VENTANA anti-p63 (4A4) Mouse Monoclonal Primary Antibody

REF 790-4509

05867061001

IVD Σ 50

REF 790-7284

10384000001

IVD Σ 250

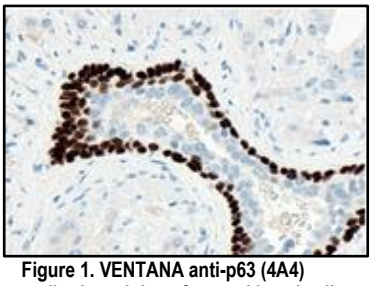

Figure 1. VENTANA anti-p63 (4A4) antibody staining of normal basal cells in prostate tissue.

INTENDED USE

VENTANA anti-p63 (4A4) Mouse Monoclonal Primary Antibody is intended for laboratory use in the qualitative immunohistochemical detection of the p63 protein by light microscopy in sections of formalin-fixed, paraffin-embedded tissue stained on a BenchMark IHC/ISH instrument.

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

The detection of p63 by immunohistochemistry (IHC) with the VENTANA anti-p63 (4A4) Mouse Monoclonal Primary Antibody (VENTANA anti-p63 (4A4) antibody) may be used for: the detection of basal cells to aid in the differentiation of benign and malignant prostate lesions, the detection of myoepithelial cells (MEC) to aid in distinguishing invasive from non-invasive breast neoplasms, and as a marker of squamous differentiation to aid in the distinction between pulmonary squamous cell carcinoma (SCCA) and pulmonary adenocarcinoma (ADC). This antibody may be used as part of a panel of IHC studies.

The human tumor protein 63 (TP63, p63) is a 77 kDa protein localized to the cellular nucleus and member of the p53 family of transcription factors.[1] The p63 protein is expressed in the basal or progenitor cells of epithelial tissues and glandular structures including the prostate, breast, and bronchi.[2,3,4] In the prostate, p63 is expressed in the basal cells of almost all normal and benign glands but is not present in the neuroendocrine or luminal secretory cells.[5] In breast, p63 is expressed in the basal MEC layer in normal tissue as well as in benign lesions.[4] Invasive lesions that evolve from and involve the prostate or breast can disrupt and eventually breach the basal membrane thus eliminating the presence of prostatic basal cells or breast MECs.[4,6]

The IHC-based detection of p63 in prostatic basal cells is a feature of normal and benign processes and the absence of p63 is indicative of carcinoma of the prostate.[6] The detection of p63 in prostatic basal cells with VENTANA anti-p63 (4A4) antibody may be used to aid in the differentiation of benign and malignant prostate lesions. The detection of p63 in breast MECs is a hallmark of non-invasive processes and the absence of p63 is indicative of invasive neoplasms.[7,8] The detection of p63 in breast MECs with VENTANA anti-p63 (4A4) antibody may be used to aid in distinguishing invasive from non-invasive breast neoplasms.

In lung, p63 is expressed in the basal cell compartment.[3] It has been speculated that squamous cell carcinoma (SCCA) of the lung originates from the basal compartment.[9] Thus, the overexpression of p63 in non-small cell lung cancer (NSCLC) can be an indicator of malignant squamous differentiation.[10,11,12] The detection of p63 with VENTANA anti-p63 (4A4) antibody may be used as a marker of squamous differentiation to aid in the distinction between pulmonary SCCA and pulmonary ADC.

PRINCIPLE OF THE PROCEDURE

VENTANA anti-p63 (4A4) antibody is a mouse monoclonal antibody produced against a recombinant fragment of the N-terminal sequence of the human p63 protein. VENTANA anti-p63 (4A4) antibody binds to the p63 protein in formalin-fixed, paraffin-embedded (FFPE) tissue sections and exhibits a nuclear staining pattern. This antibody can be visualized using *ultra*View Universal DAB Detection Kit (Cat. No. 760-500 / 05269806001) or OptiView DAB IHC Detection Kit (Cat. No. 760-700 / 06396500001). Refer to the respective method sheets for further information.

MATERIAL PROVIDED

VENTANA anti-p63 (4A4) antibody contains sufficient reagent for 50 tests.

