MDT switch detection

PCAWG (Kallisto TPM)

GTEx (Kallisto TPM)

For each gene, order transcripts by expression

MDT ?*

no

STOP

yes

MDT?

yes

MDT switch ?**

no

STOP

yes

*
1st ranked transcript has TPM ≥ 2 and ≥2x more expression than 2nd ranked transcript?

**
1. MDT unique to PCAWG ?
2. GTEx has sister transcript as MDT ?
3. GTEx has MDT for ≥ 50% of cases ?
4. MDT's relative expression is significantly different to relative expression in GTEx?

Impact prediction for MDT

MDT disrupting interactions

yes

MDT disrupts PPI ?

no

MDT has no impact

CanIsoNet: Isoform-specific interaction network

Protein interaction disrupted

Add annotations

Closest CGC gene in STRING

Network density

Cancer Gene Census (CGC)

COSMIC

$$NDS(a) = int(a) + \sum_{s=1}^{3} \sum_{b=1}^{B} \left(\frac{1}{2^s} * int(b_s) * score(b_s, b_{s-1}) \right)$$

Breadth-first search

no

Transcript has domain sequence ?

Known transcripts

ENSEMBL

yes

No disruption of interactions

Extract sequence of domain

yes

Domains interact ?

no

Skip

Get PFAM annotations from STRING, PFAM, pfam_scanl.pl

Pairs of interacting PFAM domains

3did

yes

High confident inter-action?

no

Skip

Functional protein protein interactions

STRING