

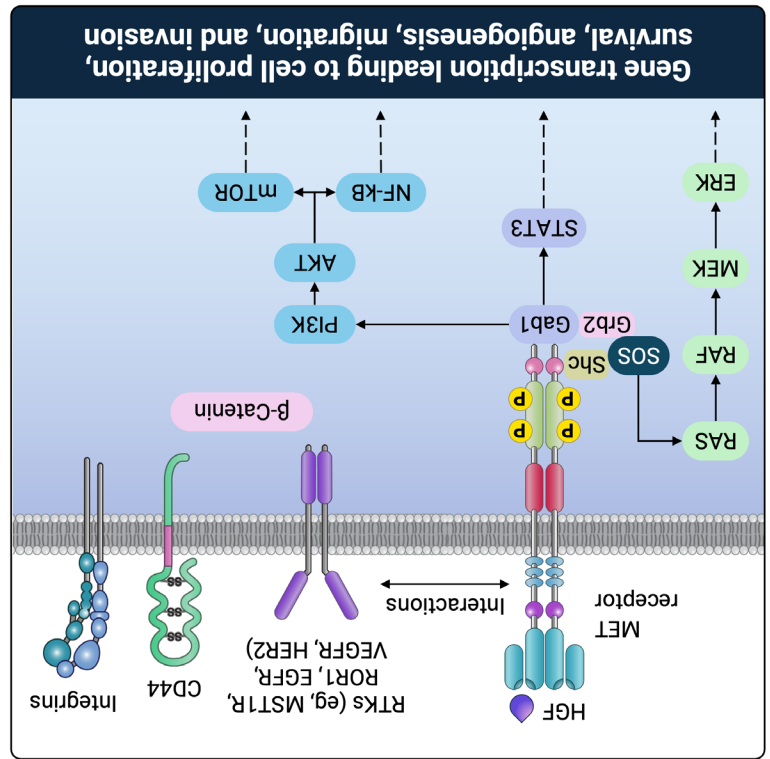
AKT=protein kinase B (or PKB); CD44=cluster of differentiation 44; EGFR=epidermal growth factor; ERK=extracellular signal-regulated kinases; Gab1=GRB2-associated-binding protein 1; Grb2=growth factor receptor-bound protein 2; HER2=human epidermal growth factor receptor 2; HGF=hepatocyte growth factor; HGF=hepatocyte growth factor receptor; MEK=mitogen-activated protein kinase; MST1R=macrophage-stimulating protein receptor 1; mTOR=mammalian target of rapamycin; NF-κB=nuclear factor-κB=rapidly accelerated fibrosarcoma; RAS=rat sarcoma virus protein; 3-kinases; RAF=rapidly accelerated fibrosarcoma; RAS=rat sarcoma virus protein; kapp-light-chain-enhancer of activated B cells; P=phosphate; PIK3=phosphatidylinositol 3-kinases; RAS=rapidly accelerated fibrosarcoma; RAS=rat sarcoma virus protein; ROR1=receptor tyrosine kinase-like orphan receptor 1; RTK=receptor tyrosine kinase; Shc=Src homology 2 domain-containing adaptor protein; SOS=son of sevenless protein (or guanine nucleotide exchange factor); STAT3=signal transducer and activator of transcription 3; VEGFR=vascular endothelial growth factor.

Image adapted from Spitaleri G, et al. *Cancers (Basel)*. 2023;15(19):4779.

References: 1. Alntas DM, Comoglio PM. *Cancers (Basel)*. 2023;15(18):4672. 2. Liang H, Wang M. *Oncotargets Ther*. 2020;13:2491-2510. 3. Park S, et al. *Histol Histopathol*. 2012;27(2):197-207. 4. Sun W, et al. *J Biomed Res*. 2013;27(3):220-230.

The MET gene encodes the c-Met (also known as MET or HGF) receptor tyrosine kinase, a protein that influences cell growth, survival, and migration when activated by its ligand, HGF-14

The HGF/MET pathway plays an important role in various vital cell processes, including embryonic development, tissue repair, carcinogenesis, and tumor progression. It can also interact with other ligands or cellular receptors.



Learn more at
DISCOVER MET
A Pathology Resource

MET Biomarkers in NSCLC

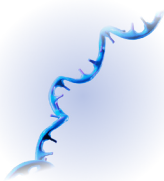
FOLD

HGF/MET Signaling

Learn more at
DISCOVER MET
A Pathology Resource

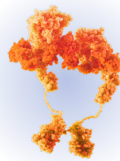


In NSCLC, HGF/MET signaling can be dysregulated through various aberrations associated with the receptor, including:



MET Exon 14 Skipping Mutations (METex14 Skipping)

- Caused by **genetic alterations, primarily point mutations or insertions/deletions (indels)**¹
- Typically identified via **genetic sequencing, including DNA and RNA NGS** methods¹



Increased c-Met Protein Expression

- Refers to **elevated levels of the c-Met receptor** on the surface of tumor cells compared to normal cells²
- Measured via **immunohistochemistry (IHC)** staining intensity of tumor cells³



MET Focal Gene Amplification (MET Amp)*

- Refers to **increase in MET gene copies** without an accompanying rise in chromosome 7 copies⁴
- Can be detected via:^{4,5}
 - **Fluorescence in situ hybridization (FISH)** using MET:CEP7 ratio
 - **DNA and RNA NGS** methods to assess gain in MET copy number

*Emerging biomarker.

