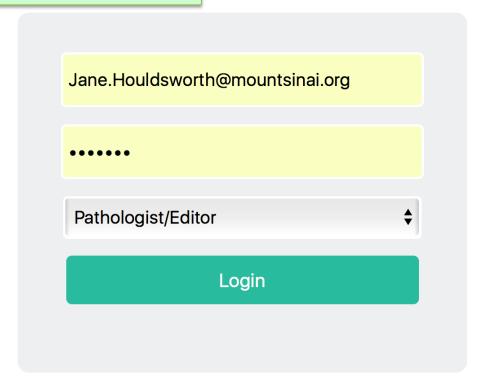
# Login

User name: email address

Select role: Pathologist/Editor (Admin)

PSW:12345678 (for all editor by default)



• Editor end

#### Welcome Jane:

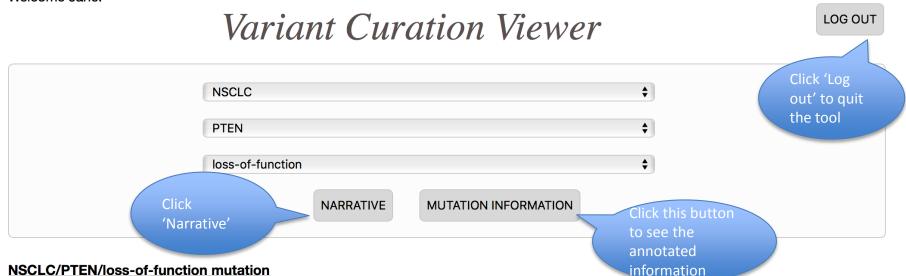
# Variant Curation Viewer

Select 'Tumor type'	Please select tumor type	<b>\$</b>
	Genes	<b>\$</b>
	Mutations	<b>\$</b>
	NARRATIVE MUTATION INFORMATION	

## Interface and steps of viewer:

- 1. Select 'Tumor type'
- 2. Select 'Gene'
- 3. Select 'Mutation'
- 4. Click 'NARRATIVE' / MUTATION INFORMATION'

Welcome Jane:



PTEN is mutated in 4-8% of non-small cell lung cancers [PMID: 20018398, PMID: 9598803, PMID: 20881644]. PTEN encodes a tumor suppressor that works as a phosphatase to convert PIP3 to PIP2 at the cell membrane [PMID: 18767981]. The loss-of-function mutations of PTEN result in PIP3 accumulation and AKT/mTOR signaling constitutive activation [PMID: 12040186].

#### NSCLC/PTEN/LOF mutation/Buparlisib (BKM120) (score R)

Buparlisib is a small molecule pan-Pl3K inhibitor of p110α/β/δ/γ [PMID: 24900266]. A phase II clinical trial evaluating buparlisib in pretreated metastatic NSCLC displaying Pl3K pathway activation showed no significant improved PFS [PMID: 26098748].



#### **NSCLC/PTEN/loss-of-function mutation**

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#### 1: NSCLC/PTEN/loss-of-function mutation

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Jane.Houldsworth@mountsinai.org: 2017-09-16 20:28:30: Testing NSCLC



#### 2: NSCLC/PTEN/LOF mutation/Buparlisib (BKM120) (score R)

Buparlisib is a small molecule pan-PI3K inhibitor of p110 $\alpha/\beta/\delta/\gamma$  [PMID: 24900266]. A phase II clinical trial evaluating buparlisib in pretreated metastatic NSCLC displaying PI3K pathway activation showed no significant improved PFS [PMID: 26098748].

Jane.Houldsworth@mountsinai.org: 2017-09-16 20:29:36: 2nd testing



# Version made by Admin and displayed in Editor end

## Modification of the narrative

#### MTC/RET/A883F

[Editing the comments from ADMIN 1st...][Editing the comments from ADMIN END 1st version of 2nd run]RET c.2647\_2648GC>TT is a missense mutation in exon 15 (codon 883). This mutation yields an alanine to phenylalanine change (A883F) in the intracellular tyrosine kinase domain. This mutation is causative for multiple endocrine neoplasia type 2b (MEN2B) [PMID: 16849421]. RET A883F occurs in 2-3% of MEN2B cases[PMID: 23059849].

