

Med&Omix

Second Meeting Query-ing

Previously Discussed in Med&Omix Meeting

- How to use cBioPortal
- How to apply on our hypothesis

So, I basically will do simple dry-testing of an hypothesis

Let's Decide A Simple Hypothesis

- I found this article on «**Utilizing Publicly Available Cancer Clinicogenomic Data on CBioPortal to Compare Epidermal Growth Factor Receptor Mutant and Wildtype Non-Small Cell Lung Cancer**»

Utilizing Publicly Available Cancer Clinicogenomic Data on CBioPortal to Compare Epidermal Growth Factor Receptor Mutant and Wildtype Non-Small Cell Lung Cancer

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<https://www.cureus.com/articles/57441-utilizing-publicly-available-cancer-clinicogenomic-data-on-cbioportal-to-compare-epidermal-growth-factor-receptor-mutant-and-wildtype-non-small-cell-lung-cancer#references>


Let's Decide A Simple Hypothesis

- Then looked for an alternative disease with alternative mutation...
Later, found this «**Oncogenic driver mutations predict outcome in a cohort of head and neck squamous cell carcinoma (HNSCC) patients within a clinical trial**»

HPV status

Article | [Open Access](#) | [Published: 06 October 2020](#)

Oncogenic driver mutations predict outcome in a cohort of head and neck squamous cell carcinoma (HNSCC) patients within a clinical trial

[Javier Fernández-Mateos](#), [Jéssica Pérez-García](#), [Raquel Seijas-Tamayo](#), [Ricard Mesía](#), [Jordi Rubió-Casadevall](#), [Carlos García-Girón](#), [Lara Iglesias](#), [Alberto Carral Maseda](#), [Juan Carlos Adansa Klain](#), [Miren Taberna](#), [Silvia Vazquez](#), [María Asunción Gómez](#), [Edel del Barco](#), [Alberto Ocana](#), [Rogelio González-Sarmiento](#)  & [Juan Jesús Cruz-Hernández](#) 

[Scientific Reports](#) **10**, Article number: 16634 (2020) | [Cite this article](#)

1882 Accesses | **4** Citations | [Metrics](#)

<https://www-nature-com.libproxy1.nus.edu.sg/articles/s41598-020-72927-2>

Let's Decide A Simple Hypothesis

- They are the ones referred in the article, so I will test how much consistent across all these datasets

Next-generation sequencing (NGS) has helped to identify genetic alterations that could be used as a molecular vulnerability for therapeutic discovery and target optimization. In addition, they could have a prognosis utility as biomarkers of response in different tumour types including head and neck squamous cell carcinomas^{16,17}. For instance, the analysis of *The Cancer Genome Atlas* (TCGA) described the molecular landscape of HPV-positive and HPV-negative HNSCC as having molecular alterations not reported before¹⁸. Since the first description of the recurrently mutated genes in HNSCC¹⁹, additional studies have included other genes such as *TP53*, *NOTCH1*, *PIK3CA*, *CDKN2A*, *CCDN1*, *HRAS*, *FAT1*, *FBXW7* and *FGFR3*, among others^{20,21}. For this reason, targeted sequencing has become a flexible tool to study those genes previously reported as mutated in HNSCC²¹.

To contribute to the understanding of how somatic mutations influence the outcome of HNSCC treatment, we have studied a panel of 26 genes (Table S1) by next-generation sequencing in a homogeneously treated locally advanced HNSCC Spanish cohort. In this study

Sections	Figures	References
		Rizzo, G., Black, M., Mymryk, J. S., Barrett, J. W. & Nichols, A. C. Defining the genomic landscape of head and neck cancers through next-generation sequencing. <i>Oral Dis.</i> 21 , e11–e24 (2015). CAS PubMed Article Google Scholar
		Stransky, N. <i>et al.</i> The mutational landscape of head and neck squamous cell carcinoma. <i>Science</i> 333 , 1157–1160 (2011). ADS CAS PubMed PubMed Central Article Google Scholar
		Network, T. C. G. A. Comprehensive genomic characterization of head and neck squamous cell carcinomas. <i>Nature</i> 517 , 576–582 (2015). ADS Article CAS Google Scholar

