MET exon 14 skipping

Detection and Validation

4baseCare
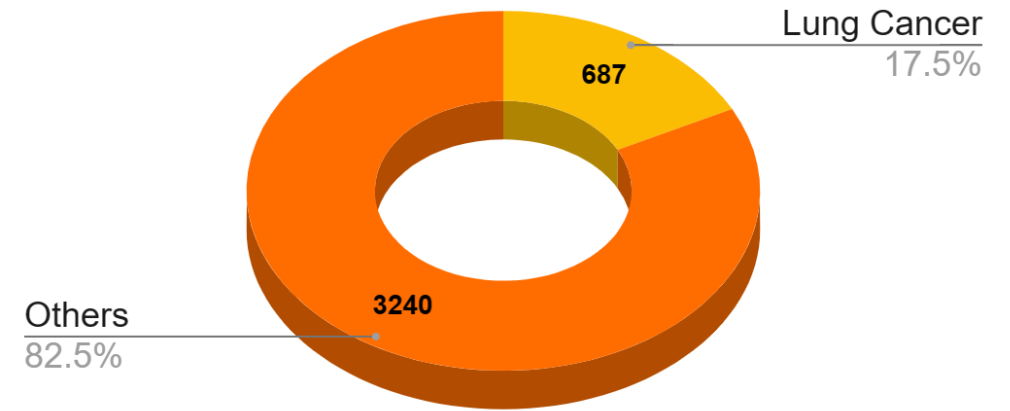*Together, We Beat Cancer*

Introduction

1. MET exon 14 skipping is a molecular alteration found in certain types of cancer.
2. It involves the skipping of exon 14 during the splicing process of the MET gene.
3. MET exon 14 skipping has been primarily observed in non-small cell lung cancer (NSCLC). Although they have been also reported in other cancers.
4. It is associated with a subset of NSCLC patients who have increased MET signaling and reduced response to targeted therapies.
5. Identification of MET exon 14 skipping is important for patient stratification and personalized treatment approaches.

Detection Methods

1. **DNA sequencing:** This method identifies specific alterations in the MET gene sequence.
2. **RNA sequencing:** It helps detect abnormal splicing patterns, including exon 14 skipping.
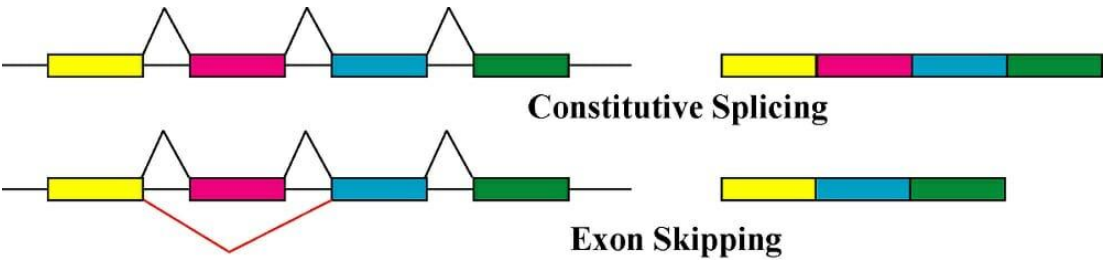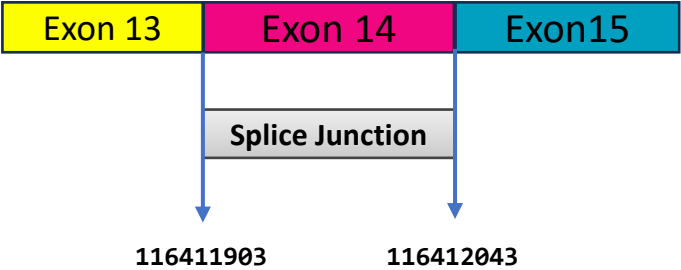
Cancer Type Distribution for DNA Analysis

Lung Cancer 17.5%
687

Others 82.5%
3240

Total Samples = 3927

4baseCare
Together, We Beat Cancer

MET exon 14 skipping: Splicing

Splicing?

