NEW ANTIBODIES AND PRODUCTS FOR MOLECULAR PATHOLOGY

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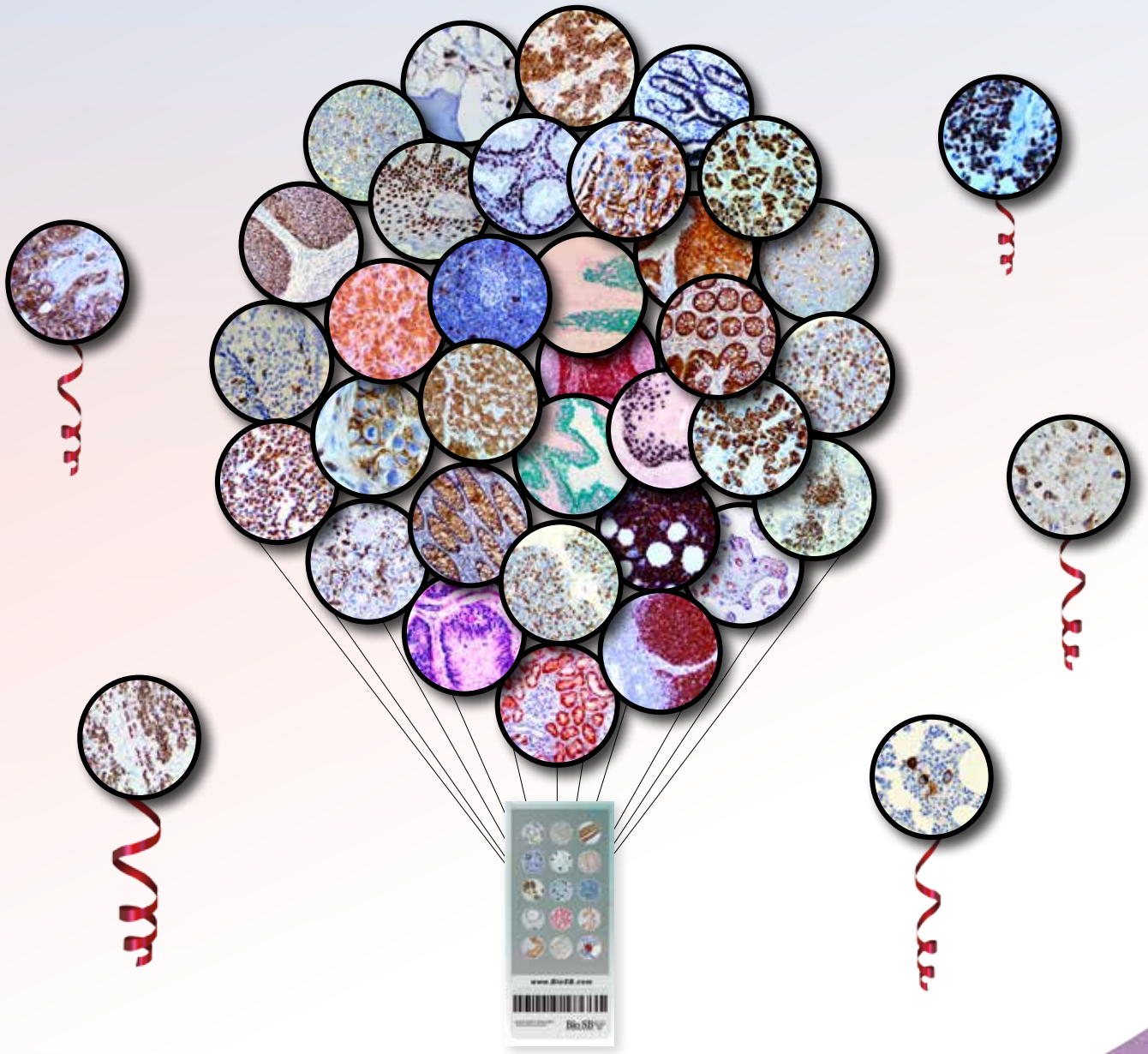
27 New IVD Biomarkers for Use in Immunohistochemistry



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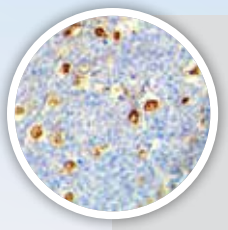
New Antibodies for Immunohistochemistry

