

# Dynamic Cell Biology

**Abbreviation:** Dyn. Cell Biol.

**Print:** ISSN 1749-0561

**Scope and target readership:** *Dynamic Cell Biology* focuses on a dynamic approach to the study of cellular processes, which may include any of the following:

- 1) Angiogenesis;
- 2) Apoptosis, senescence and (programmed) cell death: mechanisms and roles in various human diseases (e.g. cancer, autoimmune disease, viral infection, AIDS, cardiovascular disease, neurodegenerative disorders, osteoporosis and ageing);
- 3) Cancer and metastasis (causes, control, and prevention at the cellular/tissue level);
- 4) Cell: blastomere aggregation, cell membranes, cell differentiation, chromosome replication, function and dynamics of subnuclear compartments, genetics of subcellular organelles, malignant transformation, nuclear envelope and nucleocytoplasmic interactions, nuclear transfer, structure and dynamics of chromatin, X chromosome inactivation;
- 5) Cell cycle control/regulation; cell signalling pathways;
- 6) Cellular immunology; induction, modulation and exploitation of immune response;
- 7) Cellular repair and regeneration, connective tissue, stem cells, re-generative medicine;
- 8) Cytokines and growth factors in areas as diverse as signal transduction in the study of immunology, tumorigenesis and clinical medicine;
- 9) Cytology for aetiology, diagnosis, disease management;
- 10) Immunogenetics of cell surface antigens; ontogeny and phylogeny of the immune system; immunogenetics of cell interactions; functional aspects of cell surface molecules and their natural ligands, such as cytokines, adhesion molecules and activation antigens; role of tissue antigens in immune reactions *in vitro* and *in vivo*, including experimental and clinical transplantation; and relationships between normal tissue antigens and tumor-associated antigens; genetic control of immune response, disease susceptibility and genetics, biochemistry and molecular biology of alloantigens and leukocyte differentiation. Research on molecules expressed on lymphoid cells, myeloid cells, platelets and non-lineage-restricted antigens is welcome. The immunogenetics of histocompatibility antigens in humans and experimental animals and their tissue distribution, regulation and expression in normal and malignant cells and antigens as markers for disease are of major interest; immunotherapy;
- 11) Karyology and histochemistry;
- 12) Mathematical modeling of cellular events;
- 13) Microbial and host (mammalian and insect)-cell biology, cell responses elicited by the interaction with microorganisms (prokaryotic, viral, eukaryotic);
- 14) Remodelling of tissues and tissue engineering;
- 15) Subcellular and supracellular biology in neurobiology, neuroendocrinology, endocrinology, reproductive biology, skeletal and immune systems: integrative actions of gene products and their impact on the formation of tissue structure and function;
- 16) Toxicity and toxic response of cellular systems (cytotoxicity, mutagenicity, carcinogenicity, teratogenicity).

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**Cover photos:** (A, B) Dual immunolabeling for the phosphorylated c-Myc (a: red fluorescence) and fibrillarin (b: green fluorescence) in untreated control HeLa cells; (C) Merged image showing the co-localization of phosphorylated c-Myc and fibrillarin in the nucleoli of the control HeLa cells; (D) early apoptotic HeLa cell in an etoposide-treated culture demonstrating that fibrillarin first moves into the cytoplasm, where-as phosphorylated c-Myc does not locate in the nucleolus anymore, but is still present in the nucleus; (E) late karyorrhexic apoptotic HeLa cell in an etoposide-treated culture showing that fibrillarin locates in peripheral blebs, whereas phosphorylated c-Myc still aggregates in the center of the cytoplasm. Bar = 10 µm. More details in Biggiogera *et al.*, pp 65-71.

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Printed in Japan on acid-free paper.

