

School of Medicine

UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

¹Department of Medicine, Division of Medical Oncology, University of Colorado - Anschutz Medical Campus, Aurora, CO

RESULTS

- | Fusion | Overall
Frequency | TCGA
PanCancer
(N= 10,967) | MSK IMPACT
(N= 10,945) | AACR GENIE
(N=96,324) |
|--------|----------------------|----------------------------------|---------------------------|--------------------------|
| EGFR | 0.6% (752) | 0.3% (27) | 0.8% (88) | 0.6% (637) |
| ERBB2 | 0.1% (173) | 0.5% (50) | <0.1% (10) | 0.1% (113) |
| ERBB4 | <0.1% (45) | <0.1% (7) | <0.1% (4) | <0.1% (34) |

Fusion Partner	TCGA	MSK IMPACT	AACR GENIE	Total
EGFR-SEPT14	13	2	12	27
SEPT14-EGFR			17	17
EGFR-VSTM2A	1		2	3
EGFR-LAMA2			3	3
VOPP1-EGFR			3	3
SEC61G-EGFR	2			2
EGFR-GBAS			2	2
EGFR-SEC61G			2	2
EGFR-TNS3			2	2
EGFR-VOPP1			2	2
EGFR-VSTM2A			2	2
ELDR-EGFR			2	2
ZNF713-EGFR			2	2

Mutation	Group 1 (Blue)	Group 2 (Black)
TP53	44	25
PTEN	15	22
RB1	7	5
BRCA1	2	1
BRCA2	1	1
NF1	4	4
GNAQ2	5	3
PIK3CA	12	8
EGFR	33	40
ERBB2	3	2
ERBB3	4	3
ERBB4	4	2

EGFR MSK IMPACT

Cancer Type	Frequency (%)
Breast Cancer	~0.05
Colorectal Cancer	~0.05
Prostate Cancer	~0.05
Non-Small Cell Lung Cancer	~0.25
Endometrial Cancer	~0.25
Cancer of Unknown Primary	~0.40
Skin Cancer, Non-Melanoma	~0.60
Glioma	~1.10

ERBB2 MSK IMPACT

Cancer Type	Frequency (%)
Non-Small Cell Lung Cancer	~0.05
Colorectal Cancer	~0.05
Prostate Cancer	~0.10
Breast Cancer	~0.20
Bladder Cancer	~0.20
Melanoma	~0.25
Esophagogastric Cancer	~0.25
Cancer of Unknown Primary	~0.50

ERBB4 MSK IMPACT

Cancer Type	Frequency (%)
Colorectal Cancer	~0.10
Non-Small Cell Lung Cancer	~0.12
Glioma	~0.18

EGFR TCGA

Cancer Type	Frequency (%)
Non-Small Cell Lung Cancer	~0.20
Hepatocellular Carcinoma	~0.20
Esophagogastric Adenocarcinoma	~0.30
Head and Neck Squamous Cell Carcinoma	~0.40
Bladder Urothelial Carcinoma	~0.60
Diffuse Glioma	~0.80
Glioblastoma	~1.80

ERBB2 TCGA

Cancer Type	Frequency (%)
Colorectal Adenocarcinoma	~0.10
Hepatocellular Carcinoma	~0.10
Ovarian Epithelial Tumor	~0.10
Head and Neck Squamous Cell Carcinoma	~0.10
Endometrial Carcinoma	~0.10
Non-Small Cell Lung Cancer	~0.10
Esophageal Squamous Cell Carcinoma	~0.10
Pancreatic Adenocarcinoma	~0.10
Cervical Squamous Cell Carcinoma	~0.10
Bladder Urothelial Carcinoma	~0.10
Esophagogastric Adenocarcinoma	~0.10
Invasive Breast Carcinoma	~0.10
Cervical Adenocarcinoma	~0.10
Undifferentiated Stomach Adenocarcinoma	~4.50

ERBB4 TCGA

Cancer Type	Frequency (%)
Non-Small Cell Lung Cancer	~0.08
Endometrial Carcinoma	~0.12
Ovarian Epithelial Tumor	~0.12
Head and Neck Squamous Cell Carcinoma	~0.15
Invasive Breast Carcinoma	~0.25

EGFR AACR GENIE

Cancer Type	Frequency (%)
Non-Small Cell Lung Cancer	~0.10
Hepatocellular Carcinoma	~0.10
Esophagogastric Adenocarcinoma	~0.20
Head and Neck Squamous Cell Carcinoma	~0.30
Bladder Urothelial Carcinoma	~0.40
Diffuse Glioma	~0.80
Glioblastoma	~1.80