One 5 mL dispenser of VENTANA anti-p63 (4A4) antibody contains approximately 1 µg of a mouse monoclonal antibody.

VENTANA anti-p63 (4A4) antibody contains sufficient reagent for 250 tests.

One 25 mL dispenser of VENTANA anti-p63 (4A4) antibody contains approximately 5 µg of a mouse monoclonal antibody.

The antibody is diluted in Tris-HCl with carrier protein and 0.10% ProClin 300, a preservative.

Specific antibody concentration is approximately 0.2 µg/mL. There is no known non-specific antibody reactivity observed in this product.

VENTANA anti-p63 (4A4) is a recombinant mouse monoclonal antibody produced from purified cell culture supernatant.

Refer to the appropriate VENTANA detection kit method sheets for detailed descriptions of: Principle of the Procedure, Material and Methods, Specimen Collection and Preparation for Analysis, Quality Control Procedures, Troubleshooting, Interpretation of Results, and 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 method sheet may be available in all geographies. Consult your local support representative.

The following reagents and materials may be required for staining but are not provided:

1. Recommended control tissue
2. Microscope slides, positively charged
3. Negative Control (Monoclonal) (Cat. No. 760-2014 / 05266670001)
4. *ultra*View Universal DAB Detection Kit (Cat. No. 760-500 / 05269806001)
5. OptiView DAB IHC Detection Kit (Cat. No. 760-700 / 06396500001)
6. EZ Prep Concentrate (10X) (Cat. No. 950-102 / 05279771001)
7. Reaction Buffer Concentrate (10X) (Cat. No. 950-300 / 05353955001)
8. LCS (Predilute) (Cat. No. 650-010 / 05264839001)
9. ULTRA LCS (Predilute) (Cat. No. 650-210 / 05424534001)
10. Cell Conditioning Solution (CC1) (Cat. No. 950-124 / 05279801001)
11. ULTRA Cell Conditioning Solution (ULTRA CC1) (Cat. No. 950-224 / 05424569001)
12. Hematoxylin II (Cat. No. 790-2208 / 05277965001)
13. Bluing Reagent (Cat. No. 760-2037 / 05266769001)
14. General purpose laboratory equipment
15. BenchMark IHC/ISH Instrument

STORAGE AND STABILITY

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 FFPE tissues are suitable for use with this primary antibody when used with VENTANA detection kits and BenchMark IHC/ISH instruments. The recommended tissue fixative is 10% neutral buffered formalin.[13] Sections should be cut at approximately 4 µm in thickness and mounted on positively charged slides. Slides should be stained immediately, as antigenicity of cut tissue sections may diminish over time. Ask

your Roche representative for a copy of "Recommended Slide Storage and Handling" for more information.

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. Do not use beyond the specified number of tests.
4. ProClin 300 solution is used as a preservative in this reagent. It is classified as an irritant and may cause sensitization through skin contact. Take reasonable precautions when handling. Avoid contact of reagents with eyes, skin, and mucous membranes. Use protective clothing and gloves.
5. Positively charged slides may be susceptible to environmental stresses resulting in inappropriate staining. Ask your Roche representative for more information on how to use these types of slides.
6. Materials of human or animal origin should be handled as biohazardous materials and disposed of with proper precautions. In the event of exposure, the health directives of the responsible authorities should be followed.[14,15]
7. Avoid contact of reagents with eyes and mucous membranes. If reagents come in contact with sensitive areas, wash with copious amounts of water.
8. Avoid microbial contamination of reagents as it may cause incorrect results.
9. For further information on the use of this device, refer to the BenchMark IHC/ISH instrument User Guide, and the instructions for use of all necessary components located at navifyportal.roche.com.
10. Consult local and/or state authorities with regard to recommended method of disposal.
11. Product safety labeling primarily follows EU GHS guidance. Safety data sheets available on request.
12. To report suspected serious incidents related to this device, contact the local Roche representative and the competent authority of the Member State or Country in which the user is established.

This antibody or assay contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Table 1. Hazard information.

