

**Table S1: Summary descriptions of ten core IGN members analyzed in this study**

**Imprinted genes coexpressed in adult stem cells**

Gene	Expressed allele	Gene function	Mouse phenotype	Putative role in hematopoiesis or hematopoietic malignancy	Refs
<b>Cdkn1c</b>	Maternal	Encodes p57( Kip2), a cyclin-dependent kinase inhibitor. In vitro evidence suggests that p57 inhibits the activity of specific cyclin/CDK complexes. Additional functions include regulation of the cytoskeleton and promotion of apoptosis.	KO: Multiple malformations, neonatal lethal	Highly expressed in quiescent LT-HSCs but downregulated in proliferative short-term HSCs. In human CD34+ cord blood cells, <i>CDKN1C</i> is induced by TGF-beta and is critical for TGF-beta dependent cell cycle arrest.	[1,2,3,4,5,6]
<b>Dlk1 (Pref1)</b>	Paternal	Encodes a delta-like ligand that can be either soluble or membrane bound. It is thought to inhibit Notch signaling and plays a role in regulating differentiation of adipocytes and mesenchymal stem cells.	KO: Growth restriction, accelerated adiposity OE: "Callipyge" phenotype	Expressed in human CD34+ hematopoietic stem cells and upregulated in some cases of hematopoietic malignancy, particularly myelodysplasia and myeloid leukemia. Expressed by stromal cells that support hematopoiesis, suggesting that it plays a role in the interactions between stem cells and their niche.	[7,8,9,10,11,12,13]
<b>Grb10</b>	Maternal	Adapter protein for receptor tyrosine kinases, with roles in insulin and insulin-like growth factor signaling. Conflicting reports regarding repression or enhancement of receptor signaling, likely dependent on cellular context.	KO: Overgrowth, increased muscle mass / reduced adiposity, altered glucose homeostasis	Binds to the chimeric BCR-ABL tyrosine kinase expressed in chronic myelogenous leukemia. May be involved signaling from the c-Kit tyrosine kinase receptor.	[14,15,16,17,18]
<b>Gtl2 (Meg3)</b>	Maternal	Non-coding RNA that harbors two miRNA clusters and a snoRNA cluster. Part of a large reciprocally imprinted domain including <i>Dlk1</i> , <i>anti-Rtl1</i> , and <i>Dio3</i> . Several miRNAs from this cluster are downregulated in ovarian cancer, suggesting a possible tumor suppressor role.	KO: Depends on parent of origin	?	[19,20,21,22,23,24]
<b>H19</b>	Maternal	Non-coding RNA that harbors miR-675. The precise targets are unclear. Likely functions as a tumor suppressor, but conflicting reports. H19 transcript is upregulated during cell proliferation (possibly due to reduced miRNA processing).	KO: Confounded by effects on Igf2 expression; OE: Repressed growth	Downregulated in CD34+/CD33- bone marrow cells from patients with Polycythemia vera and downregulated in several different leukemias and myeloproliferative disorders.	[25,26,27,28,29,30,31,32,33]
<b>Igf2</b>	Paternal	Secreted growth factor that promotes fetal growth. Likely involved in both paracrine/endocrine signaling. Upregulated in many different cancers, in many cases due to loss of imprinting.	KO: Growth restriction, complicated by effects on placental function OE: Overgrowth, multiple malformations	Growth factor for fetal hematopoietic stem cells. Downregulated in several different leukemias.	[33,34,35,36,37,38,39]
<b>Mest (Peg1)</b>	Paternal	Expressed in embryonic mesoderm, mesodermal derivatives, and the central nervous system. May have enzymatic function as an epoxide hydrolase based on protein homology. Upregulated in obese adipose tissue.	KO: Intrauterine growth restriction	?	[40,41,42]
<b>Ndn</b>	Paternal	MAGE protein, initially discovered in post-mitotic neurons thought to arrest growth and regulate apoptosis. Multiple biochemical interactions. Implicated in differentiation of neuronal and mesenchymal tissues.	KO: Conflicting data, early post-natal lethality due to respiratory failure, possible strain differences	Likely transcriptional target of p53 and plays modest role in regulating HSC quiescence, primarily during regeneration.	[43,44,45,46,47,48,49,50,51,52]
<b>Peg3 (Pw1)</b>	Paternal	Zinc-finger transcription factor expressed in the embryonic mesoderm and brain, plays a role in TNF-alpha/NF-kB signaling and p53-mediated apoptosis. Implicated in muscle stem cell function.	KO: Intrauterine growth restriction	?	[53,54,55,56,57]
<b>Plagl1 (Zac1 / Lof1)</b>	Paternal	Zinc-finger transcription factor that inhibits the growth of tumor cells in vitro through repression of cell cycle and induction of apoptosis. Frequently deleted or down-regulated in cancer, co-regulates p53-responsive promoters.	KO: Intrauterine growth restriction	?	[58,59,60,61,62,63]

## References associated with Table S1

1. Pateras IS, Apostolopoulou K, Niforou K, Kotsinas A, Gorgoulis VG (2009) p57KIP2: "Kip"ing the cell under control. *Molecular cancer research : MCR* 7: 1902-1919.
