

anti-Thyroid Transcription Factor-1 (SP141) Rabbit Monoclonal Primary Antibody

REF 790-4756
06640613001

IVD  50

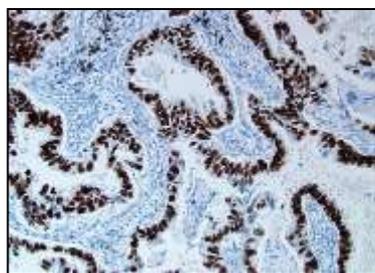


Figure 1. anti-Thyroid Transcription Factor-1 (SP141) staining neoplastic cells in lung adenocarcinoma tissue.

This product should be interpreted by a qualified pathologist in conjunction with histological examination, relevant clinical information, and proper controls.

This antibody is intended for *in vitro* diagnostic (IVD) use.

SUMMARY AND EXPLANATION

TTF-1 is a 38 kDa nuclear protein member of the family of homeodomain transcription factors.¹ TTF-1 expression was originally demonstrated in follicular cells of the thyroid gland and subsequently found in the respiratory cells of the lung.^{2,3,4} Expression in epithelial cells of the thyroid gland and lung allows TTF-1 to be a useful antibody for the classification of tumors arising in these organs.¹ In context with other data, TTF-1 becomes useful in the investigation of metastatic adenocarcinomas of an unknown origin.⁵ Expression of TTF-1 has now been identified in tissues and tumors previously thought to be negative with the use of newer clones and detection systems. Literature published over the past few years has demonstrated expression of TTF-1 being detected in neoplastic tissue beyond lung and thyroid.^{5,6,7}

The demonstration of these staining characteristics in lung (normal and abnormal) and other tissue types has been shown to be different than the established TTF-1 (8G7G3/1) clone.^{5,6,7} (See Table 4 under Specificity for footnote regarding staining in proximal and terminal bronchiole staining in normal lung.)

NOTE: Internal studies conducted at Ventana, as outlined in the Performance Characteristics section, provide additional support for these findings.

In addition, the performance profile of this clone in the diagnosis of mesothelioma is distinct from that of the 8G7G3/1 clone, which should be taken into account.⁸ Validation of any antibody clone is vital in assessing its potential diagnostic use. Specifically, awareness of the full range of normal tissue and tumor expression expected for an antibody is pivotal to diagnostic application. Interpretation needs to take into account expression of a panel of appropriate immunohistochemical antibodies along with clinicopathological features and tumor morphology before reaching a diagnosis.

PRINCIPLE OF THE PROCEDURE

Anti-TTF-1 (SP141) binds to thyroid transcription factor protein in paraffin embedded tissue sections and exhibits a nuclear staining pattern. This antibody can be visualized using OptiView DAB IHC Detection Kit (Cat. No. 760-700/06396500001), *ultraView* Universal DAB Detection Kit (Cat. No. 760-500/05269806001) or *ultraView* Universal Alkaline Phosphatase Red Detection Kit (Cat. No. 760-501/05269814001). Refer to the OptiView DAB IHC Detection Kit, *ultraView* Universal DAB Detection Kit or *ultraView* Universal Alkaline Phosphatase Red Detection Kit package inserts for further information.

REAGENT PROVIDED

Anti-TTF-1 (SP141) contains sufficient reagent for 50 tests.

One 5 mL dispenser of anti-TTF-1 (SP141) contains approximately 28.5 µg of a rabbit monoclonal antibody.

The antibody is diluted in Tris buffer, pH 7.5, with carrier protein, non-ionic detergent, and 0.09% sodium azide as preservative.

Total protein concentration of the reagent is approximately 3 mg/mL. Specific antibody concentration is approximately 5.7 µg/mL. There is no known non-specific antibody reactivity observed in this product.

Anti-TTF-1 (SP141) is a recombinant rabbit monoclonal antibody produced as purified cell culture supernatant.

Refer to the appropriate VENTANA detection kit package insert for detailed descriptions of: (1) Principles of the Procedure, (2) Materials and Reagents Needed but Not Provided, (3) Specimen Collection and Preparation for Analysis, (4) Quality Control Procedures, (5) Troubleshooting, (6) Interpretation of Results, and (7) General Limitations.

MATERIALS REQUIRED BUT NOT PROVIDED

Staining reagents, such as VENTANA detection kits and ancillary components, including negative and positive tissue control slides, are not provided.

Not all products listed in the package insert may be available in all geographies. Consult your local support representative.

STORAGE

Upon receipt and when not in use, store at 2-8°C. Do not freeze.

To ensure proper reagent delivery and the stability of the antibody, replace the dispenser cap after every use and immediately place the dispenser in the refrigerator in an upright position.

Every antibody dispenser is expiration dated. When properly stored, the reagent is stable to the date indicated on the label. Do not use reagent beyond the expiration date.