How to apply on

- Selected these datasets available

The screenshot shows the cBioPortal website interface. At the top, there is a navigation bar with links: Data Sets, Web API, R/MATLAB, Tutorials/Webinars, FAQ, News, Visualize Your Data, About, and cBioPortal Installations. A 'Login' button is on the right. Below the navigation bar, there is a 'Query' section with 'Quick Search Beta!' and 'Download' links. A citation prompt says 'Please cite: Cerami et al., 2012 & Gao et al., 2013'. The main content area is titled 'Select Studies for Visualization & Analysis:'. It shows '3 studies selected (629 samples)' and a 'Deselect all' link. A search bar is present. On the left, a list of cancer types is shown with sample counts: CNS/Brain (23), Cervix (2), Esophagus/Stomach (17), Eye (5), Head and Neck (14), Kidney (17), Liver (9), Lung (29), and Lymphoid (20). The 'Head and Neck' category is selected. In the center, a list of studies is shown under the heading 'Head and Neck'. The studies are: 'Recurrent and Metastatic Head & Neck Cancer (MSKCC, JAMA Oncol ...)' (151 samples), 'Head and Neck Squamous Cell Carcinoma' (74 samples), 'Head and Neck Squamous Cell Carcinoma (Johns Hopkins, Science...)' (32 samples), 'Head and Neck Squamous Cell Carcinoma (TCGA, Firehose Legacy)' (530 samples), 'Head and Neck Squamous Cell Carcinoma (TCGA, Nature 2015)' (279 samples), 'Head and Neck Squamous Cell Carcinoma (TCGA, PanCancer Atlas)' (523 samples), and 'Oral Squamous Cell Carcinoma (MD Anderson, Cancer Discov 2013)' (40 samples). The 'Head and Neck Squamous Cell Carcinoma' and 'Head and Neck Squamous Cell Carcinoma (Johns Hopkins, Science...)' studies are selected. Below this, the 'Nasopharyngeal Carcinoma' category is shown with one study: 'Nasopharyngeal Carcinoma (Singapore, Nat Genet 2014)' (56 samples). At the bottom, there are buttons for 'Query By Gene' and 'Explore Selected Studies'. On the right side of the interface, there is a 'What's New' section with a tweet from @cbioportal and a 'Subscribe' button. Below that, there is an 'Example Queries' section with a list of queries: 'Primary vs. metastatic prostate cancer', 'RAS/RAF alterations in colorectal cancer', 'BRCA1 and BRCA2 mutations in ovarian cancer', 'POLE hotspot mutations in endometrial cancer', 'TP53 and MDM2/4 alterations in GBM', 'PTEN mutations in GBM in text format', 'Patient view of an endometrial cancer case', and 'All TCGA Pan-Cancer'.

3 studies selected (629 samples) Deselect all

Search...

Select all listed studies matching filter (14)

Head and Neck

☐ Recurrent and Metastatic Head & Neck Cancer (MSKCC, JAMA Oncol ...)

151 samples

Head and Neck Squamous Cell Carcinoma

☒ Head and Neck Squamous Cell Carcinoma (Broad, Science 2011)

74 samples

☒ Head and Neck Squamous Cell Carcinoma (Johns Hopkins, Science...)

32 samples

☐ Head and Neck Squamous Cell Carcinoma (TCGA, Firehose Legacy)

530 samples

☐ Head and Neck Squamous Cell Carcinoma (TCGA, Nature 2015)

279 samples

☒ Head and Neck Squamous Cell Carcinoma (TCGA, PanCancer Atlas)

523 samples

☐ Oral Squamous Cell Carcinoma (MD Anderson, Cancer Discov 2013)

40 samples

Nasopharyngeal Carcinoma

☐ Nasopharyngeal Carcinoma (Singapore, Nat Genet 2014)

56 samples

3 studies selected (629 samples) Deselect all

Query By Gene OR Explore Selected Studies

What's New @cbioportal

cBioPortal @cbioportal

Work on Open Source Software for a summer and support Cancer Research!

