

B pre-mRNATRANSCRIPTS

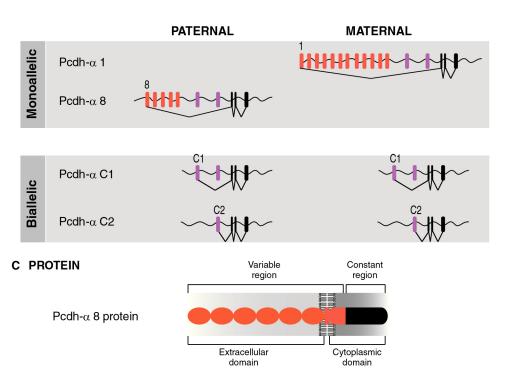


Figure 4. Alternative splicing produces variable Pcdh isoforms. (A) Hypothetical example showing the expression pattern of the Pcdh- α cluster in a single neuron, in which one of the alternative promoters is activated in a seemingly stochastic fashion on each chromosome. An enlargement of the exon 1 promoter region shows the two CCCTC-binding factor (CTCF) binding sites (conserved sequence element [CSE] and exonic CTCF binding site [eCBS]). The enlargement of the HS5-1 enhancer shows the two CTCF binding sites (a and b) and the neuron-restrictive silencer factor (NRSF) binding sequence, neuron-restrictive silencer element (NRSE). (B) The pre-mRNAs produced the maternal and paternal alleles, showing monoallelic expression of variable exons α 1 and α 8, but biallelic expression of the C-type exons. The variable pre-mRNAs contain all the variable exons located downstream from the selected promoter, which are subsequently spliced to the Con1-3 exons. Only the exon located immediately downstream from the selected promoter will be spliced to the exons encoding the intracellular constant region. (C) Each variable exon encodes for six ecto- (cadherin) domains involved in self-recognition, most probably through homotypic repulsion.