Hmgn proteins

- Bind as dimers to nucleosomes
- Regulate the deposition of histone modifications
- Compete with linker histones
- Interact with several transcription factors.

Summary: Hmgn1 and Hmgn2 are ubiquitously highly expressed in embryonic tissue, and are progressively downregulated during embryogenesis. Using RNAi, we have shown that Hmgn proteins are essential for the expression of key pluripotency genes, including Oct4 and Nanog, in embryonal carcinoma cells. CHIP experiments show that levels of H3K4me3 at the promoters of Oct4 and Nanog are decreased in Hmgn2 knockdown cells, whereas levels of H3K27me3 are increased. This provides a molecular basis for the observations that an Hmgn2 knockout is embryonic lethal, and that manipulating the Hmgn content of early Xenopus embryos causes major developmental defects.

We have also shown that Hmgn proteins are very highly expressed in neural stem cells, both during embryogenesis and in the adult mouse brain. We studied the effects of Hmgn knockdown on the neuronal differentiation of embryonal carcinoma cells in vitro. The expression levels of various neural stem cell and neuronal genes were altered following Hmgn knockdown, showing that Hmgn proteins are important for accurate neuronal differentiation and function.

siRNA knockdown of Hmgn1 or Hmgn2 reduces the expression of pluripotency markers in pluripotent embryonal carcinoma cells.

PCR array analyses reveal that several markers of early differentiation are upregulated in Hmgn knockdown EC cells. The expression of several genes required for ES self renewal and pluripotency is also disrupted.

Upregulated genes in Hmgn knockdown cells

- Oct4
- Sox2
- Nanog
- NSE
- NMDAR
- Nse
- Glyt1a
- Glyt2
- Zfp521
- Nse
- NMDA R2

Downregulated genes in Hmgn knockdown cells

- Hmgn1
- Hmgn2
- Oct4
- Sox2
- Nanog
- NSE
- NMDAR
- Nse
- Glyt1a
- Glyt2
- Zfp521
- Nse
- NMDAR

Hmgn2 is expressed in neural progenitor cells during embryogenesis

Hmgn2 levels increase during neural differentiation of EC cells

Expression of several neuronal genes is significantly altered in day 3 immature neuronal cells following Hmgn1 and/or Hmgn2 knockdown.

Hmgn proteins are enriched across the Oct4 and Nanog gene loci

CHIP-seq reveals peaks of Hmgn2 and H3 upstream of Nanog

Knockdown of Hmgn2 reduces H3K4me3 on Oct4 and Nanog

Knockdown of Hmgn2 increases H3K27me3 on Oct4 and Nanog

Retinoic acid-induced differentiation of EC cells down the neuronal lineage.

Pluripotency markers Oct4, Sox2 and Nanog are repressed during differentiation.

- Induction of neuronal markers Map2, NF-160, nestin, NSE and NMDAR-2 is observed from day 3.
- Induction of glial marker GFAP from day 9.