

Table S1. Genes upregulated in skin expressing an inhibitor of Notch signaling versus a constitutively activated Notch

GenBank	Unigene	Δ	Description	Human ortholog	Mouse phenotype or human symptom	References
BC042303.1	XI.20089	362	Foxi1, winged-helix transcription factor	FOXI1	Loss of PSCs in kidney, epididymis and inner ear in mouse, deafness and Pendred syndrome in humans	PMID: 17503324 (Yang et al., 2007), 16932748 (Blomqvist et al., 2006), 15173882 (Blomqvist et al., 2004), 12642503 (Hulander et al., 2003)
BJ090165	XI.22874	153	ubp1, Grainyhead family of transcription factors	LBP1A	Loss of placental angiogenesis in mouse	PMID: 15282311 (Parekh et al., 2004)
CB564456	XI.5948	231	Fetuin B-like, cystatin, Histidine-rich protein	fetuin B	None reported	
BJ054524	XI.16561	128	Similar to CLC-K, voltage-dependent chloride channel	CLCN2	Blindness and infertility in mouse, expressed in epithelia affected by cystic fibrosis	PMID: 11250895 (Bosl et al., 2001), 9520461 (Schwiebert et al., 1998)
BJ079632	XI.8929	115	ATP6V1C2, proton pump subunit	ATP6V1C2, DFNB47	Human recessive autosomal deafness	PMID: 16261342 (Hassan et al., 2006)
BM172535	XI.10887	107	Pendrin-like, anion exchanger	Pendrin, SLC26A4	Loss of hearing, kidney bicarbonate transport in mice, Pendred syndrome, autosomal deafness/enlarged vestibular aqueduct in humans	PMID: 11274445 (Royaux et al., 2001), 9398842 (Everett et al., 1997)
BG555028	XI.2715	100	ATP6V0A4, proton pump subunit	ATP6V0A4	Distal renal tubular acidosis in humans	PMID: 10577919 (Karet et al., 1999b)
BF072092	XI.10362	81	Carbonic anhydrase XII	CA12	None reported	
BC041213.1	XI.15327	64	Carbonic anhydrase IIA	CA2	Renal tubular acidosis in mice and humans	PMID: 3126501 (Lewis et al., 1988), 1301935 (Hu et al., 1992)
BJ051736	XI.11114	56	ATP6AC45, proton pump subunit	ATPase, H ⁺ transporting, lysosomal accessory protein 1	None reported	
BJ089334	XI.8939	55	ATP6V0D2, proton pump subunit	ATP6V0D2	None reported, expressed in kidney and epididymis	PMID: 12384298 (Smith et al., 2002), 16192400 (Pietrement et al., 2006)
CB560639	XI.9576	43	Carbonic anhydrase IIB	CA2	Renal tubular acidosis in mice and humans	PMID: 3126501 (Lewis et al., 1988), 1301935 (Hu et al., 1992)
BC043831.1	XI.17895	38	Highly conserved coiled-coiled protein	LOC80127	None reported	
BI314316	XI.18310	34	cyp3c1, p450 enzyme	CYP3A4	Pharmacokinetic defects	PMID: 10668853 (Sata et al., 2000)
BJ076278	XI.15867	32	ATP6V1B1, proton pump subunit	ATP6V1B1	Distal renal tubular acidosis in mice and humans, deafness in humans	PMID: 16174750 (Finberg et al., 2005), 9916796 (Karet et al., 1999a)
BJ088745	XI.24143	28	CLC7 chloride channel protein 7	CLCN7	Osteopetrosis in mice and humans due to poor extracellular acidification	PMID: 11207362 (Kornak et al., 2001)
AF419159.1	XI.17387	27	neuralized, Notch pathway	neuralized	None reported	
CB558944	XI.24365.1	11	ATP6V1H proton pump subunit	ATP6V1H	None reported	
BE189176	XI.5223	8.3	ATP6V1E2 proton pump subunit	ATP6V1E2	None reported, expressed in epididymis	PMID: 16192400 (Pietrement et al., 2006), 12036578 (Imai-Senga et al., 2002)
BJ076846	XI.13563.1	8.3	Anion Exchanger 1, Band 3	AE1, SLC4A1	Distal renal tubular acidosis in mice and humans	PMID: 17409310 (Stehberger et al., 2007), 12539048 (Devonald et al., 2003)
BG161319	XI.6664.1	7	ATP6V1F proton pump subunit	ATP6V1F	None reported	
BM192083	XI.24352	6	ATP6V0B proton pump subunit	ATP6V0B	None reported	
BJ086424	XI.26301.1	5.5	ATP6AP2 proton pump subunit	ATP6AP2	None reported	
BC043805.1	XI.8573	4.1	ATP6V0C proton pump subunit	ATP6V0C	None reported	

All four blastomeres of *X. laevis* embryos at the 4-cell stage were injected with either *ICD* or *HMM^{mut}* RNA. At stage 10, ectoderm was isolated and cultured on fibronectin-coated coverslips. RNA was isolated at stage 22 and analyzed by Affymetrix arrays. The expression levels of RNAs from three separate experiments were compared pairwise, and average fold change determined. Shown are all of the top genes in terms of fold change, many of which encode proteins involved in ion transport. The lower collection of genes represents other potential INC genes with lower fold changes on the array. The complete microarray dataset has been submitted to the Gene Expression Omnibus (GEO; <http://www.ncbi.nlm.nih.gov/geo/>) under accession number GSE23844.