#### MTC/RET/M918T/Sorafenib (score 2)

Sorafenib is a small molecule multi-targeted kinase inhibitor of Raf-1, BRAF, VEGFR2, KIT and RET [PMID: 15466206]. Although there is no specific RET inhibitor available and no FDA approved for treatment of MTC, some multikinase inhibitors including sorafenib are recommended for treatment of patients with MTC if clinical trials, vandetanib, or cabozantinib are not available or appropriate, or if the patient progresses on vandetanib or cabozantinib [NCCN Guidelines Version 2. 2017 Thyroid Carcinoma].

#### MTC/RET/M918T/Sunitinib (score 2)

Sunitinib is a small molecule multi-targeted RTK inhibitor of VEGFR2, KIT, PDGFR β and RET [PMID: 12646019]. Although there is no specific RET inhibitor available and no FDA approved for treatment of MTC, some multikinase inhibitors including sunitinib are recommended for treatment of patients with MTC if clinical trials, vandetanib, or cabozantinib are not available or appropriate, or if the patient progresses on vandetanib or cabozantinib [NCCN Guidelines Version 2. 2017 Thyroid Carcinoma].

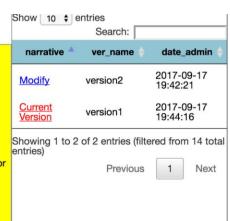
#### MTC/RET/M918T/Vandetanib (score 2)

Vandetanib is a small molecule multi-targeted kinase inhibitor of VEGFR2, EGFR and RET [PMID: 12183421]. Vandetanib is recommended for treatment of medullary thyroid cancer [NCCN Guidelines Version 2. 2017 Thyroid Carcinoma].

### paragraph 1:

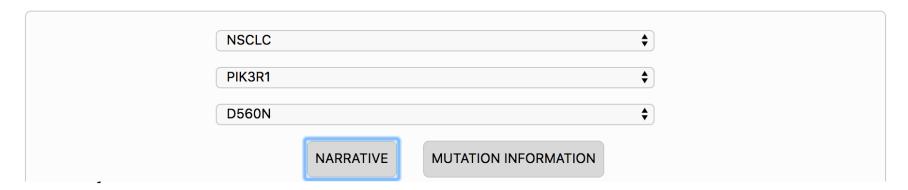
- jinlian.wang@mssm.edu: 2017-09-15 21:43:54: Testing... MTC
- jinlian.wang@mssm.edu: 2017-09-17 19:34:44: 2nd testing... MTC
- jinlian.wang@mssm.edu: 2017-09-17 19:34:55: 2nd testing... MTC
- jinlian.wang@mssm.edu: 2017-09-17 19:35:47: continue testing... MTC

paragraph 2:



# ADMIN END

# Admin End



#### 1: NSCLC/PIK3R1/D560N

PIK3R1 encodes the regulatory subunit (p85) of PI3K. Its mutations were found in 1.7% of NSCLCs [PMID: 27158780]. *PIK3R1* c.1678G>A is a missense mutation in the iSH2 domain and yields an aspartic acid to aasparagine change (D560N). The PIK3R1 D560N mutation accounts for about 5% of all PIK3R1 mutations in lung cancers [PMID: 27158780]. PIK3R1 D560N mutation likely results in loss of inhibition of the PI3K catalytic subunit and aberrant activation of downstream signaling pathways such as AKT/mTORpathway [PMID: 20713702, PMID: 9450999, PMID: 11606375, PMID: 15932879, PMID: 17626883, PMID: 18079394, PMID: 19962665, PMID: 21984976].

jinlian.wang@mssm.edu: 2017-09-17 19:16:16: last testing....

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Buparlisibis a small molecule pan-PI3K inhibitor of p110α/β/δ/γ [PMID: 24900266]. A phase II clinical trial evaluating buparlisibin pretreated metastatic NSCLC displaying PI3K pathway activation showed no significant improved PFS [PMID: 26098748].

jinlian.wang@mssm.edu: 2017-09-17 19:16:26: Color code works now



# Admin edit narrative

jinlian.wang@mssm.edu: 2017-09-17 19:16:16: last testing....

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Show 10 \$ entries

Showing 0 to 0 of 0 en

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Search:

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**Current Version** 

date admin

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jinlian.wang@mssm.edu: 2017-09-17 19:16

## Modify the narrative

## NSCLC/PIK3R1/D560N

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narrative highlighted

vellow

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#### paragraph 1:

jinlian.wang@mssm.edu: 2017-09-17 19:16:16: last testing....

#### paragraph 2:

jinlian.wang@mssm.edu: 2017-09-17 19:16:26: Color code works now

ALL COMMENTS SAVE NEW VERSION

Save any changes to current version