ERBB2 AACR GENIE

Cancer Type	Frequency (%)
Pancreatic Cancer	~0.05
Glioma	~0.05
Colorectal Cancer	~0.05
Thyroid Cancer	~0.05
Melanoma	~0.05
Non-Small Cell Lung Cancer	~0.05
Hepatobiliary Cancer	~0.05
Prostate Cancer	~0.05
Mixed Cancer Types	~0.05
Head and Neck Cancer	~0.05
Cancer of Unknown Primary	~0.05
Skin Cancer, Non-Melanoma	~0.05
Endometrial Cancer	~0.05
Cervical Cancer	~0.05
Small Cell Lung Cancer	~0.05
Ovarian Cancer	~0.05
Bladder Cancer	~0.05
Breast Cancer	~0.10
Esophagogastric Cancer	~0.30
Vaginal Cancer	~0.50

ERBB4 AACR GENIE

Cancer Type	Frequency (%)
Glioma	~0.05
Colorectal Cancer	~0.05
Melanoma	~0.05
Prostate Cancer	~0.05
Cancer of Unknown Primary	~0.05
Non-Small Cell Lung Cancer	~0.05
Mature B-Cell Neoplasms	~0.05
Bladder Cancer	~0.05
Breast Cancer	~0.05
Leukemia	~0.05
Endometrial Cancer	~0.05
Thyroid Cancer	~0.05
Ovarian Cancer	~0.05
Mixed Cancer Types	~0.05
Soft Tissue Sarcoma	~0.05
CNS Cancer	~0.18

Fusion Partner	TCGA	MSK IMPACT	AACR GENIE	Total
ERBB2-				
PPP1R1B	10		1	11
ERBB2-IKZF3	6		4	10
ERBB2-CTTN	8			8
GRB7-ERBB2		2	4	6
C17orf37-ERBB2		2	2	4
ERBB2-PSMB3	3			3
ERBB2-TCAP	1		1	2
ERBB2-WIPF2	1		1	2
RARA-ERBB2		1	1	2
SHC1-ERBB2		1	1	2
ERBB2-CDK12			2	2
ERBB2-PGAP3			2	2
ERBB2-STARD3			2	2
IKZF3-ERBB2			2	2

Cancer Type	Blue Bar (%)	Black Bar (%)	Yellow Bar (%)
TP53	75	50	65
PTEN	20	20	20
RB1	10	10	2
BRCA1	2	10	3
BRCA2	8	7	9
NF1	10	10	2
CDKN2A	7	10	5
PIK3CA	18	10	4
EGFR	8	10	4
ERBB2	2	12	18
ERBB3	2	4	5
ERBB4	2	2	3

Cancer Type	Adenocarcinoma (%)	Squamous Cell Carcinoma (%)	Other (%)
TP53	55	55	55
PTEN	75	55	55
RB1	25	0	0
RRM1	0	15	0
ERCC4	0	0	0
NF1	25	15	15
KRAS	0	0	8
PIK3CA	28	25	12
EGFR	0	0	3
ERBB2	25	0	6
ERBB3	0	0	3
ERBB4	50	30	12

Fusion Partner	TCGA	MSK IMPACT	AACR GENIE	Total
ERBB4-TRIM33				3
ERBB4-PARD3B		1	1	
ERBB4-PXMP2		1	1	

ERBB2

TCGA

■ 16.67%
■ 80.00%
■ 3.33%

Total=30

ERBB2

MSK IMPACT

■ 40.00%
■ 60.00%

Total=6

ERBB2

AACR GENIE

■ 16.47%
■ 49.64%
■ 33.89%

Total=86

ERBB2

Total

■ 16.67%
■ 80.00%
■ 3.33%

Total=129

ERBB4

TCGA

■ 22.94%
■ 54.72%
■ 20.70%
■ 1.89%

Total=63

ERBB4

MSK IMPACT

■ 50.00%
■ 30.00%
■ 20.00%

Total=10

ERBB4

AACR GENIE

■ 28.57%
■ 50.00%
■ 10.00%
■ 11.43%

Total=70

ERBB4

Total

■ 28.57%
■ 50.00%
■ 10.00%
■ 11.43%

Total=133

ERBB4

TCGA

■ 57.14%
■ 42.86%

Total=7

ERBB4

MSK IMPACT

■ 100.00%

Total=2

ERBB4

AACR GENIE

■ 91.67%
■ 8.33%

Total=12

ERBB4

Total

■ 91.67%
■ 8.33%

Total=21

Figure 5. Co-occurring mutation rates in selected tumor suppressor genes and oncogenes.

- *EGFR*, *HER2* and *HER4* fusions are individually rare events but collectively represent up to 1% of all cancers, a significant number of patients with potentially actionable genomic alterations.
- These data highlight the importance of assaying for these mutations during clinical sequencing and suggest that further investigation into HER fusion biology and potential treatment options would be impactful.