References.

- Bosl, M. R., Stein, V., Hubner, C., Zdebik, A. A., Jordt, S. E., Mukhopadhyay, A. K., Davidoff, M. S., Holstein, A. F. and Jentsch, T. J.** (2001). Male germ cells and photoreceptors, both dependent on close cell-cell interactions, degenerate upon CIC-2 Cl⁻ channel disruption. *EMBO J.* **20**, 1289-1299.
- Everett, L. A., Glaser, B., Beck, J. C., Idol, J. R., Buchs, A., Heyman, M., Adawi, F., Hazani, E., Nassir, E., Baxevanis, A. D. et al.** (1997). Pendred syndrome is caused by mutations in a putative sulphate transporter gene (PDS). *Nat. Genet.* **17**, 411-422.
- Finberg, K. E., Wagner, C. A., Bailey, M. A., Paunescu, T. G., Breton, S., Brown, D., Giebisch, G., Geibel, J. P. and Lifton, R. P.** (2005). The B1-subunit of the H⁺ ATPase is required for maximal urinary acidification. *Proc. Natl. Acad. Sci. USA* **102**, 13616-13621.
- Hassan, M. J., Santos, R. L., Rafiq, M. A., Chahrour, M. H., Pham, T. L., Wajid, M., Hijab, N., Wambangco, M., Lee, K., Ansar, M. et al.** (2006). A novel autosomal recessive non-syndromic hearing impairment locus (DFNB47) maps to chromosome 2p25.1-p24.3. *Hum. Genet.* **118**, 605-610.
- Hu, P. Y., Roth, D. E., Skaggs, L. A., Venta, P. J., Tashian, R. E., Guibaud, P. and Sly, W. S.** (1992). A splice junction mutation in intron 2 of the carbonic anhydrase II gene of osteopetrosis patients from Arabic countries. *Hum. Mutat.* **1**, 288-292.
- Imai-Senga, Y., Sun-Wada, G. H., Wada, Y. and Futai, M.** (2002). A human gene, ATP6E1, encoding a testis-specific isoform of H⁺-ATPase subunit E. *Gene* **289**, 7-12.
- Karet, F. E., Finberg, K. E., Nayir, A., Bakkaloglu, A., Ozen, S., Hulton, S. A., Sanjad, S. A., Al-Sabban, E. A., Medina, J. F. and Lifton, R. P.** (1999a). Localization of a gene for autosomal recessive distal renal tubular acidosis with normal hearing (rdRTA2) to 7q33-34. *Am. J. Hum. Genet.* **65**, 1656-1665.
- Karet, F. E., Finberg, K. E., Nelson, R. D., Nayir, A., Mocan, H., Sanjad, S. A., Rodriguez-Soriano, J., Santos, F., Cremers, C. W., Di Pietro, A. et al.** (1999b). Mutations in the gene encoding B1 subunit of H⁺-ATPase cause renal tubular acidosis with sensorineural deafness. *Nat. Genet.* **21**, 84-90.
- Kornak, U., Kasper, D., Bosl, M. R., Kaiser, E., Schweizer, M., Schulz, A., Friedrich, W., Delling, G. and Jentsch, T. J.** (2001). Loss of the CIC-7 chloride channel leads to osteopetrosis in mice and man. *Cell* **104**, 205-215.
- Lewis, S. E., Erickson, R. P., Barnett, L. B., Venta, P. J. and Tashian, R. E.** (1988). N-ethyl-N-nitrosourea-induced null mutation at the mouse Car-2 locus: an animal model for human carbonic anhydrase II deficiency syndrome. *Proc. Natl. Acad. Sci. USA* **85**, 1962-1966.
- Sata, F., Sapone, A., Elizondo, G., Stocker, P., Miller, V. P., Zheng, W., Raunio, H., Crespi, C. L. and Gonzalez, F. J.** (2000). CYP3A4 allelic variants with amino acid substitutions in exons 7 and 12, evidence for an allelic variant with altered catalytic activity. *Clin. Pharmacol. Ther.* **67**, 48-56.
- Schwiebert, E. M., Cid-Soto, L. P., Stafford, D., Carter, M., Blaisdell, C. J., Zeitlin, P. L., Guggino, W. B. and Cutting, G. R.** (1998). Analysis of CIC-2 channels as an alternative pathway for chloride conduction in cystic fibrosis airway cells. *Proc. Natl. Acad. Sci. USA* **95**, 3879-3884.
- Smith, A. N., Borthwick, K. J. and Karet, F. E.** (2002). Molecular cloning and characterization of novel tissue-specific isoforms of the human vacuolar H⁺-ATPase C, G and d subunits, and their evaluation in autosomal recessive distal renal tubular acidosis. *Gene* **297**, 169-177.
- Yang, T., Vidarsson, H., Rodrigo-Blomqvist, S., Rosengren, S. S., Enerback, S. and Smith, R. J.** (2007). Transcriptional control of SLC26A4 is involved in Pendred syndrome and nonsyndromic enlargement of vestibular aqueduct (DFNB4). *Am. J. Hum. Genet.* **80**, 1055-1063.