 

# Conserved KRAB protein domain identified upstream from the zinc finger region of Kox 8

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The human genome encodes several hundred zinc finger proteins (1). Recently, thirty Kox cDNAs encoding zinc finger motifs were isolated from human T cell lines and characterized (2). Twenty-seven Kox genes have been mapped to nine different chromosomes with apparent clustering (3). Kox 1 has been assigned to chromosome 12q and Kox 8 to chromosome 7q or 22q11 (3). Detailed sequence analysis of Kox 1 revealed that it encodes a protein domain upstream from the zinc finger region consisting of heptad repeats of methionine/leucines which resembles the leucine zipper structure and is reminiscent of the coiled coil structure observed in interfilament proteins (2). Concurrently, an evolutionarily conserved protein domain of about 75 amino acids, designated KRAB domain (**K**rüppel **a**ssociated **b**ox), was identified and estimated to be shared by about one third of the zinc finger genes present in the human genome (4). Screening the panel of thirty Kox cDNAs with the conserved KRAB domain, followed by detailed sequence analysis, demonstrated that the heptad repeats of methionine/leucines observed in Kox 1 is part of the KRAB domain (4). Further analysis of the Kox cDNAs revealed that Kox 8, in addition to Kox 1, also encodes a KRAB domain (4). In this report we show a comparison of the predicted amino acid sequence of the KRAB domains of Kox 1 and Kox 8 with the KRAB domain exemplified by HTF 9 (Figure 1). Based on the high conservation observed in different KRAB domains, it is tempting to postulate that zinc finger proteins containing KRAB domains interact with highly conserved structures present in the nucleus of eukaryotic cells. The specificity of the postulated protein–protein interactions might be specified by less well conserved amino acids of the KRAB consensus (4). The genomic organization of Kox 1 indicates that the KRAB domain is encoded by exons separate from the exons which encode the zinc finger region (data not shown). The genomic structure of KRAB domains further suggests that differential promoter utilization or alternative splicing could give rise to proteins containing the same zinc finger gene domain associated or not with the KRAB domain (4).

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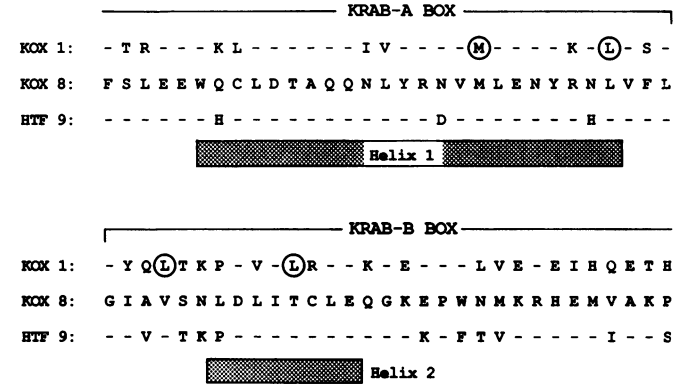


**Figure 1.** Comparison of KRAB domains present in Kox 1 and Kox 8 with the KRAB domain exemplified by HTF 9 (4). Methionine and leucine residues described as a heptad repeat of methionine/leucines in Kox 1 (2) have been encircled. The KRAB domain has been subdivided into two parts, the KRAB A and KRAB B boxes (4). The presence of amphiphilic alpha-helices was predicted by computer analysis (4). Identical amino acids are indicated by a dash (–).