2. Vlachos P, Joseph B (2009) The Cdk inhibitor p57(Kip2) controls LIM-kinase 1 activity and regulates actin cytoskeleton dynamics. *Oncogene* 28: 4175-4188.
3. Zhang P, Liegeois NJ, Wong C, Finegold M, Hou H, et al. (1997) Altered cell differentiation and proliferation in mice lacking p57KIP2 indicates a role in Beckwith-Wiedemann syndrome. *Nature* 387: 151-158.
4. Passegue E, Wagers AJ, Giuriato S, Anderson WC, Weissman IL (2005) Global analysis of proliferation and cell cycle gene expression in the regulation of hematopoietic stem and progenitor cell fates. *The Journal of experimental medicine* 202: 1599-1611.
5. Umemoto T, Yamato M, Nishida K, Yang J, Tano Y, et al. (2005) p57Kip2 is expressed in quiescent mouse bone marrow side population cells. *Biochemical and biophysical research communications* 337: 14-21.
6. Scandura JM, Boccuni P, Massague J, Nimer SD (2004) Transforming growth factor beta-induced cell cycle arrest of human hematopoietic cells requires p57KIP2 up-regulation. *Proc Natl Acad Sci U S A* 101: 15231-15236.
7. Baladron V, Ruiz-Hidalgo MJ, Nueda ML, Diaz-Guerra MJ, Garcia-Ramirez JJ, et al. (2005) dlk acts as a negative regulator of Notch1 activation through interactions with specific EGF-like repeats. *Experimental cell research* 303: 343-359.
8. Abdallah BM, Boissy P, Tan Q, Dahlgaard J, Traustadottir GA, et al. (2007) dlk1/FA1 regulates the function of human bone marrow mesenchymal stem cells by modulating gene expression of pro-inflammatory cytokines and immune response-related factors. *The Journal of biological chemistry* 282: 7339-7351.
9. Davis E, Jensen CH, Schroder HD, Farnir F, Shay-Hadfield T, et al. (2004) Ectopic expression of DLK1 protein in skeletal muscle of padumnal heterozygotes causes the callipyge phenotype. *Current biology : CB* 14: 1858-1862.
10. Nueda ML, Baladron V, Sanchez-Solana B, Ballesteros MA, Laborda J (2007) The EGF-like protein dlk1 inhibits notch signaling and potentiates adipogenesis of mesenchymal cells. *Journal of molecular biology* 367: 1281-1293.
11. Moon YS, Smas CM, Lee K, Villena JA, Kim KH, et al. (2002) Mice lacking paternally expressed Pref-1/Dlk1 display growth retardation and accelerated adiposity. *Molecular and cellular biology* 22: 5585-5592.
12. Sakajiri S, O'Kelly J, Yin D, Miller CW, Hofmann WK, et al. (2005) Dlk1 in normal and abnormal hematopoiesis. *Leukemia* 19: 1404-1410.