SPECIMEN PREPARATION

Routinely processed, formalin-fixed, paraffin-embedded tissues are suitable for use with this primary antibody when used with VENTANA detection kits and VENTANA BenchMark XT and BenchMark ULTRA automated slide stainers. The recommended tissue fixative is 10% neutral buffered formalin.⁹ Slides should be stained immediately, as antigenicity of cut tissue sections may diminish over time.

It is recommended that positive and negative controls be run simultaneously with unknown specimens.

WARNINGS AND PRECAUTIONS

1. For *in vitro* diagnostic (IVD) use.
2. For professional use only.
3. Materials of human or animal origin should be handled as biohazardous materials and disposed of with proper precautions.
4. Avoid contact of reagents with eyes and mucous membranes. If reagents come in contact with sensitive areas, wash with copious amounts of water.
5. Avoid microbial contamination of reagents as it may cause incorrect results.
6. Consult local and/or state authorities with regard to recommended method of disposal.
7. For supplementary safety information, refer to the product Safety Data Sheet and the Symbol and Hazard Guide located at www.ventana.com.

STAINING PROCEDURE

VENTANA primary antibodies have been developed for use on VENTANA BenchMark GX, VENTANA BenchMark XT and BenchMark ULTRA automated slide stainers in combination with VENTANA detection kits and accessories. Refer to Table 1, Table 2, and Table 3 for recommended staining protocols.

This antibody has been optimized for specific incubation times but the user must validate results obtained with this reagent.

The parameters for the automated procedures can be displayed, printed and edited according to the procedure in the instrument Operator's Manual. Refer to the appropriate VENTANA detection kit package insert for more details regarding immunohistochemistry staining procedures.

Table 1. Recommended Staining Protocol for anti-TTF-1 (SP141) with *ultraView* Universal DAB Detection Kit on a BenchMark GX instrument, BenchMark XT instrument or BenchMark ULTRA instrument.

Procedure Type	Method
Deparaffinization	Selected
Cell Conditioning (Antigen Unmasking)	Cell Conditioning 1, Standard
Antibody (Primary)	BenchMark GX instrument 16 minutes, 37°C BenchMark XT instrument 16 minutes, 37°C BenchMark ULTRA instrument 24 minutes, 36°C
Counterstain	Hematoxylin II, 4 minutes
Post Counterstain	Bluing, 4 minutes

Table 2. Recommended Staining Protocol for anti-TTF-1 (SP141) with OptiView DAB IHC Detection Kit on a BenchMark GX instrument, BenchMark XT instrument or BenchMark ULTRA instrument.

Procedure Type	Method
Deparaffinization	Selected
Cell Conditioning (Antigen Unmasking)	BenchMark GX instrument Cell Conditioning 1, 48 minutes BenchMark XT instrument Cell Conditioning 1, 48 minutes BenchMark ULTRA instrument Cell Conditioning 1, 64 minutes
Pre Primary Peroxidase Inhibitor	Selected
Antibody (Primary)	BenchMark GX instrument 16 minutes, 37°C BenchMark XT instrument 16 minutes, 37°C BenchMark ULTRA instrument 24 minutes, 36°C
Counterstain	Hematoxylin II, 4 minutes
Post Counterstain	Bluing, 4 minutes

Table 3. Recommended Staining Protocol for anti-TTF-1 (SP141) with *ultraView* Universal Alkaline Phosphatase Red Detection Kit on a BenchMark GX instrument, BenchMark XT instrument or BenchMark ULTRA instrument

Procedure Type	Method
Deparaffinization	Selected
Cell Conditioning (Antigen Unmasking)	Cell Conditioning 1, Standard
Antibody (Primary)	BenchMark GX instrument 16 minutes, 37°C BenchMark XT instrument 16 minutes, 37°C BenchMark ULTRA instrument 24 minutes, 36°C
Counterstain	Hematoxylin II, 4 minutes
Post Counterstain	Bluing, 4 minutes

Due to variation in tissue fixation and processing, as well as general lab instrument and environmental conditions, it may be necessary to increase or decrease the primary antibody incubation, cell conditioning or protease pretreatment based on individual specimens, detection used, and reader preference. For further information on fixation variables, refer to "Immunohistochemistry Principles and Advances."¹⁰

POSITIVE TISSUE CONTROL

Examples of positive control tissues for anti-TTF-1 (SP141) are lung adenocarcinoma tissue, normal lung or normal thyroid tissue.

STAINING INTERPRETATION / EXPECTED RESULTS

The cellular staining pattern for anti-TTF-1 (SP141) is nuclear.

SPECIFIC LIMITATIONS

The user must validate individual laboratory optimized results obtained with this reagent.

PERFORMANCE CHARACTERISTICS

Staining tests for specificity, sensitivity, and repeatability were conducted and the results are listed in Table 4, Table 5, and in the Repeatability section.

Specificity

Table 4. Specificity of anti-TTF-1 (SP141) was determined by testing formalin-fixed, paraffin-embedded normal tissues.