Paid internship - any age any background! Flexible schedule (175h or 350h projects)

Read more: github.com/cbioportal/gsoc


Sign up for low-volume email news alerts

Subscribe

Example Queries

- Primary vs. metastatic prostate cancer
- RAS/RAF alterations in colorectal cancer
- BRCA1 and BRCA2 mutations in ovarian cancer
- POLE hotspot mutations in endometrial cancer
- TP53 and MDM2/4 alterations in GBM
- PTEN mutations in GBM in text format
- Patient view of an endometrial cancer case
- All TCGA Pan-Cancer

How to apply on



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Query

Quick Search **Beta!**

Download

Please cite: [Cerami et al., 2012](#) & [Gao et al., 2013](#)

Selected Studies:

Modify

Head and Neck Squamous Cell Carcinoma (Broad, Science 2011)
Head and Neck Squamous Cell Carcinoma (TCGA, PanCancer Atlas)
Head and Neck Squamous Cell Carcinoma (Johns Hopkins, Science 2011) (629 total samples)

Select Molecular Profiles:

☒ Mutations ☒ Structural variants ☒ Copy number alterations

Select Patient/Case Set:
To build your own case set,
try out our enhanced Study View.

All (629)

x ▼

Enter Genes:

Hint: [Learn Onco Query Language \(OQL\)](#)
to write more powerful queries [↗](#)

User-defined List


x ▼

CDKN2A, TP53, NOTCH1, PIK3CA, CDKN2A, , HRAS, FAT1, FBXW7, FGFR3

☒ All gene symbols are valid.

How to apply on

Interesting relationships... For example, TP53 and HRAS are mutually exclusive, and TP53 and FAT1 co-occurs. However, FAT1 and HRAS co-occurs, too. (Need to check pathway details for this)



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Login

Modify Query



Combined Study (629 samples)
Querying 629 patients/samples in 3 studies **CDKN2A, TP53 & 6 other genes**

Queried genes are altered in 547 (87%) of queried patients/samples

[OncoPrint](#) [Cancer Types Summary](#) [Mutual Exclusivity](#) [Plots](#) [Mutations](#) [Comparison/Survival](#) [CN Segments](#) [Pathways](#) [Download](#)