13. Qi X, Chen Z, Liu D, Cen J, Gu M (2008) Expression of Dlk1 gene in myelodysplastic syndrome determined by microarray, and its effects on leukemia cells. *International journal of molecular medicine* 22: 61-68.
14. Riedel H (2004) Grb10 exceeding the boundaries of a common signaling adapter. *Frontiers in bioscience : a journal and virtual library* 9: 603-618.
15. Charalambous M, Smith FM, Bennett WR, Crew TE, Mackenzie F, et al. (2003) Disruption of the imprinted Grb10 gene leads to disproportionate overgrowth by an Igf2-independent mechanism. *Proceedings of the National Academy of Sciences of the United States of America* 100: 8292-8297.

16. Smith FM, Holt LJ, Garfield AS, Charalambous M, Koumanov F, et al. (2007) Mice with a disruption of the imprinted Grb10 gene exhibit altered body composition, glucose homeostasis, and insulin signaling during postnatal life. *Molecular and cellular biology* 27: 5871-5886.
17. Bai RY, Jahn T, Schrem S, Munzert G, Weidner KM, et al. (1998) The SH2-containing adapter protein GRB10 interacts with BCR-ABL. *Oncogene* 17: 941-948.
18. Jahn T, Seipel P, Urschel S, Peschel C, Duyster J (2002) Role for the adaptor protein Grb10 in the activation of Akt. *Molecular and cellular biology* 22: 979-991.
19. Cavaille J, Seitz H, Paulsen M, Ferguson-Smith AC, Bachellerie JP (2002) Identification of tandemly-repeated C/D snoRNA genes at the imprinted human 14q32 domain reminiscent of those at the Prader-Willi/Angelman syndrome region. *Human molecular genetics* 11: 1527-1538.
20. Seitz H, Royo H, Bortolin ML, Lin SP, Ferguson-Smith AC, et al. (2004) A large imprinted microRNA gene cluster at the mouse Dlk1-Gtl2 domain. *Genome Res* 14: 1741-1748.
21. Kircher M, Bock C, Paulsen M (2008) Structural conservation versus functional divergence of maternally expressed microRNAs in the Dlk1/Gtl2 imprinting region. *BMC genomics* 9: 346.
22. Zhang L, Volinia S, Bonome T, Calin GA, Greshock J, et al. (2008) Genomic and epigenetic alterations deregulate microRNA expression in human epithelial ovarian cancer. *Proceedings of the National Academy of Sciences of the United States of America* 105: 7004-7009.
23. Steshina EY, Carr MS, Glick EA, Yevtodiyyenko A, Appelbe OK, et al. (2006) Loss of imprinting at the Dlk1-Gtl2 locus caused by insertional mutagenesis in the Gtl2 5' region. *BMC genetics* 7: 44.
24. Takahashi N, Okamoto A, Kobayashi R, Shirai M, Obata Y, et al. (2009) Deletion of Gtl2, imprinted non-coding RNA, with its differentially methylated region induces lethal parent-origin-dependent defects in mice. *Human molecular genetics* 18: 1879-1888.
25. Hao Y, Crenshaw T, Moulton T, Newcomb E, Tycko B (1993) Tumour-suppressor activity of H19 RNA. *Nature* 365: 764-767.
26. Ariel I, Ayesh S, Perlman EJ, Pizov G, Tanos V, et al. (1997) The product of the imprinted H19 gene is an oncofetal RNA. *Molecular pathology* : MP 50: 34-44.
27. Cai X, Cullen BR (2007) The imprinted H19 noncoding RNA is a primary microRNA precursor. *Rna* 13: 313-316.
28. Looijenga LH, Verkerk AJ, De Groot N, Hochberg AA, Oosterhuis JW (1997) H19 in normal development and neoplasia. *Molecular reproduction and development* 46: 419-439.
29. Yamamoto Y, Nishikawa Y, Tokairin T, Omori Y, Enomoto K (2004) Increased expression of H19 non-coding mRNA follows hepatocyte proliferation in the rat and mouse. *Journal of hepatology* 40: 808-814.
