



Figure 8. Two *cis*-acting silencing mechanisms at imprinted gene clusters. (A) Insulator model for the *Igf2* cluster. The expression pattern for endoderm is shown. On the maternal chromosome, the unmethylated ICE binds the CTCF protein and forms an insulator that prevents the common endoderm enhancers (E) from activating *Igf2* and *Ins2*. Instead the enhancers activate the nearby *H19* lncRNA promoter. On the paternal chromosome, the methylated ICE cannot bind CTCF and an insulator does not form; hence the *Igf2* and *Ins2* mRNA genes are expressed only on this chromosome. The *H19* lncRNA is methylated, most likely because of spreading from the 2-kb distant methylated ICE, and silenced. (B) lncRNA model for the *Igf2r* cluster. The expression pattern for placenta is shown. On the maternal chromosome, the methylated ICE contains the *Airn* lncRNA promoter that is directly silenced by the DNA methylation imprint. The *Igf2r*, *Slc22a2*, and *Slc22a3* mRNA genes are expressed only on this chromosome. *Mas1* and *Slc22a1* are not expressed in placenta (filled diamond). On the paternal chromosome, the *Airn* lncRNA promoter lying in the unmethylated ICE is expressed and silences *Igf2r* (in part by kicking off RNA polymerase II), *Slc22a2*, and *Slc22a3* in *cis*. Note that in both models, the DNA methylation imprint silences the lncRNA and permits mRNA expression. ICE, imprint control element; gray arrow, expressed allele of an imprinted gene; slashed circle, repressed allele of an imprinted gene; thick gray arrows, long distance effect in *cis*.