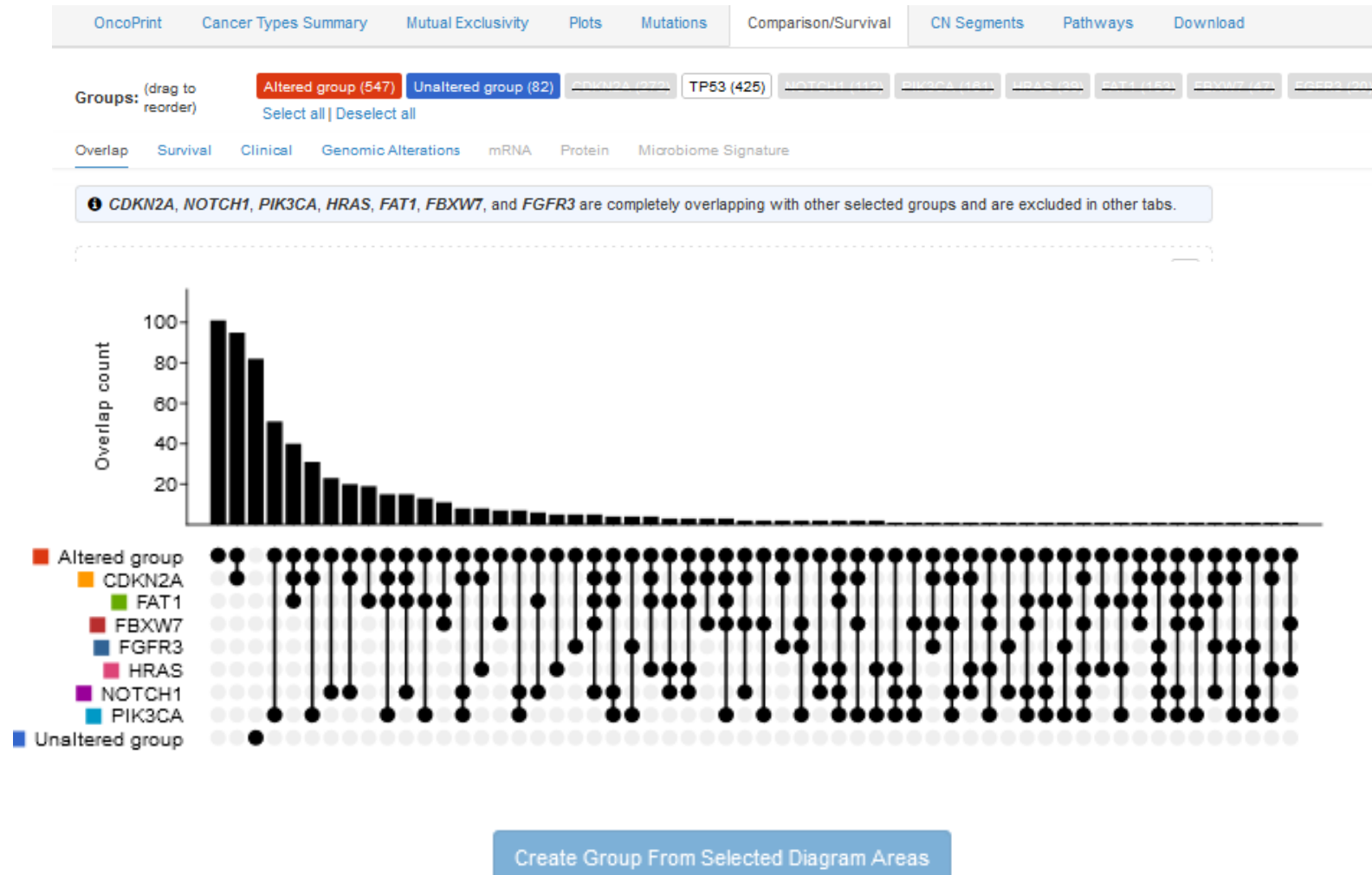
The analysis tested **28** pairs between the **8** tracks in the OncoPrint.

☒ Mutual exclusivity ☒ Co-occurrence ☐ Significant only

  Columns

A	B	Neither	A Not B	B Not A	Both	Log2 Odds Ratio	p-Value	q-Value ▲	Tendency
CDKN2A	TP53	149	45	197	224	1.913	<0.001	<0.001	Co-occurrence
CDKN2A	FAT1	288	175	58	94	1.415	<0.001	<0.001	Co-occurrence
TP53	HRAS	170	407	24	14	-2.037	<0.001	<0.001	Mutual exclusivity
FAT1	FBXW7	440	128	23	24	1.843	<0.001	<0.001	Co-occurrence
NOTCH1	FAT1	395	68	110	42	1.149	<0.001	0.002	Co-occurrence
CDKN2A	NOTCH1	300	205	46	64	1.026	<0.001	0.003	Co-occurrence
TP53	FAT1	160	303	34	118	0.874	0.003	0.011	Co-occurrence
NOTCH1	HRAS	481	96	24	14	1.547	0.003	0.011	Co-occurrence
TP53	FGFR3	182	414	12	7	-1.963	0.004	0.012	Mutual exclusivity
HRAS	FAT1	441	22	136	16	1.238	0.011	0.032	Co-occurrence
PIK3CA	FGFR3	449	147	10	9	1.459	0.029	0.075	Co-occurrence

How altered group is selected



If I look the survival data for all the genes

- It seems CDKN2A (correlated to HPV stats) alteration might be related to poor outcome in 0-50months period of survival, whereas HRA& NOTCH1 alteration has minimal or no direct effect on the survival.

	Number of Cases, Total	Number of Events	Median Months Overall (95% CI)
Unaltered group	60	16	68.48 (56.94 - NA)
CDKN2A	10	7	13.35 (10.75 - NA)
TP53	59	23	47.01 (26.43 - NA)
NOTCH1	5	0	NA
PIK3CA	24	5	210.97 (57.47 - NA)
HRAS	3	0	NA
FAT1	2	1	65.82
FBXW7	2	0	NA
FGFR3	2	0	NA

