SnapShot: Imprinted Gene Clusters

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Cell

Imprinted Gene Loci[1]	Associated Imprinted ncRNAs	Other Associated Imprinted Genes[2]	Germline DMRs[3]	Imprinting Mechanism[4]	Mouse Locus/ Human Locus[5]	Association with Human Disease or Syndrome[6]
Igf2	H19	Ins2[7]	H19 DMD (ICR)	CTCF-dependent insulator	7qF5/11p15.5	Beckwith-Wiedemann syndrome, Silver-Russell syndrome
Igf2r[8]	Air[8,*]	Slc22a2[7,9], Slc22a3[7,9]	Air promoter (ICR)	long ncRNA transcription	17qA1/6q25.3	
Snrpn	Ube3a-ATS*, snoRNAs[10]	Atp10a, Ube3a[7], Snurf, Ndn, Magel2, Mkrn3, Peg12	Snrpn promoter and exon1: PWS-IC (ICR)[11]	long ncRNA transcription?	7qB5/15q11.2	Prader-Willi syndrome, Angelman syndrome[12]
Cdkn1c	Kcnq1ot1*	Osbp15[7], Nap1l4[7,9], Phlda2[7,9], Slc22a18, Msuit1[9], Kcnq1[7], Cd81[7,9], Ascl2[7,9], Tssc4[7,9]	Kcnq1ot1 promoter: KvDMR1 (ICR)	long ncRNA transcription	7qF5/11q15.4	Beckwith-Wiedemann syndrome
Dlk1	Gtl2, anti-Rtl1 microRNAs[8], Rian snoRNAs[8], Mirg microRNAs[8,10]	Rtl1[8], Dio3	Intergenic DMR: IG-DMR (ICR)	ND	12qF1/14q32.2	
Gnas[7]	Nespas, Gnas exon 1A	Gnasxl, Nesp	Gnasxl and Nespas promoter DMR (primary ICR), Gnas exon 1a promoter DMR (secondary ICR)	ND	2qH4/20q13.32	Albright hereditary osteodystrophy, Pseudohypoparathyroidism 1a + 1b, McCune-Albright syndrome
Peg3		Zim2, Zim1[14], Usp29, Zim3, Zfp264	Peg 3 promoter and exon1	ND	7qA1/19q13.43	
Plagl1 (Zac1)[7]	Hymai[7,9]		Hymai exon1	ND	10qA2/6q24.2	Transient neonatal diabetes mellitus
Peg10		Sgce, Ppp1r9a[7], Asb4[9]	Peg10 and Sgce promoter	ND	6qA1/7q21.3	Myoclonus-dystonia syndrome[13]
Mest (Peg1)	Copg2as[8]	Copg2[9], Klf14	Mest-promoter-exon1	ND	6qA3.3/7q32.2	
Rasgrf1[7,9]	4930524O08Rik[7,9]		–30 kb Rasgrf1 DMR-Repeat (ICR)	CTCF-dependent insulator?	9qE3.1/15q25.1	
Grb10[7]		Grb10 brain isoform[7]	Grb10 CpG Island 2	ND	11qA1/7p12.2	
Zrsr1 (U2af1-rs1)[14]		Commd1[7]	Zrsr1 CpG Island	ND	11qA3.2/5q22.2	
Xlr3b[14]		Xlr4b[14], Xlr4c[14]		ND	XqA7.3	
Xist[7,9]	Tsix[7,9]			long ncRNA transcription	XqD/Xq13.2	

■ Paternally expressed genes
■ Maternally expressed genes
■ Differentially methylated regions (DMRs) methylated on the paternal allele
■ DMRs methylated on the maternal allele

*Transcription of ncRNAs essential for imprinting control of the locus.

The majority of imprinted genes are found in conserved clusters in the mammalian genome. Shown are mouse imprinted genes that are part of larger imprinting clusters (variations in human are noted). Each cluster has a prominent gene indicated in the left most column and one or more noncoding (nc)RNAs, which in many cases are critical for the domain-wide regulation of the cluster. Also shown are other associated imprinted genes that typically are jointly regulated through a common imprinting control region (ICR). Single imprinted gene loci are not included in this table and can be found using the following web resources: MRC, Harwell, Mammalian Genetics Unit, Genomic Imprinting: http://www.mgu.har.mrc.ac.uk/research/imprinting; University of Otago, Catalogue of Parent of Origin Effects: http://igc.otago.ac.nz/home.html. The official gene names are shown, with some more familiar names indicated parentheses.

[1]The prominent protein-coding gene within each cluster is listed in this column. The exception to this is Xist, which encodes a long ncRNA that coats the inactive X chromosome in females and is responsible for X inactivation.

[2]In most cases these associated genes are jointly regulated through the linked ICR.

[3]ICR indicates that the DMR has been validated as an imprinting control region by gene targeting studies in mice: deletion or mutation of the DMR results in loss of imprinting of at least one gene.

[4]The mechanism of imprinting is unknown for most of the clusters (designated as not determined, ND) but currently two types of clusters have been identified. In one type of cluster a CTCF-dependent methylation-sensitive insulator controls imprinted ge expression. In the second type of cluster imprinting requires transcription of a long ncRNA that is usually initiated from a hypomethylated DMR/promoter. A question mark indicates that the mechanism is still largely speculative.

[5]UCSC Mouse build February 2006 and Human build March 2006.

[6]Deletion, mutation, or aberrant expression of the genes in the cluster results in the listed human disease. Additionally, ICR deletions and methylation abnormalities can cause these syndromes. For most human imprinted loci, maternal and/or uniparen disomies are associated with distinct abnormal phenotypes. Only proven associations are shown.

[7]Tissue-specific imprinting.

[8]Not imprinted in human.

[9]Imprinting status in human is unknown or conflicting.

[10]All short ncRNAs at this locus may be part of a longer ncRNA.

[11]The ICR regulating the paternally expressed genes has been identified for mouse and human (PWS-IC) whereas the ICR that regulates the maternally expressed genes has been identified in humans but not in mice (AS-IC). However, Ube3a-ATS transcripti appears to be important for regulating both paternal and maternal genes at this locus.

[12]Loss of multiple paternally expressed genes is responsible for Prader-Willi syndrome (PWS) and loss of Ube3a expression is responsible for Angelman syndrome (AS).

[13]Mutations in SGCE are found in patients with Myoclonus dystonia syndrome.

[14]No human ortholog present at locus.

See online version for references and acknowledgements.

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