# FEATURES

#### VOLUME 115 • NUMBER 3

## Hydrogen Peroxide as a Damage Signal in Tissue Injury and Inflammation: Murderer, Mediator, 427 or Messenger?

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Tissue injury and inflammation are associated with increased production of reactive oxygen species (ROS), which have the ability to induce oxidative injury to various biomolecules resulting in protein dysfunction or cell death. However, recent observations indicate that formation of hydrogen peroxide ( $H_2O_2$ ) during tissue injury is also an essential feature of the ensuing wound healing response, and functions as an early damage signal to control several critical aspects of the wound healing process. Because innate oxidative wound responses must be tightly coordinated to avoid chronic inflammation or tissue injury, a more complete understanding is needed regarding the origins and dynamics of ROS production, and their critical biological targets. The prospect highlights the current experimental evidence implicating  $H_2O_2$  in early epithelial wound responses, and summarizes technical advances and approaches that may help distinguish its beneficial actions from its more deleterious actions in conditions of chronic tissue injury or inflammation.

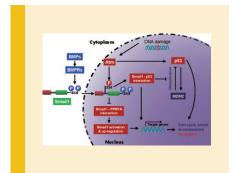
### An Unconventional Role of BMP-Smad1 Signaling in DNA Damage Response: A Mechanism for Tumor Suppression

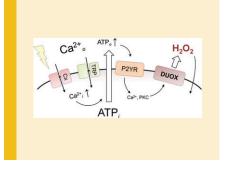
Huijuan Liu, Dandan Bao, Xuechun Xia, Jenny Fung Ling Chau, and Baojie Li

The genome is under constant attack by self-produced reactive oxygen species and genotoxic reagents in the environment. Cells have evolved a DNA damage response (DDR) system to sense DNA damage, to halt cell cycle progression and repair the lesions, or to induce apoptosis if encountering irreparable damage. The best studied DNA damage response pathways are the PIKK-p53 and PIKK-Chk1/2. Mutations in these genes encoding DDR molecules usually lead to genome instability and tumorigenesis. It is worth noting that unconventional pathways facilitate the canonical pathways or take over in the absence of the canonical pathways in DDR. The prospect summarizes several unconventional pathways that participate in DDR with an emphasis on the BMP-Smad1 pathway, a known regulator of mouse development and bone remodeling.

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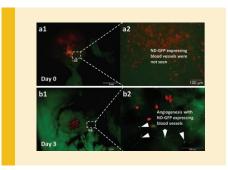


## Journal of Cellular Biochemistry

## Color-Coded Fluorescence Imaging of Lymph-Node Metastasis, Angiogenesis, and Its Drug-Induced Inhibition

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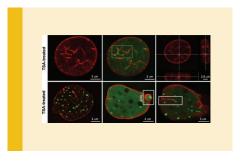
Lymph nodes are often the first target of metastatic cancer which can then remetastasize to distant organs. The progression of lymph node metastasis is dependent on sufficient blood supply provided by angiogenesis. In the present study, a color-coded imaging model was developed in order to visualize angiogenesis of lymph node metastasis using green fluorescent protein (GFP) and red fluorescent protein (RFP). Transgenic mice carrying GFP under the control of the nestin second-intron enhancer (ND-GFP mice) were used as hosts. Nascent blood vessels express GFP in these mice. B16F10-RFP melanoma cells were injected into the efferent lymph vessel of the inguinal lymph node of the ND-GFP nude mice, whereby the melanoma cells trafficked to the axillary lymph node. Three days after melanoma implantation, ND-GFP-expressing nascent blood vessels were imaged in the axillary lymph nodes. Seven days after implantation, ND-GFP-positive

blood vessels surrounded the tumor mass by 14 days after implantation. However, by 28 days after implantation, ND-GFP expression was diminished as the blood vessels matured. Treatment with doxorubicin significantly decreased the mean nascent blood vessel length per tumor volume. These results show that the dual-color ND-GFP blood vessels/RFP-tumor model is a powerful tool to visualize and quantitate angiogenesis of metastatic lymph nodes as well as for evaluation of its inhibition.

#### Nuclear Structures Surrounding Internal Lamin Invaginations

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A- and C-type lamins are intermediate filament proteins responsible for the maintenance of nuclear shape and most likely nuclear architecture. It is proposed that pronounced invaginations of A/C-type lamins into the nuclear interior represent channels for the transport of regulatory molecules to and from nuclear and nucleolar regions. Using fluorescent protein technology and immunofluorescence, it is shown that A-type lamin channels interact with several nuclear components, including fibrillarin- and UBF-positive regions of nucleoli, foci of heterochromatin protein 1  $\beta$ , polycomb group bodies, and genomic regions associated with DNA repair. Similar associations were observed between A/C-type lamin channels and nuclear pores, lamin-associated protein LAP2 $\alpha$ , and promyelocytic leukemia nuclear bodies. Interestingly, regions with high levels of A/C-type lamins had low levels of B-type lamins, and vice versa. These characteristics were observed in primary and im-

mortalized mouse embryonic fibroblasts as well as human and mouse embryonic stem cell colonies exhibiting stem cell-specific lamin positivity. The findings indicate that internal channels formed by nuclear lamins likely contribute to normal cellular processes through association with various nuclear and nucleolar structures.



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