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**Cécile Brocard, Andreas Hartig (Austria)** Peroxins: A Proliferation Romance amongst Supposition and Disposition (pp 1-11)

#### ABSTRACT

**Special Feature:** Since the discovery of peroxisomes over half a century ago, the fundamental mechanism of their biogenesis has remained a matter of debate. The outcome of recent investigations focusing on macromolecular associations coupled with peroxisome formation offers new insight for understanding this process. Peroxisome biogenesis includes the induction and import of membrane and matrix proteins, as well as proliferation and inheritance. When they become superfluous, peroxisomes are rapidly and selectively degraded via pexophagy. Many of the crucial components have been identified in genetic screens. The yeast *Saccharomyces cerevisiae* presents the advantage of being able to grow under conditions in which peroxisomes do not seem necessary such as fermentative growth on glucose media. Physiologically, the survival of a few peroxisomes possibly enables the cell to rapidly respond to new environmental conditions that require the full peroxisomal function. Accordingly, the expression of genes encoding various peroxisomal proteins is repressed by glucose and induced by the presence of fatty acids in the culture medium. Peroxisome biogenesis is controlled by a set of proteins, the peroxins. Most peroxins were originally identified in yeast species. This review aims to discuss the involvement of a range of peroxins in the process of proliferation which is essential to adapt the number of peroxisomes to the cellular needs. Among the known participants, PEX11 is the most prominent and best-studied and its homologues PEX25 and PEX27 have been involved, as well. We also consider the role of the recently identified yeast peroxins namely, PEX28, PEX29, PEX30, PEX31 and PEX32.

**Nella L. Kiyachko (Russia)** Actin Dynamics in the Plant Cell (pp 12-19)

#### ABSTRACT

**Invited Review:** Dynamic rearrangements of the actin cytoskeleton are one of the fastest responses of the plant cell to environmental signals and an important part of developmental programs. The turnover rate of actin microfilaments and supramolecular structures is several orders higher than that of actin proteins and mRNAs. The high rate of actin polymerization in the cell is provided by specific nucleating machineries, primarily by the Arp2/3 complex and formins. A wide set of actin-binding proteins capping, severing, cross-linking, and bundling actin filaments are involved in actin polymerization and depolymerization, accelerating these processes or protecting microfilaments against breakdown. The actin cytoskeleton is not only a target for various signals but also an effector for diverse physiological processes. Recently, some novel players in signaling to the plant actin cytoskeleton have been revealed, the WAVE complex and RIC proteins among them. The deciphering of signaling pathways from the actin cytoskeleton is only at the start. In this review, not all the relevant literature but mainly new developments in the field is summarized.

**Ulrich Salzer, Mario Mairhofer, Rainer Prohaska (Austria)** Stomatin: A New Paradigm of Membrane Organization Emerges (pp 20-33)

#### ABSTRACT

**Invited Review:** Stomatin, originally identified as a major protein of the human erythrocyte membrane, is widely expressed in various tissues. Orthologues are found in vertebrates, invertebrates, plants, and microorganisms. Related proteins exhibit a common core structure, termed the prohibitin (PHB) domain, with varying extensions. Stomatin has an unusual topology, similar to caveolin-1, with a hydrophobic domain embedded at the cytoplasmic side of the membrane. Additional anchoring is provided by palmitoylation and the membrane affinity of the PHB domain. Stomatin associates with cholesterol-rich microdomains (lipid rafts), forms oligomers, and thereby displays a scaffolding function by generating large protein-lipid complexes. It regulates the activity of various membrane proteins by reversibly recruiting them to lipid rafts. This mechanism of regulation has been shown for GLUT-1 and may also apply for ion channels. Stomatin is located at the plasma membrane, particularly in microvilli, in endocytic and exocytic vesicles, and cytoplasmic granules. Stomatin-carrying endosomes are highly dynamic and interact with lipid droplets suggesting a role in intracellular lipid transport. This subcellular distribution and the caveolin-like protein structure suggest important membrane organizing functions for stomatin. A general picture emerges now that cell membranes contain cholesterol-rich domains that are generated and regulated by scaffolding proteins like caveolins, stomatins, and flotillin/reggie proteins.