Hazard	Code	Statement
WARNING 	H317	May cause an allergic skin reaction.
	H412	Harmful to aquatic life with long lasting effects.
	P261	Avoid breathing mist or vapours.
	P273	Avoid release to the environment.
	P280	Wear protective gloves.
	P333 + P313	If skin irritation or rash occurs: Get medical advice/ attention.
	P362 + P364	Take off contaminated clothing and wash it before reuse.
	P501	Dispose of contents/ container to an approved waste disposal plant.

This product contains CAS # 55965-84-9, a reaction mass of: 5-chloro-2-methyl-2H-isothiazol-3-one and 2-methyl-2H-isothiazol-3-one (3:1).

STAINING PROCEDURE

VENTANA primary antibodies have been developed for use on BenchMark IHC/ISH instruments in combination with VENTANA detection kits and accessories. Refer to 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 User Guide. Refer to the appropriate VENTANA detection kit method sheet for more details regarding immunohistochemistry staining procedures.

For more details on the proper use of this device, refer to the inline dispenser method sheet associated with P/N 790-4509 (50 test) and P/N 790-7284 (250 test).

Table 2. Recommended staining protocol for VENTANA anti-p63 (4A4) antibody with *ultra*View Universal DAB Detection Kit on BenchMark IHC/ISH instruments.

Procedure Type	Method	
	GX	ULTRA or ULTRA PLUS[a]
Deparaffinization	Selected	Selected
Cell Conditioning (Antigen Unmasking)	CC1, Standard	ULTRA CC1, 64 minutes, 95 °C
Antibody (Primary)	24 minutes, 37 °C	20 minutes, 36 °C
Counterstain	Hematoxylin II, 4 minutes	
Post Counterstain	Bluing, 4 minutes	

[a] Concordance was demonstrated between BenchMark ULTRA and BenchMark ULTRA PLUS instruments using representative assays.

Table 3. Recommended staining protocol for VENTANA anti-p63 (4A4) antibody with OptiView DAB IHC Detection Kit on BenchMark IHC/ISH instruments.

Procedure Type	Method	
	GX	ULTRA or ULTRA PLUS[a]
Deparaffinization	Selected	Selected
Cell Conditioning (Antigen Unmasking)	CC1, 32 minutes	ULTRA CC1, 32 minutes, 100 °C
Pre-Primary Peroxidase Inhibitor	Selected	Selected
Antibody (Primary)	32 minutes, 37 °C	32 minutes, 36 °C
OptiView HQ Linker	8 minutes	
OptiView HRP Multimer	8 minutes	
Counterstain	Hematoxylin II, 4 minutes	
Post Counterstain	Bluing, 4 minutes	

[a] Concordance was demonstrated between BenchMark ULTRA and BenchMark ULTRA PLUS instruments using representative assays.

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."[16]

NEGATIVE REAGENT CONTROL

In addition to staining with VENTANA anti-p63 (4A4) antibody, a second slide should be stained with the appropriate negative control reagent.

POSITIVE TISSUE CONTROL

Optimal laboratory practice is to include a positive control section on the same slide as the test tissue. This helps identify any failures applying reagents to the slide. Tissue with weak positive staining is best suited for quality control. Control tissue may contain both positive and negative staining elements and serve as both the positive and negative control. Control tissue should be fresh autopsy, biopsy, or surgical specimen, prepared or fixed as soon as possible in a manner identical to test sections.

Known positive tissue controls should be utilized only for monitoring performance of reagents and instruments, not as an aid in determining specific diagnosis of test samples.

If the positive tissue controls fail to demonstrate positive staining, results of the test specimen should be considered invalid.

Examples of positive control tissues for this antibody are normal prostate and normal tonsil.

STAINING INTERPRETATION / EXPECTED RESULTS

The cellular staining pattern for VENTANA anti-p63 (4A4) antibody is nuclear.

SPECIFIC LIMITATIONS

OptiView detection system is generally more sensitive than *ultra*View detection kit. The user must validate the results obtained with this reagent and detection systems.

All assays might not be registered on every instrument. Please contact your local Roche representative for more information.

PERFORMANCE CHARACTERISTICS

ANALYTICAL PERFORMANCE

Staining tests for specificity, sensitivity, and repeatability were conducted and the results are listed below.

