

# FEATURES

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## Risks and Benefits of Bisphosphonate Therapies

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Bisphosphonates are the mainstay of osteoporosis treatment but also play a fundamental role in treating other bone diseases such as Osteogenesis Imperfecta, Pagets' disease, and in the prevention of adverse skeletal effects in certain cancers such as prostate cancer or multiple myeloma. In the last decades, the refinement of bisphosphonates and an increase in the number of new bisphosphonates commercialized has altered the clinical management of these diseases. Despite differences between randomized controlled trials and observational studies, overall all bisphosphonates licensed have proven to reduce the risk of fracture through the inhibition of bone resorption. Other beneficial effects include pain reduction in bone metastasis and potentially a decrease in mortality. However, the chronic nature of most of these disorders implies long-term treatments, which can be associated with long-term adverse effects. Some of the adverse effects identified include an increased risk of atypical femur fractures, osteonecrosis of the jaw, gastrointestinal side effects, or atrial fibrillation. The harm/benefit thinking and the constant update regarding these medications are vital in the day-to-day decision-making in clinical practices. The aims of this review are to compile the basic characteristics of these drugs and outline the most important benefits and side effects and provide a clinical context as well as a research agenda to fill the gaps in our knowledge.

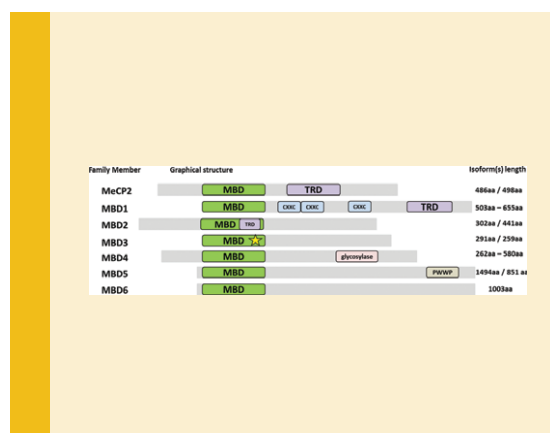
## Methyl-CpG-Binding Protein (MBD) Family: Epigenomic Read-Outs Functions and Roles in Tumorigenesis and Psychiatric Diseases

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Epigenetics is the study of the heritable changes on gene expression that are responsible for the regulation of development and that have an impact on several diseases. However, it is of equal importance to understand how epigenetic machinery works. DNA methylation is the most studied epigenetic mark and is generally associated with the regulation of gene expression through the repression of promoter activity and by affecting genome stability. Therefore, the ability of the cell to interpret correct methylation marks and/or the correct interpretation of methylation plays a role in many diseases. The major family of proteins that bind methylated DNA is the methyl-CpG binding domain proteins, or the MBDs. Here, we discuss the structure that makes these proteins a family, the main functions and interactions of all protein family members and their role in human disease such as psychiatric disorders and cancer.



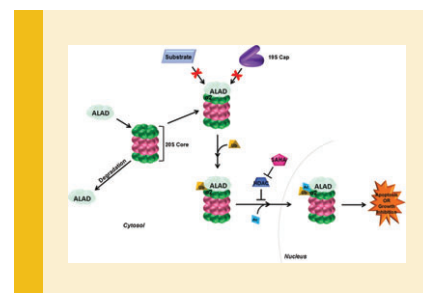
**Involvement of ALAD-20S Proteasome Complexes in Ubiquitination and Acetylation of Proteasomal  $\alpha 2$  Subunits**

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The ubiquitin-proteasome pathway has gained attention as a potential chemotherapeutic target, owing to its importance in the maintenance of protein homeostasis and the observation that cancer cells are more dependent on this pathway than normal cells. Additionally, inhibition of histone deacetylases (HDACs) by their inhibitors like Vorinostat (SAHA) has also proven a useful strategy in cancer therapy and the concomitant use of proteasome and HDAC inhibitors has been shown to be superior to either treatment alone. It has also been reported that delta-aminolevulinic acid dehydratase (ALAD) is a proteasome-associated protein, and may function as an endogenous proteasome inhibitor. While the role of ALAD in the heme biosynthetic pathway is well characterized, little is known about its interaction with, and the mechanism by which it inhibits, the proteasome. In the present study, this ALAD-proteasome complex was further characterized in cultured prostate cancer cells and the effects of SAHA treatment on the regulation of ALAD were investigated.



**Regulation of Adipose Tissue Stem Cells Angiogenic Potential by Tumor Necrosis Factor-Alpha**

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Tissue regeneration requires coordinated “teamwork” of growth factors, proteases, progenitor and immune cells producing inflammatory cytokines. Mesenchymal stem cells (MSC) might play a pivotal role by substituting cells or by secretion of growth factors or cytokines, and attraction of progenitor and inflammatory cells, which participate in initial stages of tissue repair. Due to obvious impact of inflammation on regeneration it seems promising to explore whether inflammatory factors could influence proangiogenic abilities of MSC. In this study we investigated effects of TNF- $\alpha$  on activity of adipose-derived stem cells (ADSC). We found that treatment with TNF- $\alpha$  enhances ADSC proliferation, F-actin microfilament assembly, increases cell motility and migration through extracellular matrix.

