RECENT ADVANCES IN BIOMARKER RESEARCH IN LUNG CANCER WITH SPECIAL REFERENCE TO NEW TARGETED THERAPIES.
Fred R. Hirsch, MD,PhD
Professor of Medicine and Pathology,
Univ. of Colorado Cancer Center, Aurora, CO, USA
Patients with the same diagnosis & clinical features (stage IV non-small cell lung cancer)

65 y/o male Smoker Squamous
KRAS Mt
High ERCC1
High RRM1

39 y/o female Never-Smoker Adenoca
EGFR Mt
Low ERCC1
Low RRM1

44 y/o female Never-Smoker Adenoca
ALK fusion

High EGFR IHC?
EGFR MUTATION TESTING

- DNA sequencing
- Allele specific amplification (i.e. DxS Scorpion-ARMS)
- Immunohistochemistry
- Circulating T-cells/DNA
Mutation specific antibodies

**EGF Receptor (L858R Mutant Specific) (43B2) Rabbit mAb**

- **Applications:**
  - Western blot
- **Species Cross-Reactivity:**
  - W, IP, ING, P, IF-IC, IF-P, F
- **Molecular Wt.:** 175 kDa
- **IsoType:** Rabbit IgG**

**Background:**
- EGF receptor (EGFR) is a 170 kDa transmembrane receptor tyrosine kinase that belongs to the HER/EGFR protein family. Somatic mutations in the tyrosine kinase domain of EGFR may be present in a subset of lung adenocarcinomas (1-3). Two types of mutations account for approximately 50% of mutated cases: a specific point mutation (L858R) which occurs in exon 21 and short in-frame deletions in exon 19 (4, 5). A common deletion in exon 19 is the deletion of E746-A750 (6), although other variants occur.
- **Specificity/Sensitivity:**
  - EGF (L858R Mutant Specific) (43B2) Rabbit mAb detects endogenous levels of EGFR mutant L858R protein. Due to cross-reactivity of this antibody, it may need to be used in ELISA or Western blotting to confirm the specificity.
- **Source/Purification:**
  - Monoclonal antibody is produced by immunizing animals with a synthetic peptide corresponding to L858R mutated sequence of human EGFR receptor.
- **Background References:**

**EGF Receptor (E746-A750del Specific) (6B6) XP® Rabbit mAb**

- **Applications:**
  - Western blot
- **Species Cross-Reactivity:**
  - W, IP, ING, P, IF-IC, IF-P, F
- **Molecular Wt.:** 175 kDa
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**Background:**
- EGF receptor (EGFR) is a 170 kDa transmembrane receptor tyrosine kinase that belongs to the HER/EGFR protein family. Somatic mutations in the tyrosine kinase domain of EGFR are present in a subset of lung adenocarcinomas (1-3). Two types of mutations account for approximately 50% of mutated cases: a specific point mutation (L858R) which occurs in exon 21 and short in-frame deletions in exon 19 (4, 5). A common deletion in exon 19 is the deletion of E746-A750 (6), although other variants occur.
- **Specificity/Sensitivity:**
  - EGF Receptor (E746-A750del Specific) (6B6) XP® Rabbit mAb detects endogenous levels of EGFR E746-A750del mutant protein.
- **Source/Purification:**
  - Monoclonal antibody is produced by immunizing animals with a synthetic peptide (KLH-coupled) corresponding to E746-A750del mutant sequence of human EGFR Receptor.
- **Selected Application References:**
- **Background References:**
IHC with **Exon 19** Deletion-Specific antibody

IHC with **Exon 21** Point Mutation-Specific antibody
Association of the Expression of Mutant Epidermal Growth Factor Receptor Protein as Determined with Mutation-Specific Antibodies in Non-small Cell Lung Cancer with Progression-Free Survival after Gefitinib Treatment

Azuma, Koichi; Okamoto, Isamu; Kawahara, Akihiko; Taira, Tomoki; Nakashima, Kazutaka; Hattori, Satoshi; Kinoshita, Takashi; Takeda, Masayuki; Nakagawa, Kazuhiko; Takamori, Shinzo; Kuwano, Michihiko; Ono, Mayumi; Kage, Masayoshi
doi: 10.1097/JTO.0b013e3182eeba2
Veristrat®

- Pattern of proteins in pre-treatment serum measured by MALDI-TOF mass spectrometry
- Classifier trained and tested in samples from a dozen independent phase II cohorts
- Each patient's sample is classified as
  - “Good” ~ 60% of patients
  - “Bad” ~ 40% of patients
  - “Ugly” (indeterminate) ~ 1% of patients
BR.21 – Response and DCR: Proteomic Status is Predictive