Sensitivity and Specificity

Table 4. Sensitivity/Specificity of VENTANA anti-p63 (4A4) antibody was determined by testing FFPE normal tissues.

Tissue	# positive / total cases	Tissue	# positive / total cases
Cerebrum	0/7	Stomach	0/4
Cerebellum	0/4	Small intestine	0/4
Adrenal gland	0/4	Colon	0/4
Ovary	0/4	Rectum	0/1
Pancreas	0/4	Liver	0/4
Lymph node	0/4	Eye	0/2
Parathyroid gland	0/3	Salivary gland[b]	3/4
Pituitary gland	0/3	Larynx[d,f]	2/2
Testis[a]	2/4	Pharynx[d]	1/1
Thyroid	0/4	Kidney	0/4
Breast[b,c]	23/23	Prostate[f,g]	39/45
Spleen	0/3	Bladder[h]	3/3
Tonsil[d]	4/4	Endometrium	0/4
Thymus[e]	3/3	Cervix[d,f]	4/4
Bone marrow	0/3	Skeletal muscle	0/3
Lung	0/6	Skin[d]	4/4
Heart	0/3	Nerve	0/3
Esophagus[d]	4/4	Mesothelium	0/3

[a] Rare seminiferous tubule cells; [b] Myoepithelial cells; [c] Tissues evaluated include normal, cancer adjacent breast tissue, cancer adjacent breast ductal tissue, and cancer adjacent breast tissue with fibroadenoma; [d] Squamous epithelium; [e] Epithelial cells; [f] Basal cells; [g] Tissues evaluated include normal, hyperplasia, and chronic prostatitis; [h] Urothelium.

Table 5. Sensitivity/Specificity of VENTANA anti-p63 (4A4) antibody was determined by testing a variety of FFPE neoplastic tissues.

Pathology	# positive / total cases
Astrocytoma (Cerebrum)	0/1
Meningioma (Cerebrum)	0/1
Haemangioblastoma (Cerebellum)	0/1
Medulloblastoma (Cerebellum)	0/1
Inverted Papilloma (Head and neck)	1/1
Nasopharyngeal carcinoma, NPC (Head and neck, nasopharynx)	1/1
Metastatic laryngeal squamous cell carcinoma (Lymph node)	1/1
Pleomorphic adenoma (Head and neck, salivary gland)	1/1
Adenoid cystic carcinoma (Head and neck, salivary gland)	1/1
Metastatic left orbital adenocarcinoma (Head and neck, salivary gland)	1/1
Adrenocortical adenoma (Adrenal gland)	0/1
Adrenocortical carcinoma (Adrenal gland)	0/1
High grade serous carcinoma (Ovary)	0/1
Adenocarcinoma (Ovary)	0/1
Juvenile granulosa cell tumor (Ovary)	0/1
Metastatic ovary adenocarcinoma (Rectum)	0/1
Solid pseudo-papillary neoplasm (Pancreas)	0/1
Neuroendocrine neoplasm (Pancreas)	0/1
Seminoma (Testis)[a]	0/1
Embryonal carcinoma (Testis)	0/1
Follicular adenoma (Thyroid)	0/1
Medullary carcinoma (Thyroid)	0/1
Metastatic neuroendocrine carcinoma (Adrenal gland)	0/1
Intraductal papilloma (Breast)[b]	1/1
Ductal carcinoma in situ (Breast)[b]	14/15
Invasive lobular carcinoma (Breast)	0/4
Invasive carcinoma of no special type (Breast)	0/33
Metastatic breast carcinoma (Lymph node)	1/1
Metastatic breast adenocarcinoma (Cerebellum)	0/1
Squamous cell carcinoma (Lung)	24/33
Adenocarcinoma (Lung)[c]	4/24
Large cell carcinoma (Lung)	0/1
Small cell carcinoma (Lung)	0/9
Mucinous adenocarcinoma (Lung)	0/5
Papillary adenocarcinoma (Lung)	0/5
Sarcomatoid carcinoma (Lung)	0/1
Bronchioloalveolar carcinoma (Lung)	0/1
Metastatic lung squamous cell carcinoma (Brain)[d]	1/1
Metastatic lung adenocarcinoma (Multiple sites)	0/2
Squamous cell carcinoma (Esophagus)	1/1
Leiomyoma (Esophagus)	0/1
Metastatic esophageal adenocarcinoma (Lymph node)	0/1