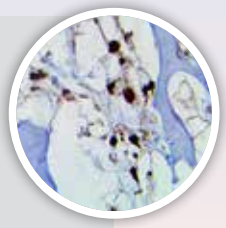


A-1-Antichymotrypsin, RMab (EP384)

Alpha-1-Antichymotrypsin antibody reacts with histiocytes and histiocytic neoplasms. Its major application is defining the presence of Alpha-1-Antichymotrypsin in histiocytes and tumors derived from them. In eosinophilic granuloma and malignant histiocytosis, the reaction for this marker is heterogeneous in intensity and distribution. In fibrous histiocytomas, under certain circumstances, a diffuse homogeneous reaction may be observed.

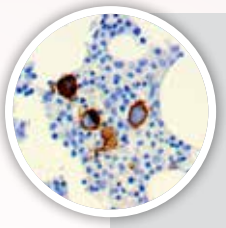
Application: Leukemia & Histiocytic, Liver Cancer

Brachyury, RMab (RBT-TBXT)



Expression of the brachyury gene has been identified as a definitive diagnostic marker of chordoma, a malignant tumor that arises from remnant notochordal cells lodged in the vertebrae. Furthermore, germ line duplication of brachyury confers major susceptibility to chordoma. The chromosomal region on 6q27 containing the brachyury gene was gained in 6 of 21 chordomas (29%), and none of the 21 chordomas analyzed showed deletions that could have affected this gene.

Application: Neural & Neuroendocrine Cancer, Liver Cancer

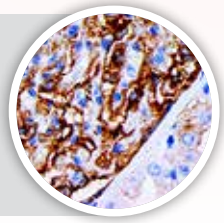


CD42b, RMab (EP409)

CD42b is a marker of megakaryocytes and platelets and used in the Diagnosis of AML-M7 to distinguish AML-M7 (CD42b+) from acute myelosis with myelofibrosis (usually CD42b -). Acute megakaryoblastic leukemia has a significantly higher proportion of blasts expressing CD42b. Patients with Histoplasma capsulatum infections have been noted with unusual IHC positivity of the platelet associated marker CD42b/GP1b expressed on the surface of this fungal organisms. Evaluation of additional cases demonstrated that a majority of histoplasmosis cases (83%) showed positive staining with CD42b/GP1b, comparable to GMS stain results.

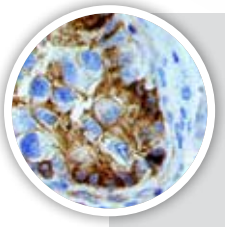
Application: Leukemia & Histiocytic

CD61, RMab (EP65)



CD61 labels the IIIa subunit of the noncovalently-linked glycoprotein heterodimer IIb/IIIa complex present on human platelets and their precursors. This antibody is useful in identifying megakaryoblastic differentiation as seen in Megakaryoblastic Leukemia.

Application: Leukemia & Histiocytic



CD146 / MUC18 / Mel-CAM, MMab (BSB-122)

The lineage-specific expression pattern of CD146 can be useful in the differential diagnosis of certain conditions including melanomas and various types of gestational trophoblastic lesions. CD146 has been suggested to play an important role in tumor progression, implantation and placentation. CD146 expression can promote tumor progression in human melanoma, possibly through enhanced interaction between melanoma cells and endothelial cells. In contrast, CD146 may act as a tumor suppressor in breast carcinoma. CD146 expression is frequently lost in breast carcinomas and overexpression of CD146 in breast carcinoma cells results in a more cohesive cell growth and the formation of smaller tumors in nude mice. During implantation and placentation, CD146 expressed by the intermediate trophoblast in the placental site binds to its putative receptor in uterine smooth muscle cells and limits trophoblastic invasion in the myometrium.