30. Milligan L, Antoine E, Bisbal C, Weber M, Brunel C, et al. (2000) H19 gene expression is up-regulated exclusively by stabilization of the RNA during muscle cell differentiation. *Oncogene* 19: 5810-5816.
31. Nunez C, Bashein AM, Brunet CL, Hoyland JA, Freemont AJ, et al. (2000) Expression of the imprinted tumour-suppressor gene H19 is tightly regulated during normal haematopoiesis and is reduced in haematopoietic precursors of patients with the myeloproliferative disease polycythaemia vera. *J Pathol* 190: 61-68.

32. Bock O, Schlue J, Kreipe H (2003) Reduced expression of H19 in bone marrow cells from chronic myeloproliferative disorders. *Leukemia : official journal of the Leukemia Society of America, Leukemia Research Fund, UK* 17: 815-816.
33. Tessema M, Langer F, Bock O, Seltsam A, Metzsig K, et al. (2005) Down-regulation of the IGF-2/H19 locus during normal and malignant hematopoiesis is independent of the imprinting pattern. *Int J Oncol* 26: 499-507.
34. Chao W, D'Amore PA (2008) IGF2: epigenetic regulation and role in development and disease. *Cytokine & growth factor reviews* 19: 111-120.
35. Rodriguez S, Gaunt TR, Day IN (2007) Molecular genetics of human growth hormone, insulin-like growth factors and their pathways in common disease. *Human genetics* 122: 1-21.
36. Kaneda A, Feinberg AP (2005) Loss of imprinting of IGF2: a common epigenetic modifier of intestinal tumor risk. *Cancer research* 65: 11236-11240.
37. Constanca M, Hemberger M, Hughes J, Dean W, Ferguson-Smith A, et al. (2002) Placental-specific IGF-II is a major modulator of placental and fetal growth. *Nature* 417: 945-948.
38. Sun FL, Dean WL, Kelsey G, Allen ND, Reik W (1997) Transactivation of Igf2 in a mouse model of Beckwith-Wiedemann syndrome. *Nature* 389: 809-815.
39. Zhang CC, Lodish HF (2004) Insulin-like growth factor 2 expressed in a novel fetal liver cell population is a growth factor for hematopoietic stem cells. *Blood* 103: 2513-2521.
40. Kaneko-Ishino T, Kuroiwa Y, Miyoshi N, Kohda T, Suzuki R, et al. (1995) Peg1/Mest imprinted gene on chromosome 6 identified by cDNA subtraction hybridization. *Nat Genet* 11: 52-59.
41. Kamei Y, Suganami T, Kohda T, Ishino F, Yasuda K, et al. (2007) Peg1/Mest in obese adipose tissue is expressed from the paternal allele in an isoform-specific manner. *FEBS letters* 581: 91-96.
42. Lefebvre L, Viville S, Barton SC, Ishino F, Keverne EB, et al. (1998) Abnormal maternal behaviour and growth retardation associated with loss of the imprinted gene Mest. *Nature genetics* 20: 163-169.
43. Hayashi Y, Matsuyama K, Takagi K, Sugiura H, Yoshikawa K (1995) Arrest of cell growth by necdin, a nuclear protein expressed in postmitotic neurons. *Biochemical and biophysical research communications* 213: 317-324.
44. Barker PA, Salehi A (2002) The MAGE proteins: emerging roles in cell cycle progression, apoptosis, and neurogenetic disease. *Journal of neuroscience research* 67: 705-712.
45. Brunelli S, Tagliafico E, De Angelis FG, Tonlorenzi R, Baesso S, et al. (2004) Msx2 and necdin combined activities are required for smooth muscle differentiation in mesoangioblast stem cells. *Circulation research* 94: 1571-1578.
46. Tseng YH, Butte AJ, Kokkotou E, Yechoor VK, Taniguchi CM, et al. (2005) Prediction of preadipocyte differentiation by gene expression reveals role of insulin receptor substrates and necdin. *Nature cell biology* 7: 601-611.
