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The imprinted gene and parent-of-origin effect database

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ABSTRACT

The database of imprinted genes and parent-of-origin effects in animals (http://www.otago.ac.nz/IGC) is a collation of genes and phenotypes for which parent-of-origin effects have been reported. The database currently includes over 220 entries, which describe over 40 imprinted genes in human, mouse and other animals. In addition a wide variety of other parent-of-origin effects, such as transmission of human disease phenotypes, transmission of QTLs, uniparental disomies and interspecies crosses are recorded. Data are accessed through a search engine and references are hyperlinked to PubMed.

INTRODUCTION

Imprinting describes those genes for which the transcriptional activity is dependent on the parent-of-origin of the allele. In addition to genomic imprinting, numerous other parent-of-origin effects have been documented, the mechanisms for which may include undiscovered gene imprinting, parental-specific mutation or other mechanisms.

THE DATABASE

In 1998 we published a catalogue of imprinted genes and parent-of-origin effects (1) which formed the basis of an online database which is larger, more comprehensive and regularly updated. The database is publicly available and provides a searchable compilation of parent-of-origin effects, most of which have been extracted from the biomedical literature. For each gene or phenotype entry, a brief summary of the parent-of-origin effect is provided, along with relevant references hyperlinked to PubMed. Searchable fields include species, chromosome, gene or phenotype name, text within the description and the date on which the entry was last modified. The database is maintained by the corresponding author, who welcomes submissions and comments.

At the time of submission, 41 genes were reported to be imprinted in human and mouse (Table 1) with 12 new imprinted genes having been reported in the first 9 months of 2000. These 41 genes are equally divided between those which show preferential or exclusive expression from the maternally- versus the paternally-derived allele. Enumeration of the actual number of imprinted genes depends on the definition of a 'gene'. Some of the imprinted genes express multiple sense and/or antisense transcripts, while several imprinted transcripts of undefined function have been reported, especially in the Prader–Willi and Angelman syndromes locus on human chromosome 15 (2). Excluding variably spliced isoforms, but including antisense transcripts and non-coding transcripts of unknown function, approximately 60 imprinted transcripts have been reported. There are some differences between the reported imprinting status of genes in mouse and human which largely reflect the lack of comparative data, but documented examples of discordance exist; for example *IGF2R* which is imprinted in mouse but not humans.

The discovery of increasing numbers of imprinted antisense or adjacent RNA transcripts parallels the earlier observations of *IGF2* and *H19* which are coordinately and oppositely imprinted, and has provided further evidence for the involvement of non-coding RNA transcripts in mechanisms to establish or maintain imprinted gene expression (3). Genomic imprinting was formally demonstrated for the first time in 1991, but parent-of-origin effects have been recorded for millennia among animal breeders (4). Ironically, historical interpretations of Mendel's work and the emphasis on the equality of alleles may have impeded the discovery of imprinted phenomena, but recently parent-of-origin effects have been reported for quantitative-trait loci (QTLs) such as back fat thickness, muscle depth and intramuscular fat content in pigs (5) and for birth weight, weaning weight, hot carcass weight and gestation in cattle (I.G.Imumorin, personal communication).

Several other parent-of-origin effects have been reported, with varying qualities of supporting evidence. For example the phenotypes associated with uniparental disomies such as Prader–Willi and Angelman syndromes (human 15q), Beckwith–Wiedemann syndrome (11p), Russell–Silver syndrome (7p) and transient neonatal diabetes (6q) indicate the presence of imprinted genes and strong candidate genes now exist for each of these syndromes. The influence of parental origin on the transmission of human disease phenotypes has been demonstrated for conditions such as hereditary paragangliomas and diabetes susceptibility, and more recently has been suggested for a wide range of phenotypes such as premature ovarian failure (6) and male transsexuality (7).

The database also records genes for which there is a parent-of-origin effect on mutation rates: for example *de novo* mutations of *RET*, *FGFR2*, *FGFR3* and *RB* preferentially occur during male gametogenesis. It also records parental effects on the direction of interspecies crosses, such as lion–tiger crosses (ligers and tigons), horse–donkey crosses (mules and hinnies) mink frog–bull frog crosses and others.

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Table 1. Imprinted genes human and mouse

Human chr.	Gene	Parent	Mouse chr(cM)	Gene	Parent
1p	p73	M			
1p	ARHI	P			
5q	U2AFBPL	NI	11(12)	Irlgs2	P
6q	HYMAI	P			
6q	PLAGL1	P	10(15)	Zac1	P
6q	IGF2R	NI	17(7)	Igf2r	M(AS)
7p	GRB10	M/P*	11(8)	Grb10	M
7q	SGCE	no data	6(1)	Sgce	P
7q	MEST	P	6(7)	Mest	P
7q	COPG2	P*	6(7)	Copg2	M(AS)
7q	Hs.6421	no data	6(7)	Mit1	P
11p	H19	M	7(69)	H19	M
11p	IGF2	P(AS)	7(69)	Igf2	P(AS)
11p	INS	no data	7(69)	Ins2	P
11p	ASCL2	M	7(69)	Mash2	M
11p	TSSC4	NI	7(69)	Tssc4	M bias
11p	MTR1	P			
11p	KCNQ1	M(AS)	7(69)	Kcnq1	M(AS)
11p	CDKN1C	M	7(69)	Cdnk1c	M
11p	SLC22A1L	M	7(69)	Orctl2	M
11p	TSSC3	M	7(69)	Tssc3	M
11p	ZNF215	M			
11p	WT1	M/P*(AS)			
13q	HTR2A	M*	14(41)	Htr2a	M
14q	DLK1	NI	12	Dlk	P
14q	MEG3	M	12(54)	Gtl2	M
15q	MKRN3	P(AS)	7(29)	Zfp127	P
15q	NDN	P	7(28)	Ndn	P
15q	MAGEL2	P	7(28)	Magel2	P
15q	SNRPN	P	7(27)	Snrpn	P
15q	IPW	P	7(28)	Ipw	P
15q	UBE3A	M(AS)	7(28)	Ube3a	M
15q	RASGRF1	no data	9(50)	Rasgrf1	P
18q	IMPACT	NI	18	Impact	P
19q	PEG3	no data	7(4)	Peg3	P
19q	KIAA0972	no data	7(4)	Zim1	M
20q	GNAS1	M/P(AS)	2(104)	Gnas	M/P(AS)
20q	NNAT	no data	2(88)	Nnat	P
Xq	XIST	P	X(42)	Xist	P
			X(57)	Esx1	M
			19(49)	Ins1	P

Parent, parent-of-origin of expressed allele; P, paternal, M, maternal; AS, expression of an imprinted antisense transcript; NI, not imprinted; asterisk, conflicting data.

Although the database attempts to include as many reports and hypotheses as possible, it cannot always judge the accuracy of these claims. Apparent imprinted gene expression can simply reflect the technical problems of allelic drop-out during RT–PCR when transcript frequency is rare, while some of the reported imprinted inheritance patterns might reflect chance skewing or biases within the families studied. Conversely, apparent absence of imprinting can merely indicate the absence of data from specific tissues at specific developmental time periods.

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