Identifying potential tumor drivers through integration of gene expression and DNA copy number in SI-NET

Samuel Backman, Elham Barazeghi, Olov Norlén, Per Hellman, Peter Stålberg
Department of Surgical Sciences, Uppsala university, Sweden

Background

- The genetics of SI-NET remains poorly understood
- Only *CDKN1B* has been found recurrently mutated
- Copy number variations are common – notably loss of chromosome 18, as well as of chromosome 11, and gain of chromosomes 4, 5 and 14.
- The molecular effects of these alterations remains unknown

Aim: To identify tumor driver genes affected by copy number alterations in SI-NETs.

Methods:

- DNA/RNA was extracted from 20 fresh frozen SI-NET samples
- Whole genome sequencing and RNA-Seq was performed, followed by gene expression quantification and copy number analysis
- Differential expression analyses were performed based on copy number calls.

Conclusions

We identify potential SI-NET driver genes affected by gene dosage.

These results could guide future functional analyses

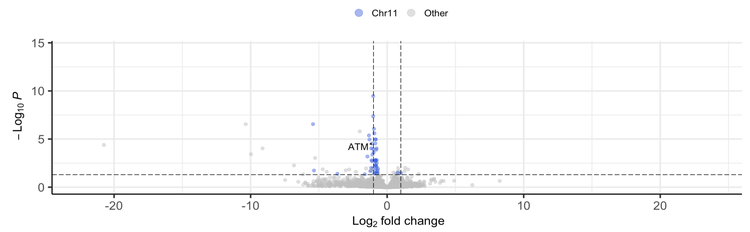
Gene	Log2(Fold Change)	Adjusted p-value
PQLC1	-0,92	4,70E-09
LINC00909	-1,21	4,83E-08
TXNL4A	-0,98	5,44E-07
MBP	-0,84	1,55E-06
CTDP1	-0,81	2,05E-06
RBFA	-0,95	3,16E-06
TMX3	-0,85	2,27E-05
ATP9B	-0,98	3,16E-05
GALR1	-5,31	3,23E-05
RTTN	-0,68	6,00E-05
TIMM21	-0,82	1,75E-04
SOCS6	-0,68	4,07E-04
PARD6G	-1,48	6,44E-04
ADNP2	-0,40	1,60E-03
ZNF407	-0,56	2,07E-03
CNDP2	-0,64	5,92E-03
LOC101927481	-2,08	1,33E-02
ZNF236	-0,56	2,10E-02
HSBP1L1	-0,82	4,53E-02
FBXO15	-0,74	4,68E-02

Table 1. Genes on chromosome 18 q22-qter affected by gene dosage

Contact: samuel.backman@uu.se

Results:

- Eleven cases had loss of chromosome 18, four had loss of chromosome 11, and six had gain of chromosome 14
- 513 genes were differentially expressed in tumors with loss of chromosome 18, including 20 in the shared region of q22-qter
- Tumours with loss of chromosome 11 had 78 differentially expressed genes, of which 52 - including tumor suppressor gene *ATM*, were located on chromosome 11



- Tumours affected by gain of chromosome 14 had differential expression of 525 genes including 60 located on chromosome 14