47. Deponti D, Francois S, Baesso S, Sciorati C, Innocenzi A, et al. (2007) Necdin mediates skeletal muscle regeneration by promoting myoblast survival and differentiation. *The Journal of cell biology* 179: 305-319.
48. Kurita M, Kuwajima T, Nishimura I, Yoshikawa K (2006) Necdin downregulates CDC2 expression to attenuate neuronal apoptosis. *The Journal of neuroscience : the official journal of the Society for Neuroscience* 26: 12003-12013.

49. Tsai TF, Armstrong D, Beaudet AL (1999) Necdin-deficient mice do not show lethality or the obesity and infertility of Prader-Willi syndrome. *Nature genetics* 22: 15-16.
50. Gerard M, Hernandez L, Wevrick R, Stewart CL (1999) Disruption of the mouse necdin gene results in early post-natal lethality. *Nature genetics* 23: 199-202.
51. Liu Y, Elf SE, Miyata Y, Sashida G, Huang G, et al. (2009) p53 regulates hematopoietic stem cell quiescence. *Cell Stem Cell* 4: 37-48.
52. Kubota Y, Osawa M, Jakt LM, Yoshikawa K, Nishikawa S (2009) Necdin restricts proliferation of hematopoietic stem cells during hematopoietic regeneration. *Blood* 114: 4383-4392.
53. Relaix F, Weng X, Marazzi G, Yang E, Copeland N, et al. (1996) Pw1, a novel zinc finger gene implicated in the myogenic and neuronal lineages. *Developmental biology* 177: 383-396.
54. Relaix F, Wei XJ, Wu X, Sassoon DA (1998) Peg3/Pw1 is an imprinted gene involved in the TNF-NFkappaB signal transduction pathway. *Nature genetics* 18: 287-291.
55. Relaix F, Wei X, Li W, Pan J, Lin Y, et al. (2000) Pw1/Peg3 is a potential cell death mediator and cooperates with Siah1a in p53-mediated apoptosis. *Proc Natl Acad Sci U S A* 97: 2105-2110.
56. Deng Y, Wu X (2000) Peg3/Pw1 promotes p53-mediated apoptosis by inducing Bax translocation from cytosol to mitochondria. *Proceedings of the National Academy of Sciences of the United States of America* 97: 12050-12055.
57. Nicolas N, Marazzi G, Kelley K, Sassoon D (2005) Embryonic deregulation of muscle stress signaling pathways leads to altered postnatal stem cell behavior and a failure in postnatal muscle growth. *Developmental biology* 281: 171-183.
58. Spengler D, Villalba M, Hoffmann A, Pantaloni C, Houssami S, et al. (1997) Regulation of apoptosis and cell cycle arrest by Zac1, a novel zinc finger protein expressed in the pituitary gland and the brain. *The EMBO journal* 16: 2814-2825.
59. Varrault A, Ciani E, Apiou F, Bilanges B, Hoffmann A, et al. (1998) hZAC encodes a zinc finger protein with antiproliferative properties and maps to a chromosomal region frequently lost in cancer. *Proceedings of the National Academy of Sciences of the United States of America* 95: 8835-8840.
60. Varrault A, Gueydan C, Delalbre A, Bellmann A, Houssami S, et al. (2006) Zac1 regulates an imprinted gene network critically involved in the control of embryonic growth. *Dev Cell* 11: 711-722.
61. Abdollahi A (2007) LOT1 (ZAC1/PLAGL1) and its family members: mechanisms and functions. *Journal of cellular physiology* 210: 16-25.
62. Basyuk E, Coulon V, Le Digarcher A, Coisy-Quivy M, Moles JP, et al. (2005) The candidate tumor suppressor gene ZAC is involved in keratinocyte differentiation and its expression is lost in basal cell carcinomas. *Molecular cancer research : MCR* 3: 483-492.
63. Huang SM, Schonthal AH, Stallcup MR (2001) Enhancement of p53-dependent gene activation by the transcriptional coactivator Zac1. *Oncogene* 20: 2134-2143.