a standard biochemical reaction called phosphorylation that activates or inactivates target proteins to orchestrate coordinated entry into subsequent phase of the cell cycle. Different cyclin-CDK combinations determine the downstream proteins targeted. CDKs are constitutively expressed in cells whereas cyclins are synthesised at specific stages of the cell cycle, in response to varied molecular signals. During the last years, several molecular-biology tools have been extensively used in scientific research for identifying new function of proteins and metabolites. Still, the identification of metabolites, specially which control the cell cycle is not trivial and is characterized by piecemeal progress, especially in plants. In this seminar, we will discuss the methodologies that we are using to identify and characterize metabolites that bind to the APC in the model plant Arabidopsis, and to potentially define their roles in plant development.

Biography

Nubia Barbosa Eloy has her expertise in Plant Development and Cell Cycle, especially in improving the ways to have better crop and production. During her academic life, she has published several peer reviewed papers about plant growth and development. Her main interest is to study the plant growth to better enhance crop productivity, using cutting edge techniques to achieve her goal.

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