Sca2 Ko Microarray

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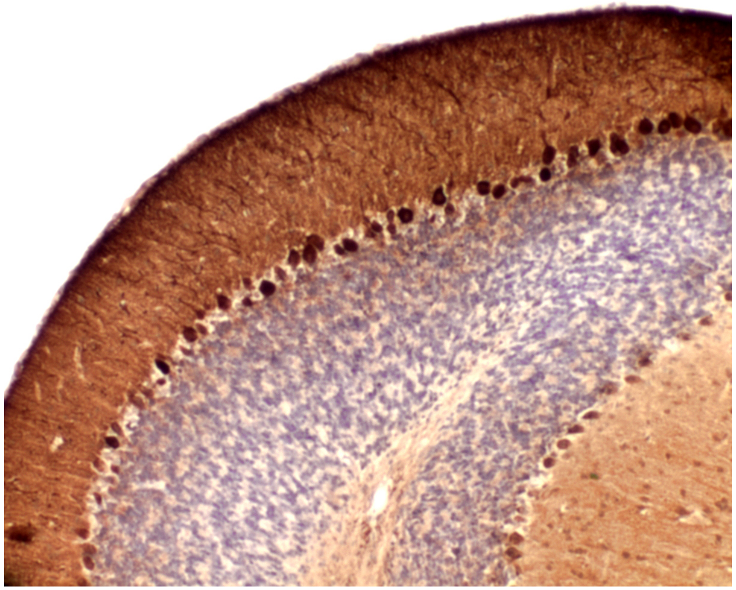
SCA2 transgenic study



- tissue : <u>whole cerebellum</u>
- time course : newborn, 7 weeks, <u>7 months</u>
- 7 months time point shows no significant difference in 4/4 and 3 /4 comparisons
- earlier time points : *not performed*
- low stringency (2/4) : upregulation <u>*erythroid differentiation regulator*</u>

SCA2 transgenic cerebellum

Number of Comparisons	Probe pairs	Luminosity	Fold change	Transcript name
2.02	54.8	11841.5	1.9	erythroid differentiation regulator
2.02	40.8	441.5	2.8	N-terminal Asn amidase
2.02	31.3	181.5	2.1	aldehyde dehydrogenase 9A

The SCA2 knockout array project

- one time point : 2 month old mice, 8 mice in each group

- Comparison of SCA2$^{(-/-)}$ vs. wt controls

- Tissues examined :
  Cerebral cortex, cerebellum, muscle, heart

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SCA2 K.O. cerebellum

growth and differentiation

4.04	78.3	2513.5	2.4	Insulin-like growth factor binding protein 2
2.02	22.3	1950	0.2	erythroid differentiation regulator
-3.03	-34.8	-1935.0	-1.7	Mouse mast cell growth factor (MGF)

energy and metabolism

4.03	58	377.5	5.2	klotho
3.03	68.8	8456.5	2	Ectonucleotide pyrophosphatase/phosphodiesterase 2
-4.04	-73.5	-2020.5	-3.9	thioredoxin-dependent peroxide reductase (tpx)

channels

3.02	56.8	1439.8	2.6	K^+ inwardly-rectifying channel, subfam. J, memb. 9

SCA2 K.O. cerebellum (cont'd.)

transcription

3.03	41	1393.5	2.1	N10 cDNA for a nuclear hormonal binding receptor
3.03	48.5	354.5	2.7	Eukaryotic translation initiation factor eIF-4A
3.02	65.8	981.5	2.2	Inactive X specific transcripts

endogenous retrovirus

4.04	68.8	1370.5	2.4	D-like endogenous retrovirus MusD2

other

4.04	78.5	4424.0	3.2	Transthyretin
3.03	65.8	1618.5	6.4	alpha-synuclein
-4.04	-75.3	-2020.8	-17.3	ataxin-2 (SCA2)
-3.03	-54.8	-1364.5	-3.5	ataxin-2 (SCA2)
-4.04	-41	-174.8	-3	Mus musculus NRK mRNA for NIK-related kinase
-3.02	-48.8	-1571.3	-3.9	Fatty acid transport protein
-3.02	-40.8	-600.5	-5.4	Ubiquitin C