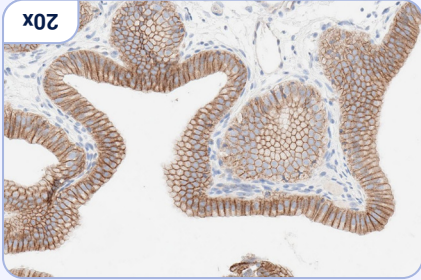
CEP7=centromeric portion of chromosome 7; HGF=hepatocyte growth factor; NGS=next-generation sequencing; NSCLC=non-small cell lung cancer.

References: 1. Socinski MA, et al. *JCO Precis Oncol*. 2021;5:653-663. 2. Sierra JR, Tsao MS. *Ther Adv Med Oncol*. 2011;3(1 Suppl):S21-S35. 3. Ding C, et al. *BMC Pulm Med*. 2023;23(1):240. 4. Coleman N, et al. *ESMO Open*. 2021;6(6):100319. 5. Qin K, et al. *Cancers (Basel)*. 2023;15(3):612.

References: 1. VENTANA MET (SP44) RxDx Assay Interpretation Guide for Non-Squamous Non-Small Cell Lung Cancer, 1018336US Rev A, 2025-05-14. 2. Yin W, et al. *Cancers (Basel)*. 2022;14(10):2433. 3. Abbvie Data on File REF-138355.
 *FNA or other cytology samples that can be spun into cell blocks. †Zinc formalin can also be acceptable.
 FNA=fine-needle aspirate; IHC=immunohistochemistry; NBF=neutral-buffered formalin; NSCLC=non-small cell lung cancer.

Images for illustrative purposes only. Contents herein should not be considered as a replacement for assay-specific interpretation manuals or guides.

Internal controls



20x

External control

Non-neoplastic gallbladder

Types of specimen

Includes resections, biopsies, and cell blocks*

Section considerations

4–5 µm sections with ≥100 viable tumor cells

Fixation considerations

Immediate fixation in 10% NBF for 6–72 hours†

Cellular components

Membrane + cytoplasmic	Membrane	Complete

Membrane staining


Basolateral	Partial	Complete

Tumor cell staining intensities

Weak (1+), moderate (2+), and/or strong (3+)

Staining Patterns^{1,2}

MET IHC



Key MET IHC Considerations

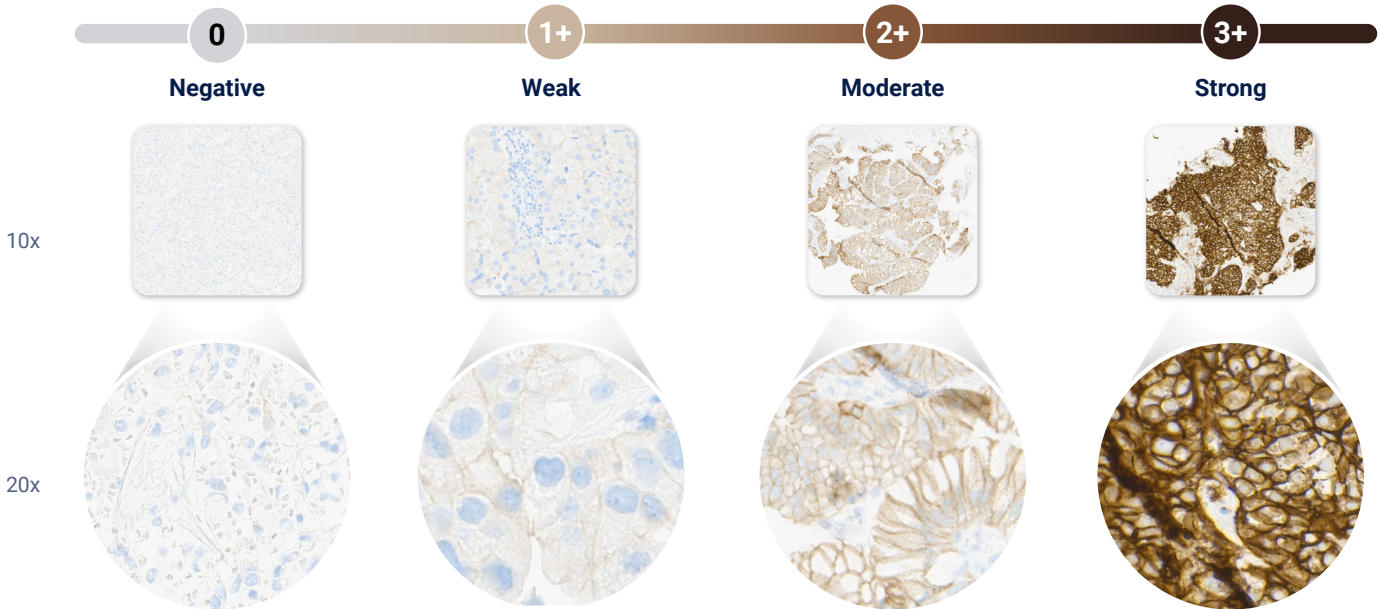
Learn more at
DISCOVER MET
 A Pathology Resource



FOLD

c-Met Protein Expression

Learn more at
DISCOVER MET
 A Pathology Resource



Images for illustrative purposes only. Contents herein should not be considered as a replacement for assay-specific interpretation manuals or guides.

References: 1. VENTANA MET (SP44) RxDx Assay Interpretation Guide for Non-Squamous Non-Small Cell Lung Cancer, 1018336US Rev A, 2025-05-14. 2. Images are provided by Caris Life Sciences. 3. Yin W, et al. *Cancers (Basel)*. 2022;14(10):2433.