<table>
<thead>
<tr>
<th></th>
<th>Proteomics Good (%)</th>
<th>Proteomics Poor (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD</td>
<td>76 (41.5%)</td>
<td>80 (73.4%)</td>
<td>156</td>
</tr>
<tr>
<td>SD</td>
<td>89 (48.6%)</td>
<td>28 (25.7%)</td>
<td>117</td>
</tr>
<tr>
<td>PR/CR</td>
<td>18 (9.8%)</td>
<td>1 (0.9%)</td>
<td>19</td>
</tr>
<tr>
<td>DCR</td>
<td>107 (58.5%)</td>
<td>29 (26.6%)</td>
<td>136</td>
</tr>
<tr>
<td>Total</td>
<td>183</td>
<td>109</td>
<td>292</td>
</tr>
</tbody>
</table>

ORR P = 0.002, DCR P = 0.0001
### Status

#### OS: Patients with Proteomics Signature Good

- **N=266**

<table>
<thead>
<tr>
<th></th>
<th>Median OS (mos)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>erlotinib</td>
<td>10.5</td>
<td>9.1 – 11.4</td>
</tr>
<tr>
<td>placebo</td>
<td>6.6</td>
<td>4.1 – 8.2</td>
</tr>
</tbody>
</table>

Hazard ratio = 0.63 (0.47 – 0.85)

*P = 0.002*

#### OS: Patients with Proteomics Signature Poor

- **N=170**

<table>
<thead>
<tr>
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<th>Median OS (mos)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>erlotinib</td>
<td>4.0</td>
<td>2.5 – 5.2</td>
</tr>
<tr>
<td>placebo</td>
<td>3.1</td>
<td>2.2 – 3.7</td>
</tr>
</tbody>
</table>

Hazard ratio = 0.77 (0.55 – 1.06)

*P = 0.107*

Interaction p value = 0.48
BR.21- Median OS erlotinib arm by biomarker

- EGFR FISH +: n=61, Median OS = 10.5 mos (CI: 7.9 - 13.0)
- EGFR FISH -: n=98, Median OS = 6.4 mos (CI: 4.7 - 8.0)
- EGFR MUT: n=34, Median OS = 10.9 mos (CI: 7.5 - 13.0)
- EGFR WT: n=170, Median OS = 7.9 mos (CI: 6.4 - 9.3)
- KRAS MUT: n=30, Median OS = 3.7 mos (CI: 2.1 - 5.6)
- KRAS WT: n=176, Median OS = 7.5 mos (CI: 6.0 - 9.0)
- Proteomic Good: n=266, Median OS = 10.5 mos (CI: 9.3 - 11.8)
- Proteomic Poor: n=170, Median OS = 3.98 mos (CI: 2.5 - 5.3)

Adapted from Zhu JCO 2008

Indicates median OS unselected patients BR21 with 95% Conf. Int.
Median OS = 6.7 mos (CI: 4.7 - 8.0)
PROSE Study

- Randomized VeriStrat stratified phase III study (275 pts.)
- Started March 2008
- Second line erlotinib versus chemotherapy
- Patients with inoperable NSCLC
- Primary endpoint: OS; secondary endpoint: PFS
- Italian multi-institutional study (Principal Investigators, V. Gregorc MD, Milan, Italy. Fred R. Hirsch MD, Colorado, Anna Spreatfico MD, Colorado )
BIOMARKER STUDIES TO BE STARTED AT A PRECLINICAL LEVEL
Gefitinib sensitive/resistant cell lines: Hierarchical clustering using genes with best prediction accuracy

Coldren CD et al; Mol Cancer Res 2006.

E-CADHERIN EXPRESSION

Coldren CD et al; Mol Cancer Res
2006.
EGFR Interacting Molecules

EGFR

ErbB3

E-CAD

HDAC

ZEB

Snail

AGGTG

CACCT

ECAD
**Hypothesis:** Entinostat will overcome resistance to erlotinib by reprogramming the tumor phenotype

**Dose & Schedule**
- ENT (10mg d1, d15 of 28d cycle) + ERL (150mg qd) vs. placebo + erlotinib (150mg qd)

**Patient Population:** N = 132
- Advanced NSCLC eligible for EGFR Therapy
- 2nd or 3rd line

**Endpoints:** 4 mos. PFS rate, PFS, ORR, OS
**Benchmark SOC:** PFS = 2.2 mos., OS = 6.7 mos.

**Biomarkers:** EGFR Mutations, KRAS, E-cadherin

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**ENCORE 401: PFS and OS in ITT Population**