Constitutive Splicing

Exon Skipping

RNA-seq

ex 13   ex 15

ex13 GSP2   ex15 GSP2

Splice Junctions

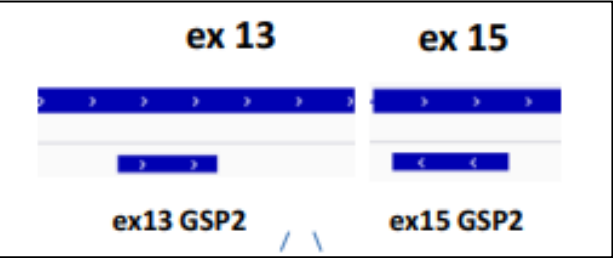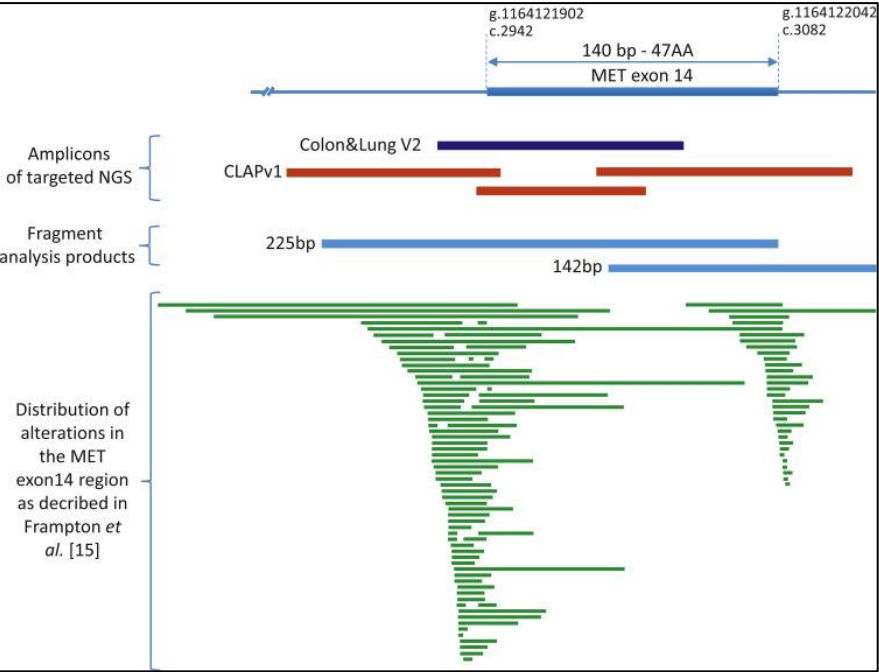| Exon 13 | Exon 14 | Exon15 |

Splice Junction

116411903   116412043

Filename.SJ.out.tab provides a list of all the splice junctions recorded in the sample, it is generated(default) by all RNA-seq pipeline in BSSH

DNA-seq

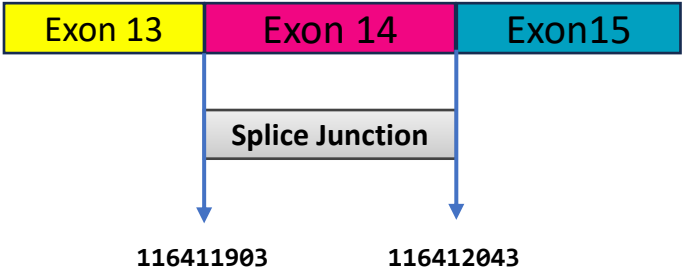g.1164121902
c.2942

g.1164122042
c.3082

140 bp - 47AA
MET exon 14

Amplicons of targeted NGS

Colon&Lung V2
CLAPv1

Fragment analysis products

225bp

142bp

Distribution of alterations in the MET exon14 region as decribed in Frampton *et al.* [15]

MET exon 14 skipping: METSkipper14

Exon 13 | Exon 14 | Exon15

Splice Junction

116411903   116412043

METSkipper14 is a tool to detect MET exon 14 skipping events from RNA-seq data.

