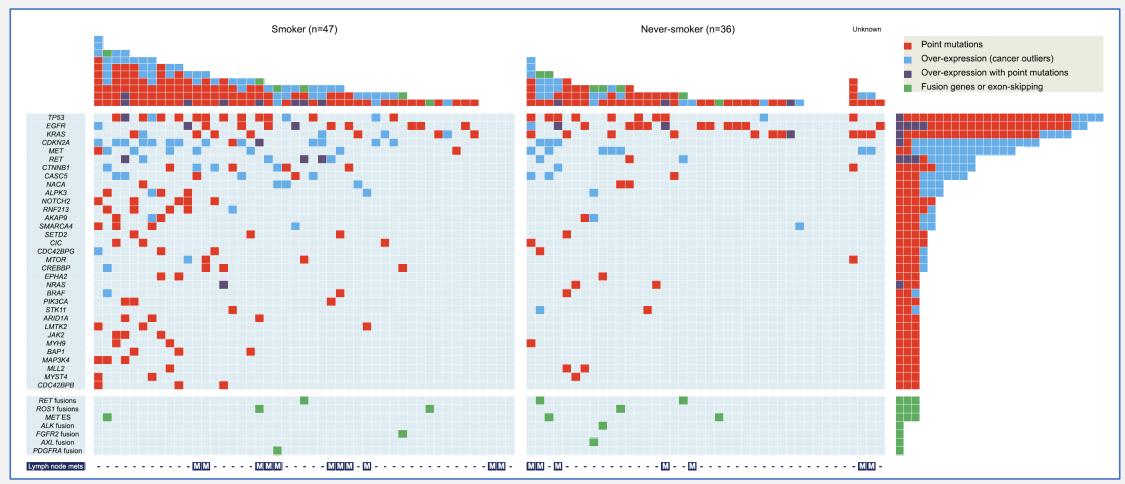
Effects of Smoking on Gene Expression in South Korean Patients with Lung Adenocarcinomas

Jess White

ANGSD 2020

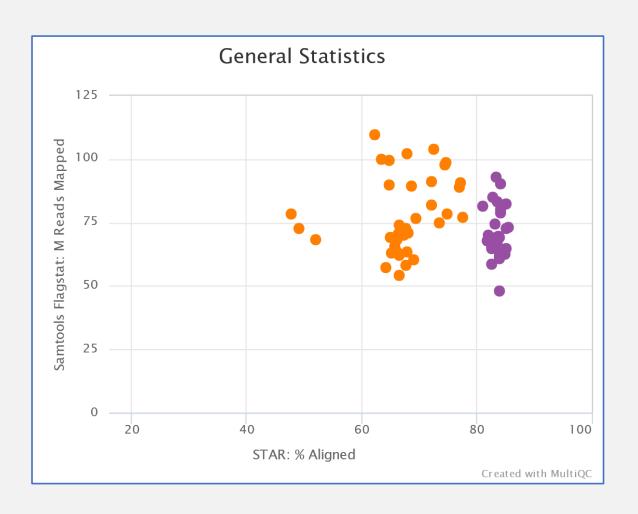
April 14, 2020

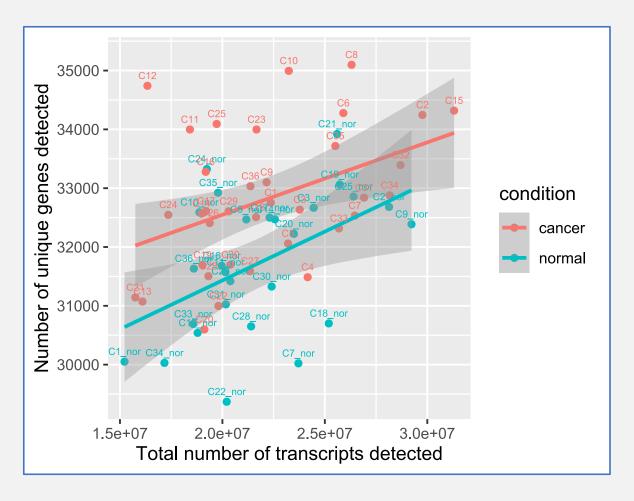
Lung adenocarcinomas of smokers are associated with a distinct genetic signature and higher mutational burden



Source: Seo et al., Genome Research, 2012.