**Progression-Free Survival**
- Placebo: median PFS 1.88 mos
- Entinostat: median PFS 1.97 mos

**Hazard ratio 0.99 (95% CI: 0.68, 1.44)**

**P = 0.98 by stratified log-rank test**

**Overall Survival**
- Placebo: median OS 6.7 mos
- Entinostat: median OS 8.9 mos

**Hazard ratio 0.91 (95% CI: 0.61, 1.36)**

**P = 0.65 by stratified log-rank test**

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**ENCORE 401: Survival by E-Cadherin Levels**

**Kaplan-Meier Estimates of OS by Subgroup**

- E-Cadherin +3 (N = 26)
  - Placebo: median OS 5.4 mos
  - Entinostat: median OS 9.4 mos
  - Hazard ratio 0.36 (95% CI: 0.14, 0.94)
  - **P = 0.03 by stratified log-rank test**

- E-Cadherin +1, +2 (N = 40)
  - Placebo: median OS 7.0 mos
  - Entinostat: median OS 4.4 mos
  - Hazard ratio 1.25 (95% CI: 2.57)
  - **P = 0.55 by stratified log-rank test**

**Kaplan-Meier Estimates of PFS by Subgroup**

- E-Cadherin +3 (N = 26)
  - Placebo: median PFS 1.9 mos
  - Entinostat: median PFS 3.7 mos
  - Hazard ratio 0.55 (95% CI: 0.22, 1.36)
  - **P = 0.19 by stratified log-rank test**

- E-Cadherin +1, +2 (N = 40)
  - Placebo: median PFS 1.9 mos
  - Entinostat: median PFS 1.7 mos
  - Hazard ratio 1.36 (95% CI: 0.70, 2.67)
  - **P = 0.36 by stratified log-rank test**

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Witta, Bunn and Hirsch et al: J Clin Oncol, June 2012
Hepatocyte growth factor (HGF)/MET signaling pathway transduces invasive growth signals from mesenchymal to epithelial cells.
OAM4558g Study Design: Global, Double-Blind, Placebo-Controlled, Phase II Study

Key Eligibility:
- Stage IIIB/IV NSCLC
- 2nd/3rd-line NSCLC
- Tissue Required
- PS 0-2

Co-Primary Objectives:
- PFS in “Met High” patients
- PFS in overall ITT population

Other Key Objectives:
- OS in “Met High” patients
- OS in Overall ITT patients
- Overall Response Rate
- Safety/Tolerability

Arm A
- Erlotinib (150 qd-oral) + MetMAb (15 mg/kg IV q3w)

Arm B
- Erlotinib (150 qd-oral) + Placebo (IV q3w)

Stratification Factors:
- Tobacco History
- Performance Status
- Histology

Addition of MetMAb* if eligible

1:1 Randomization

n = 128

n = 64

n = 64

n = 23

- Enrollment from 3/2009 to 3/2010
- Data cut off: June 8, 2010
PFS and OS: Met High Population

**PFS, HR=0.56**

- Median PFS (wk): 6.4 (Erlotinib + Placebo) vs. 12.4 (Erlotinib + MetMAb)
- Hazard ratio: 0.56
- 95% CI: 0.31–1.02
- Log-rank p-value: 0.0547
- # Events: 25 (Erlotinib + Placebo) vs. 19 (Erlotinib + MetMAb)

**OS, HR=0.55**

- Median OS (mo): 7.4 (Erlotinib + Placebo) vs. 7.7 (Erlotinib + MetMAb)
- Hazard ratio: 0.55
- 95% CI: 0.26–1.16
- Log-rank p-value: 0.1113
- # Events: 20 (Erlotinib + Placebo) vs. 13 (Erlotinib + MetMAb)

**Number at Risk:**

- Erlotinib + Placebo: 30 (PFS) vs. 30 (OS)
- Erlotinib + MetMAb: 35 (PFS) vs. 35 (OS)

**Summary:**

MetMAb+Erlotinib improves both PFS and OS in Met High NSCLC patients.
FLEX
(Pirker et al., Lancet Oncol. 2011 Nov 3)

- Eligibility Criteria: EGFR-expressing, advanced stage NSCLC; No prior CT
- Primary Endpoint: Median overall survival (845 events needed)
- Secondary Endpoints: Survival rate (1 and 2 y), PFS rate (6 and 12 mo), response rate, safety, QoL
- Sample Size: 1100 in 170 centers in EU, Latin America, Asia