Inputs – *filename.SJ.out.tab*
Output – *filename.SJ.out_output.tab*

splice_start	splice_end	portion_spliced	unique_mapping_reads
116411709	116411912	0.070921986	24
116411709	116414934	1	26

How METSkipper14 works?

- METSkipper14 assumes that the Splice Junction is a region(let's call it SJR) instead of just junction coordinates.

- It checks that how much the SJR and exon 14 are encompassing/overlapping each other calculates the portion of skipped portion in reference to exon 14.

- An ideal proportion of skipping will be 100% with good number of support reads.

MET exon 14 skipping: Detection and Validation

Results

DNA-seq

1. We detected the irregularities in exon 14 boundaries(MET) of **31(0.7%)** samples out of **3927** samples (8 out of 687 – **1.16%**)
2. Only **10(lung n=5)** samples out of these were categorized into the splicing consequence including the GT/AG site

RNA-seq

1. Out of these samples(31), the RNA-seq data was available for 24 samples, hence they were taken forward for validation using the RNA-seq algorithm
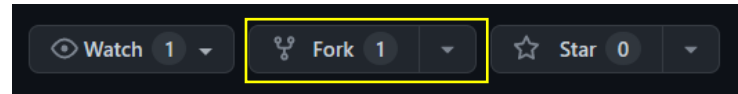2. Only **two samples** reported to have the splice junction indicating exon 14 skipping.
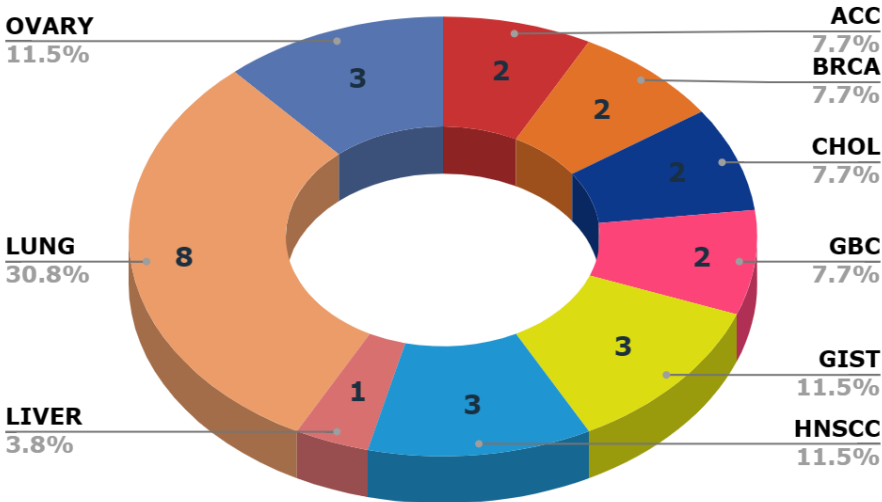
sample	Cancer	POS	VAR	DP	AB	RNA	SpliceJunction	DETECTED IN RNA	Intron-motif	ReadSupport
VF3D	CHOL	116412043	G>GACA	35	8.6	YES	116409846-116419318	YES	non-canonical	2
VEFD	**LUNG**	116411902	G>C	68	32.4	YES	116411709-116414934	**YES**	**canonical - GT/AG**	26
VK2D	**LUNG**	116411901	AGATCTGGGCAGTGAATTAG>A	207	21.7	NA	NA	NO	NA	NA

4baseCare
Together. We Beat Cancer

GitHub

https://github.com/spKrispy/metskipper

Fork the repo and make changes to the original code if required

Watch 1 Fork 1 Star 0

Raise issues, find solution. And stop facing them repeatedly

Issues Pull requests Actions
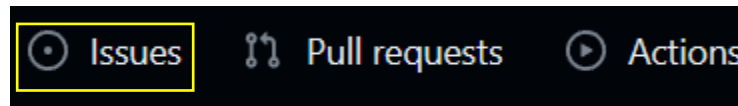
Sync new changes from original code, and stay up-to-date