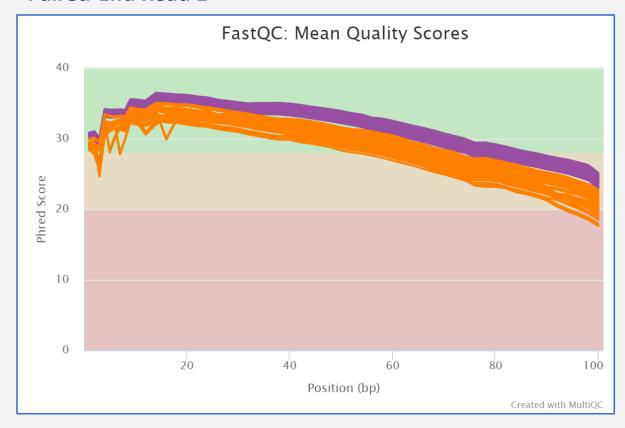
Paired-normal samples aligned at a higher rate than tumor biopsies, but tumor biopsies expressed more unique genes





Phred scores were worse for tumor biopsies and demonstrably worse for paired-end read 2 than paired-end read 1

Paired-End Read 1



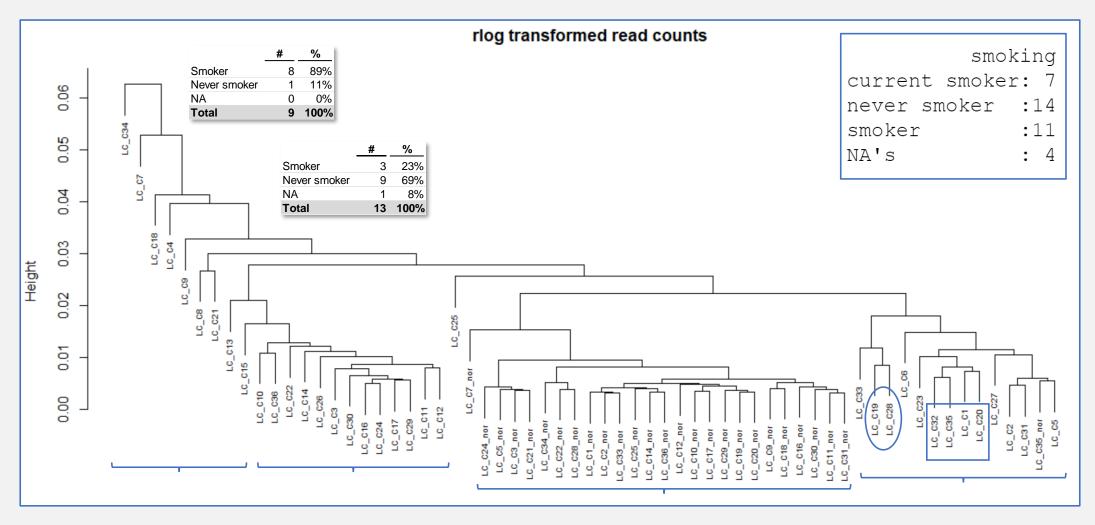
Paired-End Read 2



BLAST alignment of small subset unmapped cancer sample reads suggests tumor mutational burden complicates mapping

```
Query #4: ERR164585.41770307 0:N: 00 Query ID: lcl Query 32913 Length: 101
Sequences producing significant alignments:
                                                              Max
                                                                    Total Query
                                                                                     Per.
Description
                                                              Score Score cover Value Ident
Homo sapiens protein disulfide isomerase family A member 4...
                                                                          100% 2e-36 94.06
                                                              154
Homo sapiens protein disulfide isomerase family A member 4...
                                                                          100% 2e-36 94.06
                                                              154
Homo sapiens protein disulfide isomerase family A member 4...
                                                             154
                                                                          100% 2e-36 94.06
Homo sapiens protein disulfide isomerase family A member 4...
                                                                          100% 2e-36 94.06
                                                              154
                                                                    154
Homo sapiens protein disulfi
Homo sapiens protein disulfi Alignments:
Homo sapiens protein disulfi|>Homo sapiens protein disulfide isomerase family A member 4 (PDIA4), transcript variant 5, non-coding RNA
Homo sapiens protein disulfi Sequence ID: NR_163906.1 Length: 2597
                           Range 1: 1780 to 1880
                          Score: 154 bits(83), Expect: 2e-36,
                          Identities:95/101(94%), Gaps:0/101(0%), Strand: Plus/Plus
                          Query 1
                                       AGAGATCTGGAGCATTTGAGCAAGTTTATAGAAGAACATGCCACAATACTGAGCAGGACT
                                       AGAGATCTGGAGCATTTGAGCAAGTTTATAGAAGAACATGCCACAAAACTGAGCAGGACC 1839
                          Query 61
                                       AAGGAAGTGCTTGTAAGGCCTGAGGTCTGCTGAAGGTGGGA
                                       AAGGAAGAGCTTTGAAGGCCTGAGGTCTGCGGAAGGTGGGA
```