Pathology	# positive / total cases
Adenocarcinoma (Stomach)	0/1
Tubular adenoma (Stomach)	0/1
Metastatic stomach adenocarcinoma (Multiple sites)	0/2
Adenocarcinoma (Small intestine)	0/1
Gastrointestinal stromal tumor (GIST) (Small intestine)	0/1
Adenocarcinoma (Colon)	0/1
Tubular adenoma (Colon)	0/1
Metastatic colon mucinous adenocarcinoma (Multiple sites)	0/2
Adenocarcinoma (Rectum)	0/1
Villus tubular adenoma (Rectum)	0/1
Metastatic rectum adenocarcinoma (Bladder)	0/1
Hepatocellular carcinoma (Liver)	0/1
Cavernous hemangioma (Liver)	0/1
Metastatic hepatocellular carcinoma (Lung)	0/1
Giant cell tumor (Bone)	0/1
Osteosarcoma (Bone)	0/1
Angiomyolipoma (Kidney)	0/1
Clear cell carcinoma (Kidney)	0/1
Metastatic kidney clear cell carcinoma (Thyroid gland)	0/1
Metastatic kidney urothelial carcinoma (Testis)	1/1
Leiomyoma (Prostate)	0/1
Adenocarcinoma (Prostate)	0/38
Metastatic prostate (Bone)	0/1
Metastatic prostate (Lymph node)[e]	1/1
Inverted papilloma (Bladder)	1/1
Urothelial carcinoma (Bladder)[d]	1/1
Leiomyoma (Uterus)	0/1
Endometrioid adenocarcinoma (Uterus)	0/1
Clear cell carcinoma (Uterus)	0/1
Squamous cell carcinoma (Cervix)	1/1
Adenocarcinoma (Cervix)	1/1
Metastatic cervix squamous cell carcinoma (Colon)	1/1
Metastatic lung small cell carcinoma (Lymph node)	0/1
Diffuse large B-cell lymphoma (Lymph node)	1/1
Hodgkin's lymphoma (Lymph node)	0/1
Metastatic adenocarcinoma NOS (Skin)	0/1
Squamous cell carcinoma (Skin)	0/1
Melanoma	0/1

[a] Occasional lymphocyte staining; [b] Myoepithelial cells; [c] Rare tumor cell staining may occur; [d] Few positive tumor cells; [e] Tumor cell staining.

Precision

Precision studies for VENTANA anti-p63 (4A4) antibody were completed to demonstrate:

- Between lot precision of the antibody.
- Within run and between day precision on a BenchMark ULTRA instrument.
- Between instrument precision on the BenchMark GX and BenchMark ULTRA / ULTRA PLUS instrument.
- Between platform precision between the BenchMark GX and BenchMark ULTRA / ULTRA PLUS instrument.

All studies met their acceptance criteria.

Precision on the BenchMark ULTRA PLUS instrument was demonstrated using representative assays. Studies included Within Run Repeatability, Between Day and Between Instrument Intermediate Precision. All studies met their acceptance criteria.

CLINICAL PERFORMANCE

Clinical performance data relevant to the intended purpose of VENTANA anti-p63 (4A4) antibody were assessed by systematic review of the literature. The data gathered support the use of the device in accordance with its intended purpose.

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NOTE: A point (period/stop) is always used in this document as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

The summary of safety and performance can be found here:

https://ec.europa.eu/tools/eudamed

Symbols

Ventana uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see elabdoc.roche.com/symbols for more information).

GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

REVISION HISTORY

Rev	Updates
J	Updates to Principle of the Procedure, Material Provided, Materials Required but not Provided, Warnings and Precautions, Staining Procedure, Staining Interpretation / Expected Results, Analytical Performance, and Intellectual Property sections. Added BenchMark GX instrument. Added OptiView DAB IHC Detection Kit. Removed recommended protocols for BenchMark XT.

INTELLECTUAL PROPERTY

For USA: Rx only

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