A demethylase is an enzyme that catalyzes the removal of methyl groups from various substrates, including proteins, nucleic acids (DNA and RNA), and small molecules. In the context of epigenetics and gene regulation, the term “demethylase” is often used to refer to enzymes that remove methyl groups from histone proteins, which are involved in chromatin structure and gene expression control.

There are two primary classes of histone demethylases:

Lysine-Specific Demethylases (KDMs): These enzymes remove methyl groups from specific lysine residues on histone proteins. Each KDM typically targets a specific lysine residue with a particular number of methyl groups (mono-, di-, or trimethylated) and can either be classified as amine oxidase-dependent (such as LSD1/KDM1) or Jumonji C domain-containing (such as JMJD2 and JMJD3).

Arginine-Specific Demethylases: These enzymes remove methyl groups from arginine residues on histones.

The action of histone demethylases is crucial for the regulation of gene expression. Methylation of histone proteins can either activate or repress gene transcription, depending on the specific histone residue and the degree of methylation. Demethylases reverse these modifications, allowing for changes in chromatin structure and gene activation or repression.

Histone demethylases play a significant role in various cellular processes, including development, differentiation, DNA repair, and disease development. Dysregulation of these enzymes can be associated with various diseases, including cancer. Research into histone demethylases continues to provide insights into their functions and potential therapeutic implications.