Application: Melanoma & Skin Cancer, Breast Cancer

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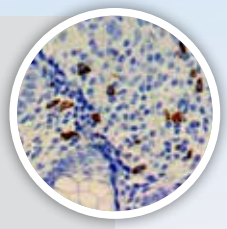
CTLA4 / CD152, RMab (RBT-CTLA4)



Mutations in this gene have been associated with insulin-dependent diabetes mellitus, Graves' disease, Hashimoto's thyroiditis, celiac disease, systemic lupus erythematosus, thyroid-associated orbitopathy, primary biliary cirrhosis and other autoimmune diseases. Polymorphisms of the CTLA-4 gene are associated with autoimmune diseases such as autoimmune thyroid disease and multiple sclerosis, though this association is often weak. In Systemic Lupus Erythematosus (SLE), the splice variant sCTLA-4 is found to be aberrantly produced and found in the serum of patients with active SLE. Germline haploinsufficiency of CTLA4 leads to CTLA4 deficiency or CHAI disease (CTLA4 haploinsufficiency with autoimmune infiltration), a rare genetic disorder of the immune system. This may cause a dysregulation of the immune system and may result in lymphoproliferation, autoimmunity, hypogammaglobulinemia, recurrent infections, and may slightly increase one's risk of lymphoma.

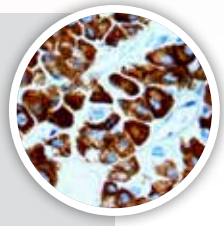
Application: Rejection & Autoimmunity, Lymphoma; Immunotherapy

Cytokeratin, MNF116, MMab (MNF116)

Mutations in this gene have been associated with insulin-dependent diabetes mellitus, Graves' disease, Hashimoto's thyroiditis, celiac disease, systemic lupus erythematosus, thyroid-associated orbitopathy, primary biliary cirrhosis and other autoimmune diseases. Polymorphisms of the CTLA-4 gene are associated with autoimmune diseases such as autoimmune thyroid disease and multiple sclerosis, though this association is often weak. In Systemic Lupus Erythematosus (SLE), the splice variant sCTLA-4 is found to be aberrantly produced and found in the serum of patients with active SLE. Germline haploinsufficiency of CTLA4 leads to CTLA4 deficiency or CHAI disease (CTLA4 haploinsufficiency with autoimmune infiltration), a rare genetic disorder of the immune system. This may cause a dysregulation of the immune system and may result in lymphoproliferation, autoimmunity, hypogammaglobulinemia, recurrent infections, and may slightly increase one's risk of lymphoma.

Application: Carcinomas of Unknown Primary Site, Undifferentiated Tumor, Breast Cancer, Melanoma & Skin Cancer, Lung Cancer, Germ Cell Tumor, Sarcoma & Soft Tissue, Testicular Cancer

FSH, RMab (EP257)



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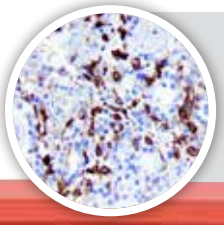
Application: Pituitary, Neural & Neuroendocrine Cancer



Herpes Simplex Virus II, MMab (BSB-116)

Herpes Simplex Virus II typically involves the genitalia, and may also affect skin or internal organs such as brain, lung, liver, adrenal gland, or GI tract of immunocompromised individuals.

Application: Infectious Diseases

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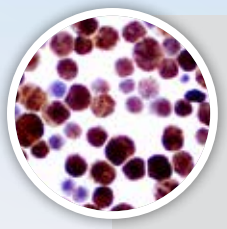
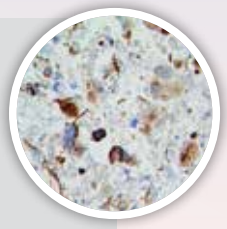


Herpes Simplex Virus I & II, MMab (10A3 / BSB-116)

The antibody reacts with antigens common to HSV types 1 and 2. The antibody reacts with all major glycoproteins present in the viral envelope and at least one core protein as determined by crossed immunoelectrophoresis. Contaminating antibodies to human and bovine serum have been removed by solid-phase absorption. The antibody shows no reaction with human and bovine plasma when tested by ELISA. The antibody shows no cross-reactivity to cytomegalovirus and Epstein-Barr virus.

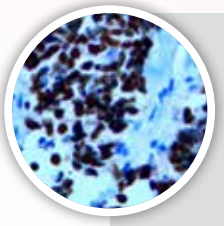
Application: Infectious Diseases

IDH1 R132H, MMab (IHC132)



Mutations involving IDH1 occur in a high proportion of diffuse gliomas, with implications on diagnosis. About 90% involve exon 4 at codon 132, replacing amino acid arginine with histidine (R132H). Preliminary studies comparing Immunohistochemistry (IHC) with IDH1-R132H mutation-specific antibodies have shown concordance with DNA sequencing and no cross-reactivity with wild-type IDH1 or other mutant proteins.