FLEX Overall Survival

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Median OS</th>
<th>1-year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT + Cetuximab (n=557)</td>
<td>11.3 mo</td>
<td>47%</td>
</tr>
<tr>
<td>CT (n=568)</td>
<td>10.1 mo</td>
<td>42%</td>
</tr>
</tbody>
</table>

HR=0.871 (95% CI 0.762–0.996), p=0.044

BMS 099 Treatment Schema
(Lynch et al., J Clin Oncol. 2010 Feb 20;28(6):911-7)

- Paclitaxel 225 mg/m² d1* or Docetaxel 75 mg/m² d1*
  + Carboplatin AUC=6 d1 Q3wk for a maximum of 6 cycles
  + Cetuximab 400 mg/m² d1 wk1; 250 mg/m² weekly

R 1:1

BMS 099 Progression-Free Survival Per IRRC

- Cetux + Taxane/Carbo; n = 338 (4.40 mos)
- Taxane/Carbo; n = 338 (4.24 mos)

HR = 0.902
95% CI = 0.761 – 1.069
Stratified log-rank p value = 0.2358

Overall Survival: All Patients

- Cetuximab + TC; n = 338 (277 events)
- TC; n = 338 (287 events)

HR (95% CI) = 0.890 (0.754 – 1.051)
Stratified log-rank P value = 0.17

9.69 mo
(95% CI 8.28–11.50)

8.38 mo
(95% CI 7.33–9.92)
EGFR IHC score first described in 2003 in relation to EGFR-targeted therapy

Epidermal Growth Factor Receptor in Non–Small-Cell Lung Carcinomas: Correlation Between Gene Copy Number and Protein Expression and Impact on Prognosis

By Fred R. Hirsch, Marileila Varella-Garcia, Paul A. Bunn Jr, Michael V. Di Maria, Robert Veve, Roy M. Bremnes, Anna E. Barón, Chan Zeng, and Wilbur A. Franklin

Purpose: The epidermal growth factor receptor (EGFR) is frequently overexpressed in non-small-cell lung carcinoma (NSCLC), and EGFR inhibitors are promising new therapeutic agents. The molecular mechanisms responsible for EGFR overexpression are poorly understood.

Materials and Methods: Gene copy number and protein status of EGFR were investigated in microarrayed tumors from 183 NSCLC patients, including squamous cell carcinoma (SCC; 89 patients) and non-SCC (94 patients) histologies. Protein expression was assessed by immunohistochemistry on a scale from 0 to 400 (percentage of positive cells × staining intensity). Gene and chromosome 7 copy numbers were identified by fluorescent in situ hybridization (FISH).

Results: EGFR protein overexpression was observed in 62% of the NSCLC (25% scored 201 to 300; 37% scored 301 to 400), more frequently in SCC than non-SCC (82% vs 44%; P < .001), and in 80% of the bronchioloalveolar carcinomas.

The prevalent FISH patterns were balanced disomy (40%) and trisomy (38%) for EGFR gene and chromosome 7 (40%), whereas balanced polysomy was seen in 13% and gene amplification was seen in 9% of the patients. Gene copy number correlated with protein expression (r = 0.4; P < .001). EGFR overexpression or high gene copy numbers had no significant influence on prognosis.

Conclusion: EGFR overexpression is frequent in NSCLC, is most prominent in SCC, and correlates with increased gene copy number per cell. High gene copy numbers per cell showed a trend toward poor prognosis. It will be important to evaluate EGFR gene and EGFR protein status and signal protein expression to properly interpret future clinical trials using EGFR inhibitors.


**FLEX: overall survival; UNSELECTED**

<table>
<thead>
<tr>
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</tr>
<tr>
<td>CT (n=568)</td>
<td>10.1 mo</td>
<td>42%</td>
</tr>
</tbody>
</table>

HR = 0.87 (95% CI: 0.76–1.0) p = 0.04

---

**Selected**

**FLEX survival: high EGFR expression**

**Caucasian patients**

<table>
<thead>
<tr>
<th></th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=282</td>
<td></td>
</tr>
<tr>
<td>CT + cetuximab</td>
<td>11.4 mo</td>
</tr>
<tr>
<td>CT</td>
<td>7.9 mo</td>
</tr>
</tbody>
</table>

HR* = 0.64 (95% CI: 0.49–0.83)

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**FLEX survival: high EGFR expression**