**Keith P. Niven, Ben R. Kiefel, Peter L. Beech (Australia)** Recent Advances in Chloroplast and Mitochondrial Division (pp 34-41)

#### **ABSTRACT**

**Invited Mini-Review:** The division of endosymbiotic organelles (mitochondria and chloroplasts, which are derived from the ancient engulfment of free-living bacteria) are complex processes requiring proteins derived from the host and symbiont. The last 12 months have seen great leaps forward in our understanding of these processes including a more detailed understanding of the components required for the recruitment of dynamin-like proteins, the elucidation of the division components applying the constrictive force required for organelle division, the discovery of an Fzo-like protein in chloroplasts and new evidence questioning the evolutionary origins of the dynamins. Here we discuss recent findings in light of our current understanding of the chloroplast and mitochondrial division processes.

**I. Bernardini, E. Bartocchini, M. Viola Magni, E. Albi (Italy)** Nuclear Lipids and Cell Fate (pp 42-47)

#### **ABSTRACT**

**Invited Mini-Review:** Lipids are known not only as components of cell membranes but also as part of the nuclear fraction. In the nucleus lipids are present with a specific composition and metabolism and their behaviour, in different physiological and pathological conditions, is completely independent from that of the cell membrane. The nuclear lipid fraction is constituted by glycerolphospholipids, sphingolipid and cholesterol which have an active metabolism thanks to the presence of lipid enzymes responsible for their synthesis and catabolism. Nuclear lipid metabolites are in equilibrium when the cells are resting whereas, when the cells are submitted to various stimuli, they interact in different ways in relation to cell type and localization: nuclear membrane, nuclear matrix and chromatin, playing different structural and/or functional roles. The focus of this mini-review is to highlight the implications of nuclear lipid metabolism on the cell fate regulation when a proliferative or apoptotic stimulus is applied.

**Hans Rotheneder, Ludwig Schwarzmayr, Peter Andorfer, Amsatou Sarr (Austria)** Transcription Factors of the E2F Family and DNA Damage Control (pp 48-59)

#### **ABSTRACT**

**Invited Review:** The ability to sense and respond to genetic lesions is pivotal to maintain the integrity of the genome. This response is composed of cell cycle checkpoints and DNA repair mechanisms that serve to ensure proper replication of the genome prior to cell division. E2F is a family of mostly heterodimeric transcription factors that can be divided into subgroups with opposing activities. E2F factors are intrinsically tied to proliferation and best known for their ability to regulate the timely expression of genes required for replication and cell cycle progression. However, recent studies suggest that E2F can also regulate transcription of genes involved in other biological processes. These include DNA damage response, DNA repair and apoptosis, mitosis and mitotic checkpoints, and differentiation. E2F activity is regulated in a cell cycle-dependent manner, primarily through its interaction with pocket proteins like the retinoblastoma tumor suppressor protein. Pocket proteins themselves are regulated through reversible phosphorylation by cyclin dependent kinases. Among the E2F proteins, the E2F1 transcription factor is of special interest because of its contrasting behavior under cellular stress conditions, which sets it apart from all other members of the family. E2F1 may act as an oncogene or as a tumor suppressor, probably depending on the genetic background and the level of expression. Upon DNA damage, E2F1 becomes the target of damage-induced kinases, which results in dramatic alteration of its stability, interaction partners, and target genes. Here we review the current understanding of the role of E2F proteins with a focus on the regulation and activity of E2F1 during DNA damage.