Application: Neural & Neuroendocrine Cancer

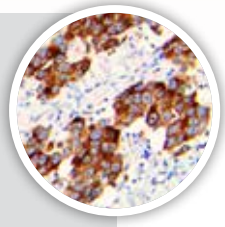


INSM1, MMab (BSB-123)

It has been reported that INSM1 expresses exclusively in SCLC specimens using immunohistochemistry, and first elucidated that INSM1 regulates the NE differentiation pathway in lung cancer. In addition, it has demonstrated an increased sensitivity and specificity compared to other NE biomarkers (Chromogranin A, Synaptophysin and CD56) in lung cancer specimens. In addition, it's been shown to be involved in NE differentiation in medullary thyroid carcinoma, pheochromocytoma, intestinal NE carcinoma, islet cell tumor, pituitary tumor, and SCLC cell lines.

Application: Lung Cancer, Neural & Neuroendocrine Cancer, Pituitary, Colon & GI Cancer

LIN28, RMab (EP150)



LIN28 has been found to be a highly sensitive marker for testicular intratubular germ cell neoplasias, classic seminomas, embryonal carcinomas, and yolk sac tumors (YST) with relatively high specificity. LIN28 can be used as a diagnostic marker for these tumors and has demonstrated a similar level of diagnostic utility as SALL4. The major advantage of LIN28 over OCT4 is in diagnosing yolk sac tumors (yolk sac tumors negative for OCT4). In another study, LIN28 was found to be a sensitive marker of ovarian primitive germ cell tumors like Gonadoblastomas, Dysgerminomas, Embryonal Carcinomas, and YSTs. LIN28 can be used to distinguish them from non- testicular germ cell tumors. High expression of Lin28 is associated with poor prognosis and high tumor aggressiveness in esophageal cancer and these effects are mediated through increased proliferation and invasiveness of esophageal cancer cells.

Application: Ovarian Cancer, Testicular Cancer, Liver Cancer, Breast Cancer, Endometrial and Genital Cancer, Colon and GI Cancer, Germ Cell Tumors

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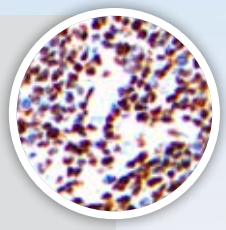
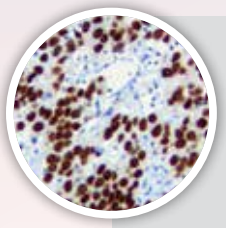
LM02, RMab (RBT-LM02)



LMO2 expression has been reported to be special feature of GC DLBCL (Diffuse Large B Cell Lymphoma of germinal center subtype) which can be used as a diagnostic marker. LMO2 has shown usefulness as part of an IHC panel of germinal center-associated markers in eliminating cases of Diffuse Follicle Center Lymphoma. This is accomplished by taking into consideration the histologic and immunoarchitectural spectrum of Nodal Marginal Zone Lymphoma (NMZL) and the immunohistochemical analysis for CD43, CD23, CD21, BCL6, HGAL, and LMO2 in the diagnosis of NMZL.

Application: Lymphoma

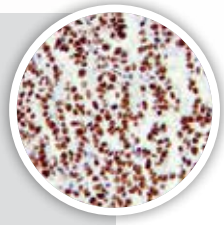


Nanog, RMab (EP225)

Nanog is highly and specifically expressed in carcinoma in situ (CIS), embryonal carcinomas, and seminomas, but not in teratomas and yolk sac tumors. Additionally, it has been reported that Human embryonic stem cell genes OCT4, NANOG, STELLAR, and GDF3 are expressed in both seminoma and breast carcinoma. Positive Nanog expression is significantly associated with high-grade ovarian serous carcinoma and is absent in benign, borderline, and low-grade serous lesions. A study suggests the expression of Nanog exhibiting cellular shuttling behavior and increasing stromal distribution during the progression of cervical cancer. Recently it was suggested that Nanog overexpression, a hazard factor of differentiation, lymph node metastasis, and tumor size, may predicate decreased overall survival (OS) and disease-free survival (DFS) for lung cancer.

