SPECIAL FOCUS EDITORIAL

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Hypometabolism and the cell cycle

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This special issue focuses on cell cycle control as it applies to cells and organisms that can transition into states of low metabolic rate. The ability to enter a hypometabolic state such as dormancy or torpor is a critical survival strategy for many organisms. When environmental conditions are not conducive to a pattern of continuous growth and development, many organisms can strongly suppress their metabolic rate and enter a hypometabolic or even ametabolic state that allows them to effectively "wait out" environmental stress conditions (e.g., too hot or too cold temperatures, oxygen limitation, desiccation, lack of food, etc.) that could otherwise be rapidly lethal. Hypometabolism is widespread in both unicellular (bacteria, yeast, etc.) and multicellular organisms and is a fundamental part of survival strategies known by many different names, including anaerobiosis (living without oxygen), anhydrobiosis (life in a dry state), diapause/dauer (arrested development), freeze tolerance (survival with 50–70% of body water frozen as extracellular ice), estivation (aerobic dormancy triggered by water or nutrient challenge, often in hot climates) and mammalian hibernation (prolonged cold torpor in response to the thermal and nutrient challenges of winter). Net metabolic rate suppression in hypometabolic states is typically >80% and often >95% as compared with normal resting metabolism. In some cases, states that are virtually ametabolic are also achieved and allow viability to be preserved over years, decades or even centuries. Periods of hypometabolism are sometimes obligatory, such as seasonal entry into hibernation or an obligate diapause at a particular developmental stage. In other instances, entry into a hypometabolic state is an opportunistic event, occurring whenever environmental conditions are poor (e.g., lack of nutrients or oxygen). A capacity for whole-body torpor is not part of the human condition, although it could be desirable as a medical treatment or to allow prolonged space flight. However, selected cell types within our bodies are maintained in a quiescent state until they are needed (e.g., lymphocytes and hematopoietic stem cells). This ensures that organisms can draw upon reserves of these replacement cells throughout their lives.

The cycle of cell division is a fundamental characteristic of life on Earth and critical to the proliferation of cells among both unicellular and multicellular organisms. The drive to continue the progress of the cell cycle in many tissues and organs is inexorable. The molecular events of the cell cycle are ordered and directional—the cycle does not seem to be reversible. However, the cell cycle can be controlled, slowed or even stopped in response to signals including environmental cues and growth factors. The cell cycle is highly energy expensive, involving the duplication of DNA and the synthesis of many new proteins and subcellular components. Not surprisingly, then, cell cycle arrest is a well-documented response of both unicellular and multicellular organisms to environmental challenges, such as nutrient or oxygen limitation. As such, regulated and coordinated cell cycle arrest should be an integral component of hypometabolic states, contributing to energy savings by strongly suppressing or halting cell division among proliferative cell types or tissues.

This special focus in *Cell Cycle* examines the regulation of the cell cycle as it specifically relates to the phenomenon of hypometabolism. How is the cell cycle reversibly regulated when cells and organisms enter into or exit from periods of dormancy or arrested development? How is cell cycle suppression integrated with known mechanisms of metabolic rate depression? Are the regulatory principles the same or different? What is universal and what is unique about cell cycle regulation in different forms of hypometabolism? We examine cell cycle responses in multiple systems including quiescence in unicellular organisms (bacteria, yeast), arrested development (diapause in nematode larvae and fish embryos), hypometabolism induced by environmental stress (anoxia, dehydration, freezing) in ectothermic vertebrates, and seasonal hibernation in ground squirrels. We hope that readers will be intrigued.

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