

## Poster H-73

### Unusually Large Conserved Syntenic Blocks at the Vertebrate Hox loci are associated with Conserved Regulatory Elements Within and Outside Hox clusters



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**Short Abstract:** By comparative analysis of human, mouse and fugu Hox loci we have uncovered unusually large evolutionary conserved syntenic blocks (up to 5.2 Mb) at these loci. Conserved putative regulatory elements spread over large regions are likely to be the evolutionary constraint that has maintained the exceptionally long syntenic blocks.

#### Long Abstract:

Hox genes code for homeodomain-containing transcription factors that determine the anterior-posterior patterning of tissues along the body axis of animals. In vertebrates, Hox genes are organized into tight clusters containing up to 14 paralogs. A remarkable feature of these clusters is that the positions of genes in the cluster are colinear with their 'spatial' and 'temporal' expression pattern along the anterior-posterior axis of the embryo. The molecular mechanisms underlying this orchestrated expression patterns of Hox genes and the selective pressure that has maintained the clustering and colinear organization of vertebrate Hox genes are still not well understood. In order to identify conserved regulatory elements within and outside Hox clusters that may be responsible for conservation of vertebrate Hox clusters, we have obtained contiguous sequences from the seven Hox loci in fugu and compared them with their orthologous sequences from human and mouse. Our analysis has uncovered unusually large syntenic blocks that have been conserved at the Hox loci over 450 Myr divergent evolutions of teleost fishes and mammals. This in contrast to the large number of short syntenic blocks comprising 3-6 genes identified in the fugu and human genomes (Aparicio et al., et al. 2002. Science 297, 1301-1310). The largest conserved syntenic blocks are found at the human and mouse HoxA and HoxD loci, containing 21 and 19 genes across 5.2 Mb and 4 Mb respectively. The corresponding regions in fugu are 19 and 12-fold smaller. The syntenic blocks contain a large number of conserved non-coding sequences (CNS) within as well as outside Hox gene clusters. These CNS include previously characterized as well as a large number of novel putative regulatory elements. The elements flanking the HoxD gene cluster overlap and extend beyond the previously characterized 5' global enhancer region of HoxD locus (Spitz, F., Gonzalez, F. & Duboule, D. 2003. Cell 113, 405-417). The clusters of conserved elements identified in the 3' region of the HoxD locus, and in the 5' and 3' regions of HoxA locus may represent hitherto uncharacterized global enhancers that are involved in the coordinated regulation of Hox clusters. These global enhancers, spread across large regions on either side of Hox gene clusters, are likely to be the major evolutionary constraint that has maintained the exceptionally long syntenic blocks

at the vertebrate Hox loci.