**Antonio Villalobo (Spain)** Enhanced Cell Proliferation Induced by Nitric Oxide (pp 60-64)

#### **ABSTRACT**

**Invited Mini-Review:** Nitric oxide (NO<sup>•</sup>) regulates multiple physiological functions including cell proliferation. The regulatory action of NO<sup>•</sup> on cell proliferation is exerted in a bimodal mode, enhancing and inhibiting the progression of the proliferative process depending on the actual concentration of NO<sup>•</sup> encountered by the cell. Although not all details are understood, the cytostatic action of NO<sup>•</sup>, when attained at high concentrations, has been studied in more depth. However, the stimulatory action of minute quantities of NO<sup>•</sup> on cell proliferation has received less attention, although its potential physiological importance is already apparent. Knowledge on the molecular mechanisms and signalling events responsible for the enhancement of cell

proliferation induced by NO<sup>•</sup> are still very limited, although new findings have started to uncover some of their details. In this review I shall describe the progress done in the last few years on this respect, and explore the physiological relevance of the enhancement exerted by NO<sup>•</sup> on the proliferation of cells relevant for the regulation of normal organismal growth and development. The action of NO<sup>•</sup> stimulating the proliferation of tumour cells has become also an important pathophysiological issue and it will be outlined. The studies concerning the action of NO<sup>•</sup> on cancerous cells could be significant to better understand the molecular mechanisms underlying this pathological process and its possible therapeutic control.

**Marco Biggioera, Barbara Cisterna, Maria Grazia Bottone, Cristiana Soldani, Carlo Pellicciari (Italy)** Nuclear RNP and Nucleolar-Associated Proteins during Apoptosis: a Politically Correct Form of Segregation? (pp 65-71)

#### ABSTRACT

**Invited Mini-Review:** During apoptosis, a major rearrangement of nuclear RNP-containing structures takes place, in parallel with chromatin changes. In the interchromatin space, nucleoplasmic RNP constituents (perichromatin fibrils and granules, and interchromatin granules) as well as the nucleolar components aggregate into heterogeneous clusters we called HERDS (for Heterogeneous Ectopic RNP-Derived Structures). In late apoptosis, these aggregates are extruded from the nucleus and released at the cell surface within apoptotic bodies; we also confirm that during apoptosis nucleolar proteins (i.e phosphorylated c-Myc, Ki-67, fibrillarin) already segregate in the nuclei and remain separated in the cytoplasm. Immunocytochemical evidence from light and electron microscopy also demonstrate that the sub-cellular particles in the apoptotic bodies may be heterogeneous in size and content, and may still include immunodetectable nuclear proteins and nucleic acids. Remarkably, the extrusion from the nucleus of a wide and heterogeneous spectrum of proteins which survive in a partially degraded (or even in an undegraded) form during the late steps of apoptosis legitimizes the growing interest toward those *novel* and ectopic molecular complexes which may play a role in the etiology of autoimmune diseases. In this paper we also confirm that the formation of HERDS is a more general phenomenon which may be triggered by transcriptional arrest.

**Ying Chang, Jianjun Guo, Yajun Gao, Jin-Gui Chen (Canada)** Modulation of Root Cell Division by the Heterotrimeric G-proteins in *Arabidopsis* (pp 72-77)

#### ABSTRACT

**Invited Mini-Review:** The root is an ideal system to study cell division *in situ*. The root system originates from a root primordium that is formed during embryogenesis. Stem cells of the root apical meristem (RAM) essentially give rise to all cell types in the primary root. Therefore, the growth of the primary root is in part a consequence of cell cycle maintenance in the RAM. Lateral roots are initiated from the pericycle cells located adjacent to protoxylem poles at some distance from the RAM. The formation of lateral roots requires meristem formation by pericycle founder cells, a process that involves re-entry or activation of the cell cycle. The cell division in the RAM and the formation of lateral roots are regulated by both intrinsic and environmental stimuli. Substantial evidence supports the notion that cell division in the RAM and the activation of pericycle founder cells use distinctive mechanisms. Recent research indicates that the heterotrimeric G-protein subunits have differential roles in the modulation of cell cycle maintenance in the RAM and in the activation of pericycle cells during lateral root formation. Future studies are expected to lead to the determination of the molecular mechanism through which the heterotrimeric G-protein complex executes its modulatory role in root cell division.