**Caucasian patients with adenocarcinoma**

<table>
<thead>
<tr>
<th></th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=94</td>
<td></td>
</tr>
<tr>
<td>CT + cetuximab</td>
<td>20.2 mo</td>
</tr>
<tr>
<td>CT</td>
<td>8.0 mo</td>
</tr>
</tbody>
</table>

HR* = 0.49 (95% CI: 0.29–0.81)

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CT, chemotherapy; HR, hazard ratio; CI, confidence interval

*Unaddressed

## Concurrent or Sequential Chemotherapy + Cetuximab in S0342: Analysis by EGFR FISH

<table>
<thead>
<tr>
<th>EGFR FISH</th>
<th>OR (CR/PR)</th>
<th>DCR (CR/PR/SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FISH-</td>
<td>26%</td>
<td>55%</td>
</tr>
<tr>
<td>FISH+</td>
<td>45%</td>
<td>81%**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(p=0.02)</td>
</tr>
</tbody>
</table>

### Progression Free Survival by FISH Score Group

- **1-4 Low**: 31/31, Median in Months: 3 (2,4)
- **5-6 High**: 41/45, Median in Months: 6 (5,7)

Logrank P-value = .0008

### Overall Survival by FISH Score Group

- **1-4 Low**: 25/31, Median in Months: 7 (4.11)
- **5-6 High**: 29/45, Median in Months: 15 (10.19)

Logrank P-value = .04

*Hirsch: JCO 26: 3351-3357. 2008*
S0819: Developing SWOG Phase III Study

PC: Paclitaxel: 200 mg/m² & Carboplatin: AUC = 6
  Cetuximab: 400 mg/m², then 250 mg/m² weekly
*In Bevacizumab Eligible: 15 mg/kg every 3 weeks (piloted in S0536)

Correlative Science:
- Tumor: EGFR/HER pathways; KRAS
- Genomic DNA: EGFR polymorphisms
- Plasma: Proteomic predictor

1505 patients (618 FISH +)

PFS is Primary Endpoint
Different Antibodies to Detect EGFR Expression

Extracellular Domain (ED)-Specific Antibodies: **3C6** or **31G7**

Intracellular Domain (ID)-Specific Antibody: **5B7**

**SOSC3** is reported to be a negative regulator of EGFR signaling.

**SOSC3** and **5B7** compete for same binding site on EGFR.
Prediction of Response to EGFR TKI Based on EGFR Protein Expression

Area Under Curve

<table>
<thead>
<tr>
<th>0.55</th>
<th>0.67</th>
<th>0.72</th>
<th>0.78</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-value</td>
<td>0.560</td>
<td>0.052</td>
<td>0.010</td>
</tr>
</tbody>
</table>
Proposed methods to detect *ALK*-positive tumors

- Four proposed methods of testing
  - Fluorescent in-situ hybridization (FISH)
  - Immunohistochemistry (IHC)
  - Reverse transcriptase polymerase chain reaction (RT-PCR)
  - DNA sequencing

Detection of ALK by IHC


Table 1. Interpretation of IHC staining on lung adenocarcinomas by three pathologists

<table>
<thead>
<tr>
<th></th>
<th>Lung Adenocarcinoma (n = 153)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>D5F3 antibody</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>100</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>99</td>
</tr>
<tr>
<td>Positive predictive value (%)</td>
<td>96</td>
</tr>
<tr>
<td>Negative predictive value (%)</td>
<td>100</td>
</tr>
<tr>
<td>κ statistic</td>
<td>0.94</td>
</tr>
</tbody>
</table>

*Of the pathologists' IHC interpretation as positive staining in predicting an ALK rearrangement
FGFR1 as a new target for therapy in lung cancer
Amplification of FGFR1 is relatively frequent in SCC

Sequencing 52 NSCLC cell lines revealed no FGFR1 kinase domain mutations
Dutt et al

Sequencing 94 SCC and 94 ADC tumors showed one mutation in ADC but no FGFR1 mutations in SCC
Weiss et al

FGFR1 Amplification may be the “Oncogenic Driving” event.

