## **SNADRIF** description

SNADRIF (SNA DRIver Finder) is a Python 3.7 software package that predicts cancer driver genes from the TCGA PanCanAtlas SNA data and classifies them into oncogenes and tumor suppressors. Driver prediction is based on calculating the ratio of functional (hyperactivating or inactivating) SNAs to passenger SNAs, whereas driver classification is based on calculating the ratio of hyperactivating SNAs to inactivating SNAs. Bootstrapping is used to calculate statistical significance and Benjamini–Hochberg procedure is used to keep false discovery rate under 5%. The pipeline can be executed fully automatically in less than two hours on a modern PC (Linux, Windows or MacOS).

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## **Pipeline overview**

First, the SNA file and the sample quality file are downloaded from <a href="https://gdc.cancer.gov/about-data/publications/PanCan-CellOfOrigin">https://gdc.cancer.gov/about-data/publications/PanCan-CellOfOrigin</a>.

Next, low quality samples and metastatic samples are filtered out.

Then, SNAs are classified into likely hyperactivating, likely inactivating, likely passenger and unclear.

Variant_Classification	Possible effect
De_novo_Start_InFrame	hyperactivating
De_novo_Start_OutOfFrame	passenger
Frame_Shift_Del	inactivating
Frame_Shift_Ins	inactivating
IGR	unclear
In_Frame_Del	hyperactivating
In_Frame_Ins	hyperactivating
Intron	unclear
Missense_Mutation	hyperactivating
Nonsense_Mutation	inactivating
Nonstop_Mutation	inactivating

RNA	unclear
Silent	passenger
Splice_Site	unclear
Targeted_Region	unclear
Translation_Start_Site	inactivating
3'Flank	unclear
3'UTR	unclear
5'Flank	unclear
5'UTR	unclear

The number of SNAs of each type is counted for each gene and two indices are calculated:

a) NSEI - Nonsynonymous SNA Enrichment Index

## **NSEI** = Number of hyperactivating SNAs + Number of inactivating SNAs + 1 / Number of passenger SNAs + 1

b) HISR - Hyperactivating to Inactivating SNA Ratio

## HISR = Number of hyperactivating SNAs + 1 / Number of inactivating SNAs + 1

Next, the gene-patient matrix is constructed, recording various combinations of hyperactivating, inactivating, passenger and unclear SNAs. Bootstrapping from this matrix is then used to obtain the realistic distribution of NSEI under the null hypothesis. P-values are then determined and Benjamini—Hochberg procedure performed to keep FDR under 5%.

Finally, the resulting driver genes are classified into oncogenes (HISR>5) or tumor suppressors (HISR<5) based on empirically determined HISR threshold.

A detailed description of pipeline steps can be found in the file SNADRIF pipeline.pdf

Instructions for executing the code can be found in the file Instructions.txt