Hierarchical clustering reveals distinct normal cluster and suggests smoking and non-smoking clusters may be distinct



Many of the most differentially expressed genes were pseudogenes or IncRNA, but some were known lung cancer targets

geneid	padj	SYMBOL
ENSG00000164330	1.56E-59	EBF1
ENSG00000234518	1.24E-56	PTGES3P1
ENSG00000175166	1.46E-53	PSMD2
ENSG00000259447	5.33E-51	RP11-462P6.1
ENSG00000262855	2.07E-45	RP11-46I8.4
ENSG00000287199	3.33E-45	NA
ENSG00000172167	4.42E-45	MTBP
ENSG00000172724	4.95E-45	CCL19
ENSG00000282975	6.30E-44	RP11-59J16.3
ENSG00000254781	9.07E-44	GVINP2
ENSG00000235232	4.98E-43	MRPS18BP2
ENSG00000245729	3.44E-41	RP11-480D4.1
ENSG00000287006	6.55E-41	NA
ENSG00000260806	7.40E-41	RP11-872J21.3
ENSG00000176083	1.02E-40	ZNF683
ENSG00000281696	2.96E-40	MIR664A
ENSG00000183631	9.01E-40	PRR32
ENSG00000260472	2.76E-39	CTD-2358C21.2
ENSG00000261293	3.68E-39	RP11-276H1.2
ENSG00000150995	5.03E-39	ITPR1
ENSG00000274937	5.06E-39	CTD-2311M21.4
ENSG00000274210	2.10E-38	U1
ENSG00000257668	2.87E-38	RP11-58A17.2
ENSG00000252943	2.90E-38	RNU6-264P
ENSG00000270241	3.79E-38	RP4-657M3.2

EBF1-mediated upregulation of ribosome assembly factor PNO1 contributes to cancer progression by negatively regulating the p53 signaling pathway

Aling Shen, Youqin Chen, Liya Liu, Yue Huang, Hongwei Chen, Fei Qi, Jiumao Lin, Zhiqing Shen, Xiangyan Wu, Meizhu Wu, Qiongyu Li, Liman Qiu, Na Yu, Thomas J. Sferra, and Jun Peng

Medicine (Baltimore). 2018 Aug; 97(35): e12021.

Published online 2018 Aug 21. doi: 10.1097/MD.000000000012021

PMCID: PMC6392579

PMID: <u>30170409</u>

Hyper expression of MTBP may be an adverse signal for the survival of some malignant tumors

A data-based analysis and clinical observation

Yantao Mao, Mei Tian, Bo Pan, Qingshan Zhu, Paiyun Li, Hongmei Liu, Weipeng Liu, Mingtao Dai, Lili Yu, and Yuan Tian, MD, PhDf,*

J Allergy Clin Immunol. 2018 Oct;142(4):1257-1271.e4. doi: 10.1016/j.jaci.2017.12.998. Epub 2018 Jan 31.

CCL19-producing fibroblastic stromal cells restrain lung carcinoma growth by promoting local antitumor T-cell responses.

Cheng HW¹, Onder L¹, Cupovic J¹, Boesch M¹, Novkovic M¹, Pikor N¹, Tarantino I², Rodriguez R³, Schneider T⁴, Jochum W³, Brutsche M⁴, Ludewig B⁵.