High Mobility Group (HMG) Proteins

Background

High mobility group (HMG) proteins are ubiquitous nuclear proteins that regulate and facilitate various DNA-related activities such as transcription, replication, recombination and repair. HMGs bind to DNA and chromatin and act as “architectural elements” that induce both short- and long-range changes in the structure of their binding sites. They affect the activities of various regulatory molecules, including hormone receptors, p53, the RAG proteins involved in V(D)J recombination, the homeotic protein HOXD9 of HIV integrase, and several transcription factors. The functional motifs of the ubiquitous HMG proteins are widespread and found in the DNA binding domains of numerous regulatory proteins.

HMG proteins may play a significant role in human disorders. Disruptions and rearrangements in the genes coding for some of the HMG proteins are associated with the etiology of common benign tumors such as uterine leiomyomas, endometrial polyps, and lipomas. HMG-1 and HMG-2 proteins are implicated in the mechanism of action of the anti-cancer drug cisplatinum. In addition, antibodies to HMG proteins are found in patients suffering from autoimmune diseases.

Thus, by modifying the architecture of DNA and chromatin the HMG proteins may contribute to the regulation of various processes that ultimately affect the cellular phenotype. Studies on the structure and function of these proteins may provide insights into the molecular mechanisms underlying the etiology of certain diseases.

Nomenclature

The high mobility group (HMG) proteins were originally isolated from mammalian cells and arbitrarily classed as a specific type of nonhistones based on the observation that these proteins are present in all mammalian and many vertebrate cells, that they share certain physical properties, and that they are associated with isolated chromatin. They were originally subdivided into 3 groups: HMG-1/-2, HMG-14/-17 and HMG-I/Y. These proteins are considered the canonical HMG proteins. Subsequent studies have revealed that the functional motifs characteristic of each of the canonical HMG proteins are widespread among nuclear proteins. Proteins containing any of the functional motifs of the canonical HMG proteins are known as HMG-motif proteins. In fact, the canonical HMG proteins can be considered to be a subclass of the HMG-motif proteins. The HMG-motif proteins are now subdivided into 3 superfamilies:

1. HMGB (formerly HMG-1/-2)
2. HMGN (formerly HMG-14/-17)
3. HMG A (formerly HMG-I/Y/C)

Each HMG family has a characteristic functional sequence motif. The functional motif of the HMGB family is named “HMG-box”, that of the HMGN family is named “nucleosomal binding domain”, and that of the HMG A family is named “AT-hook”. Proteins containing any of these functional motifs embedded in their sequence are known as HMG-motif proteins. The interrelationship between the various HMG proteins is diagrammed below.

HMG Chromosomal Proteins Homepage

For more detailed information and a list of HMG proteins, visit the HMG Chromosomal Proteins Homepage.

References

