

PRESENTAZIONI ORALI

Genome wide mapping of the MBF-1 binding sites during embryogenesis of the sea urchin reveals it is a chromatin organizer

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The Zinc-finger MBF1 factor is a transcription activator involved in the expression of the early histone genes during development of the sea urchin embryo (1). The DNA-binding domain of MBF1 shares high sequence similarity with that of the CTCF chromatin organizer but, unexpectedly, extensive *in silico* analysis failed to identify the sea urchin CTCF ortholog (2, 3). This led us to speculate that MBF1 could have co-opted the function of CTCF during evolution of the echinoderms. To support this hypothesis, we performed the genome-wide MBF1-binding sites mapping in the *P. lividus* genome, by chromatin immunoprecipitation coupled to next generation sequencing (ChIP-Seq). We observed that MBF1 binding motifs are spread across the genome, with a CCCTC core sequence showing perfect conservation with the mammalian CTCF binding element. In particular, MBF1 binds to the promoter regions of hundreds of target genes. Among others, we confirmed the specific interaction with the promoters of histone and *Hox* genes, and observed the full evolutionary conservation of these binding sites in *P. lividus* and *S. purpuratus* species. Next, to appraise globally the functional meaning of binding events we analyzed the MBF1 occupancy in chromatin samples derived from embryos exposed to compounds, such as Lithium and Zinc, that impair axial patterning. Comparison with controls revealed differential MBF1 recruitment on selected genes reflecting differentially regulated mechanisms in treated embryos. The molecular pathways impacted by Li and Zn include cell signaling, gene transcription, DNA repair, and chromatin condensation. Collectively, our observations highlight the DNA binding potency of MBF1, strongly suggesting that it could act both as a transcription factor of its target genes and a general chromatin organizer.

[1] Cavalieri, V et al. (2009) *Nucleic Acid Res.*, **37**,7407-15.

[2] Heger, P et al. (2012) *PNAS*, **109**, 17507-12.

[3] Cavalieri, V et al. (2013) *Plos Genetics*, **9**, e1003847.

NiII and ZnII Schiff base complexes: B-DNA vs. G4-DNA binding

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Last decades discoveries about implications of DNA polymorphism in cancerous events have turned on the interest of researchers about targeting non-canonical DNA structures. Among them G-quadruplexes (G4), arising from guanine-rich regions of DNA in which tetrads of guanines are linked by Hoogsteen hydrogen bonds, have been found to naturally occur in human telomeric regions where they inhibit reverse transcriptase activity of telomerase.

Figure 1. UV-Vis spectra of the reported NiII complex in presence of increasing amounts of telomeric quadruplex (left); a representative snapshot taken from the molecular dynamics simulation showing the interaction between NiII complex and telomeric quadruplex (right).