SCA2 K.O. cerebral cortex

energy and metabolism

3.03	36.3	438.0	2.8	adenylyl cyclase-associated protein (CAP)
-4.03	-51.5	-831.8	-1.4	peptidylglycine alpha-amidating monooxygenase (PAM)

growth and differentiation

4.04	53.3	7887.8	1.8	erythroid differentiation regulator
3.03	51.8	4319.8	2.1	erythroid differentiation regulator
3.02	37.8	1112.8	2.1	Bone morphogenetic protein 1

enzyme

3.03	47.3	1502.5	1.7	Esterase 10 sid478p

endogenous retrovirus

4.04	70.5	893.8	2.4	type D-like endogenous retrovirus MusD2
3.03	36.3	796.5	1.5	type IIB intracisternal A-particle (IAP) element

SCA2 K.O. cerebral cortex (cont'd.)

channels				
3.02	50	1560.8	3.1	Potassium inwardly-rectifying channel, subfamily J
3.03	53.5	2970.8	2.1	diazepam-binding inhibitor
-3.03	-45.8	-1699.5	-1.7	K+ channel beta2 subunit
transcription				
3.03	33.3	1033.3	1.7	Mus musculus WSB-1
-3.03	-41	-938.3	-2.2	putative mouse homolog of Nuclear factor I/X (CCAAT-binding transcription factor)
other				
3.03	33.3	2177.0	1.7	Proteasome beta type subunit 5, pseudogene
3.02	42.5	498.5	2.1	AKAP95 mRNA for A kinase anchor protein 95
3.03	75	2986.0	3.2	brain fatty acid-binding protein (B-FABP)
3.03	39.3	2247.8	1.7	Paneth cell enhanced expression PCEE
3.03	34.8	214.5	1.8	CD6 antigen
-4.04	-79.5	-2480.3	-20.9	ataxin-2 (SCA2)
-4.04	-58.3	-1116.3	-10	ataxin-2 (SCA2)
-4.04	-52	-533.0	-2.4	cAMP-dependent Rap1 guanine-nucleotide exchange factor
-3.03	-66	-5229.3	-2	putative mouse homolog of Myelin-associated Oligodendrocytic Basic Protein-81
-3.03	-37.5	-4606.3	-1.4	TI-225, complete cds

SCA2 K.O. : tissue overlap

<u>(Criteria :</u> at least 2 tissues, 2/4 comp., 30% pp, 1.5 fold change)

<u>Increases in Cerebellum AND cerebral cortex :</u>

type D-like endogenous retrovirus MusD2
Potassium inwardly-rectifying channel, subfamily J, member 9
erythroid differentiation regulator
Transthyretin
Inactive X specific transcripts (Xist)
slow/cardiac troponin C (cTnC)
spi2 proteinase inhibitor (spi2/eb4)
CD6 antigen
Acidic nuclear phosphoprotein 32

<u>Decreases in Cerebellum AND cerebral cortex :</u>

Ataxin-2
Putative mouse hom. of Nuclear factor I-X (CCAAT-binding transcr. factor)
Putative mouse hom. Myelin-associated/Oligodendrocytic Basic Protein-81
thioredoxin-dependent peroxide reductase (tpx)

SCA2 K.O. : tissue overlap

Increases in Cerebellum AND muscle :

transcription factor GIF
erythroid differentiation regulator
Inactive X specific transcripts (Xist)
Myocyte enhancer factor 2C
Early growth response 1
slow/cardiac troponin C (cTnC)
spi2 proteinase inhibitor (spi2/eb4)
beta-1-globin

Decreases in Cerebellum AND muscle :

Ataxin-2
male-specific histocompatibility antigen H-YDb (Uty)
Mus musculus mRNA for DBY RNA helicase
Mouse gene for 18S rRNA

SCA2 K.O. : tissue overlap

Increases in cerebral cortex AND muscle :

erythroid differentiation regulator
Inactive X specific transcripts (Xist)
slow/cardiac troponin C (cTnC)
spi2 proteinase inhibitor (spi2/eb4)
Carbonic anhydrase-like sequence

Decreases in cerebral cortex AND muscle :

Ataxin-2
Myocilin
TI-225
chromaffin granule ATPase II homolog

“Leads”, “Trails” (some examples)

- Transcription factors: NFI/CTF, NFIc1B, GIF, LRG-21, MEF-2C,
- erythroid differentiation regulator
- *Xist (*Inactive X specific transcripts)
- Intracisternal particles (= endogenous retroviruses, transposons)

Conclusions : the SCA2 knockout project

- (Very few published studies so far on knockout microarray)
- Few, seemingly unrelated targets rather than “big story” emerging
- Little overlap between tissues