SNP Array
~21% of SCC and 3% of ADC
Amplification of 8p11-12
FGFR1 in this region

FGFR1 gene copy number varies in NSCLC

- 5/57 (9%) FGFR1 >4 (clusters)
- 15/57 (26%) FGFR1 >3
- 5/57 (9%) FGFR1:CH8 Ratio >2
Disease-Free and Overall Survival

**NSCLC**

- Disease-Free Survival Probability
- Logrank p = 0.012
- FGFR1 >= 2.36
- FGFR1 < 2.36

**SCC**

- Disease-Free Survival Probability
- Logrank p = 0.091
- FGFR1 >= 2.36
- FGFR1 < 2.36
THE FUTURE
How we should view our NSCLC patients

- Unknown, 33%
- KRAS, 25%
- EGFR, 15%
- ALK, 5%
- RET, 5%
- BRAF, 3%
- PI3K, 3%
- MET, 3%
- MEK1, 1%
- AKT1, 1%
- FGFR1, 1%
- VEGFR, 1%
- PDGFR, 1%
- ROS1, 1%
- HER2, 2%
Multiplexed Mutation Assays

Tumor Tissue

Resected Specimen

Core Biopsy

Multiplex PCR

SNaPshot® (Applied Biosystem)

Mass ARRAY SNP - Sequenom, Inc

10% Sensitivity and ~20ng DNA/multiplex reaction

Dias-Santagata, EMBO Mol Med 2:146, 2010
WHAT ABOUT SQUAMOUS CELL CARCINOMAS?
# Genomic alterations in cancer

### Structural variants
- Translocations
- Fusions
- Inversion

### Copy number alterations
- Amplifications
- Deletions
- LOH

### Point mutations
- Missense
- Nonsense
- Splice site
- Frameshift

Wild type: AGTGA
Mutant: AGAGA

### Gene expression
- Outlier expression
- Isoform usage
- Pathways & signatures

Adapted from: Roychowdhury et al. Sci Transl Med; 2012
Figurative depiction of the landscape of somatic mutations present in a single cancer genome.
Squamous cell lung cancer: complexity revealed by whole genome sequencing
New Target Therapy in Squamous Cell Carcinoma of the Lung

<table>
<thead>
<tr>
<th>Gen</th>
<th>Frequency</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>FGFR1 amplification</td>
<td>22% (15% CTGA)</td>
<td>FGFR TKIs</td>
</tr>
<tr>
<td>EGFRvIII mutation</td>
<td>5%</td>
<td>EGFR TKIs</td>
</tr>
<tr>
<td>PI3KCA mutation</td>
<td>3.6%</td>
<td>PI3KCA inhib.</td>
</tr>
<tr>
<td>EGFR TK mutation</td>
<td>3.4%</td>
<td>EGFR TKIs</td>
</tr>
<tr>
<td>DDR2 mutation</td>
<td>3.2%</td>
<td>Dasatanib Nilotinib</td>
</tr>
</tbody>
</table>

Okashi and Pao, *Cancer Discovery*, April 2011
Squamous Lung Cancer Consortium
Main Mission:

- **GENERAL:**
  - Stimulate research in this subgroup of patients:
  - Unmet Need!!

- **SPECIFICALLY:**
  - Develop and/or validate prognostic and predictive biomarkers
  - Develop clinical trials
  - Learn more about SCC- biology and identify new therapeutic targets
Squamous lung cancer consortium (SLCC): The funding teams:

1) University of Colorado Cancer Center
   - Coordinating PI: Dr. Fred R. Hirsch, MD, PhD

2) University of Michigan
   - Co-PI: Dr. David Beer, PhD

3) Duke University
   - Co-PI: Dr. David Harpole, MD, PhD

4) Brigham & Womens/Harvard
   - Co-PI: Dr. Raphael Bueno, MD

5) University of California Davis
   - Co-PI: Dr. David Gandara, MD

6) Princess Margaret Hospital, Toronto, Canada
   - Co-PIs: Dr. Ming Tsao, MD/ Frances Shepherd, MD

7) Washington University, St.Louis
   - Co-PI: Ramaswamy Govindan, MD

8) Mayo Clinic
   - Co-PI: Kara Ballman, PhD
JOIN US FOR OUR UPCOMING MEETINGS

5th Latin American Conference on Lung Cancer
JULY 25–27, 2012
RIO DE JANEIRO, BRAZIL
WWW.LALCA2012.ORG

5th Asia Pacific Lung Cancer Conference
November 26–28, 2012
Fukuoka, Japan
www.aplcc2012.org

Multidisciplinary Symposium in Thoracic Oncology
September 6–8, 2012
Chicago, USA
www.thoracicsymposium.org

15th World Conference on Lung Cancer
OCTOBER 27–30, 2013
SYDNEY, AUSTRALIA
WWW.2013WORLDLUNGCANCER.ORG

BECOME A MEMBER OF IASLC WWW.IASLC.ORG