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Abstract:

Metnase is a novel bifunctional protein that contains a SET domain and a transposase domain. Metnase contains sequence-specific DNA binding activity and sequence non-specific DNA cleavage activity, as well as enhances genomic integration of exogenous DNA. Although Metnase can bind specifically to DNA sequences containing a core Terminal Inverted Repeat sequence, this does not explain how the protein could function at sites of DNA damage. Through immunoprecipitation and gel shift assays, I have identified the Pso4 protein as a binding partner of Metnase both in vitro and in vivo. Pso4 is essential for cell survival in yeast, and cells containing a mutation in Pso4 show increased sensitivity to DNA cross-linking agents. In addition, the protein has sequence-independent DNA binding activity, favoring double-stranded DNA over single-stranded DNA. I demonstrated that the two proteins form a 1:1 stochiometric complex, and once formed, Metnase can localize to DNA damage foci as shown by knockdown of Pso4 protein using in vivo immunofluorescence. In conclusion, this shows that Metnase plays an indispensable role in DNA end joining, possibly through its cleavage activity and association with DNA Ligase IV.

Description:

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