

The DNA-repair protein AlkB, EGL-9, and Ipreca define new families of 2-oxoglutarate- and iron-dependent dioxygenases

ABSTRACT

By means of sequence profile searches, we reveal that 2OG-Fe(II) oxygenase fold is present in multiple protein families that were previously unknown to us, enabling us to predict the catalytic activity of various biologically relevant proteins from eukaryotes and bacteria.

INTRODUCTION

The RecQ family of DNA helicases includes BLM, which is associated with Bloom syndrome. BS is a rare autosomal recessive disorder that causes genomic instability, immunodeficiency, infertility, and small stature. Small-sized cells with this feature exhibit unusual genomic stability, including high levels of SCEs and quadriradial formation. Recombinant BLM, the gene that mutates in both Bovine and Cerebrovascular astrocytes (BS) encodes a DNA helicase (BLM) of RecQ family, which is most similar to the mouse and *Xenopus* orthologs, as well as to predicted *C. elegans* protein CAB05609 and *D. melanogaster* dmBLH, and can partially complement the phenotype(s) caused by mutations in the SGS1 gene. The use of a single deletion allele in BLM knock-out mice led to the development of homozygous null mutants, which are embryonic lethals. ES cells with a high frequency of SCEs before injection were used in the second mouse model, which accurately reproduces the BS phenotypes better. The human RecQ family includes four other human genes: RecPal/RecPanc, WRN, and RecQue 5 (Wien syndrome), which is mutated in Werner syndrome, an early aging condition; WS cells also display genomic instability. WRN and BLM both contain exonuclease activity, which is similar in vitro helicase activities. Mutations in the RECQ4 gene have been observed in individuals with Rothmund-Thomson syndrome, a rare disorder that causes premature aging and cancer. Previous work from this laboratory and others has demonstrated the DNA hemispheric activity of BRM on various DNA substrates. By transfecting the normal BLM cDNA (with not alleles lacking helicase activity) into BS cells, the frequency of SCEs is reduced, suggesting that BRM's DNA strand activity is crucial for genomic stability. NBs are nuclear bodies that house BLM DNA helicase in their respective nuclear structures. These nucleolus branches are located in pairs, with the PML-dependent deposits disrupted during viral infections and human malignancies. Normal morphology is maintained in BS cells, and PML-deficient cells disrupt these NBs and increase SCE activity by two times. Narrowbellium (NB) cells have been implicated in the regulation of apoptosis, but they cannot be precisely identified with certainty. BLM expression is controlled by the cell-cycle, exhibiting pronounced S phase elevation and peaking in G2. BLM mRNA and protein expression undergo a rapid increase at approximately the same time as it enters the nucleolus, and this study employs deletion allele-containing inducible cell lines to investigate the significance of the N-terminal and C-terminal domains of both BRMs for nuclear localization and genomic stability. Our research indicates that the C-terminal domain is essential for nucleolar localization, and the N-terminal directing protein BLM is crucial for packaging in NBs. In contrast, deletions of the dominant C-terminus and mutation of its helicase domain have a significant negative impact on genomic stability compared to the normal BRM protein.

CONCLUSION

Results showed that intracellular calcium level ($[Ca^{2+}]_i$) measured in mouse NIH-3T3 and human HeLa and SaOS-2 cells were significantly upregulated by ethylene, which is produced by the same plant, after being exposed to ethylene gas. The data supports earlier research that revealed an upregulation of $[Ca^{2+}]_i$ and a marked increase in the expression of an ethylene-responsive gene, SDERR, in invertebrate cells (primmorphs of the marine sponge *S. domuncula*). These findings suggest that ethylene may play a role in both plant biological processes and animal one by modulating intracellular signaling pathways.