Tissue	#positive/total cases	Tissue	#positive/total cases
Cerebrum	2/3 ⁱ	Mesothelium (pleura)	0/7
Cerebellum	0/3	Myeloid (bone marrow)	0/3
Adrenal gland	0/3	Lung	17/17 ⁱⁱⁱ
Ovary	0/3	Heart	0/3
Pancreas	0/3	Esophagus	0/3
Hypophysis	0/3	Stomach	0/3
Testis	0/3	Small intestine	0/3
Thyroid	5/5 ⁱⁱ	Colon	0/3
Breast	0/3	Liver	0/3
Spleen	0/3	Salivary gland	0/3
Tonsil	0/3	Kidney	0/3
Thymus	0/3	Prostate	0/3

ⁱ Positive staining noted in scattered glial cells

ⁱⁱ Positive staining noted in follicular cells

ⁱⁱⁱ Positive staining noted in basal and columnar epithelium in both proximal bronchi and terminal bronchioles, and type 2 pneumocytes

Sensitivity

Table 5. Sensitivity of anti-TTF-1 (SP141) was determined by testing a variety of formalin-fixed, paraffin-embedded neoplastic tissues.

Pathology	# positive / total cases
Glioblastoma	0/1
Atypical meningioma	0/1
Malignant ependymoma	0/1
Malignant oligodendroglioma	0/1
Serous papillary adenocarcinoma	0/1
Mucinous papillary adenocarcinoma	0/1

Pathology	# positive / total cases
Islet cell carcinoma	0/1
Pancreatic adenocarcinoma	0/1
Seminoma	0/1
Embryonal carcinoma	0/1
Thyroid medullary carcinoma	5/6
Thyroid papillary carcinoma	26/26
Thyroid follicular carcinoma	15/18
Thyroid colloid adenoma	14/15
Thyroid fetal adenoma	10/10
Thyroid oncocytoma	4/4
Breast intraductal carcinoma	0/1
Breast invasive ductal carcinoma	0/1
Diffuse B-cell lymphoma	0/1
Lung small cell undifferentiated carcinoma	15/17
Lung squamous cell carcinoma	15/57
Lung adenocarcinoma	46/57
Lung atypical carcinoid	18/22
Lung papillary adenocarcinoma	6/8
Lung large cell carcinoma	2/6
Lung alveolar carcinoma	3/3
Esophageal neuroendocrine carcinoma	0/1
Esophageal adenocarcinoma	0/1
Gastric mucinous adenocarcinoma	0/1
Gastrointestinal adenocarcinoma	0/1
GIST	0/1
Hepatocellular carcinoma	4/67
Hepatoblastoma	0/1
Renal clear cell carcinoma	0/1
Prostatic adenocarcinoma	5/15
Prostatic transitional cell carcinoma	0/1
Leiomyoma	0/1
Endometrial adenocarcinoma	0/1
Endometrial clear cell carcinoma	0/1
Uterine squamous cell carcinoma	0/1
Embryonal rhabdomyosarcoma	0/1
Anal malignant melanoma	0/1
Basal cell carcinoma	0/1
Squamous cell carcinoma	0/1
Neurofibroma	0/1
Retroperitoneal neuroblastoma	0/1
Epithelial malignant mesothelioma	0/1
Diffuse malignant lymphoma	0/1

Pathology	# positive / total cases
Hodgkin lymphoma	0/1
Diffuse malignant lymphoma	0/1
Bladder transitional cell carcinoma	0/1
Low grade leiomyosarcoma	0/1
Osteosarcoma	0/1
Spindle cell rhabdomyosarcoma	0/1
Intermediate grade leiomyosarcoma	0/1
Malignant melanoma	0/1
Atypical meningioma	0/1
Colon adenocarcinoma	3/21
Lung squamous metaplasia	9/9
Uterine carcinosarcoma	3/6
Ovarian serous carcinoma	3/18
Ovarian endometrioid carcinoma	0/10
Thymoma (type A)	2/5
Thymoma (type AB)	0/4
Thymoma (type B1)	1/22
Thymoma (type B2)	0/10
Thymoma (type B3)	0/4
Thymic carcinoid	0/3
Thymic hyperplasia	0/4

Repeatability

Repeatability studies for anti-TTF-1 (SP141) were completed to demonstrate:

- Inter-lot reproducibility of the antibody.
- Intra-run and Inter-run reproducibility on a BenchMark XT instrument.
- Intra-platform reproducibility on the BenchMark XT instrument and the BenchMark ULTRA instrument.
- Inter-platform reproducibility between the BenchMark XT instrument and BenchMark ULTRA instrument.

All studies met their acceptance criteria.

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CONTACT INFORMATION



Ventana Medical Systems, Inc.
1910 E. Innovation Park Drive
Tucson, Arizona 85755
USA
+1 520 887 2155
+1 800 227 2155 (USA)



www.ventana.com



Roche Diagnostics GmbH
Sandhofer Strasse 116
D-68305 Mannheim
Germany