Application: Ovarian Cancer, Testicular Cancer, Germ Cell Tumor, Breast Cancer, Lung Cancer

NPM1/B23, MMab (BSB-124)



NPM1 gene is up-regulated, mutated and chromosomally translocated in many tumor types. Chromosomal aberrations involving NPM1 were found in patients with non-Hodgkin lymphoma, Acute Promyelocytic Leukemia, Myelodysplastic Syndrome, and Acute Myelogenous Leukemia. NPM1 is a nuclear protein. In approximately 50% to 60% of cytogenetically normal Acute Myeloid Leukemia (AML), NPM1 is mutated and localized in the cytoplasm. Both wild type and mutant NPM1 can be detected by immunohistochemistry (IHC). The expression of NPM1 is heterogeneous in gastric tumors. NPM1 down-regulation may have a role in gastric carcinogenesis and may help in the selection of anticancer treatment strategies. NPM1 has a critical role in the regulation of colon cancer cells migration and invasion and it may serve as a potential marker for the prognosis of colon cancer patients.

Application: Lymphoma, Leukemia & Histocytic, Colon & GI Cancer.

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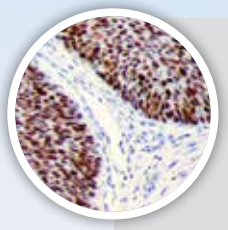
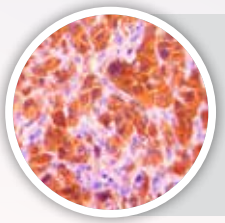


p14 ARF / CDKN2A, RMab (RBT-p14)

p14ARF, has been reported to be associated with the clinicopathological features of different cancers. Very commonly, cancer is associated with a loss of function of INK4a, ARF, Rb, or p53. Without ARF, MDM2 can inappropriately inhibit p53, leading to increased cell survival. The INK4a/ARF locus is found to be deleted or silenced in many kinds of tumors. It has been found that 41% breast carcinomas have p14ARF defects and in a separate study, 32% of colorectal adenomas were found to have p14ARF inactivation due to hypermethylation of the promoter. Homozygous deletions and other mutations of CDK2NA (ARF) have been found to be associated with Glioblastoma. p14ARF expression has been found to be significantly associated with the risk of lung cancer.

Application: Breast Cancer, Colon & GI Cancer, Cervical Cancer, Neural and Neuroendocrine Cancer

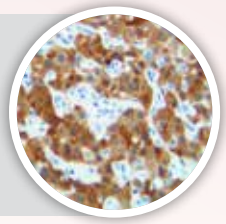


P16, MMab (16P04, JC2)

p16 is a tumor suppressor gene. p16 is an important gene in regulating the cell cycle. p16INK4a regulates the cell cycle by binding and deactivating various cyclin-CDK complexes. p16 is a G1/S-cell cycle regulator that is involved in the pathway that converges in the tumor suppressor protein Rb.

Application: Cervical Cancer, Breast Cancer, Head & Neck Cancer

P16, RMab (RBT-p16)



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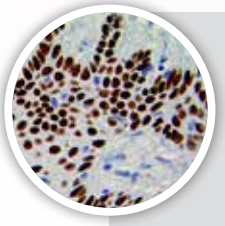
Application: Cervical Cancer, Breast Cancer, Head & Neck Cancer

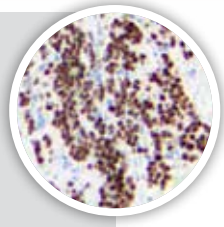


P63, MMab (4A4)

Anti-p63 to human p63 protein labels an epitope common to all six p63 isotypes (TAp63α, TAp63β, TAp63γ, ΔNp63α, ΔNp63β, ΔNp63γ). p63 labels the nuclei of myoepithelial cells in the prostate gland as well as breast tissue, making it useful in differentiating benign vs. malignant prostate lesions and breast lesions.

Application: Cervical Cancer, Breast Cancer, Head & Neck Cancer, Kidney & Urotelial Cancer, Lung Cancer, Prostate Cancer, Thyroid & Parathyroid Cancer, Melanoma & Skin Cancer, Carcinomas of Unknown Primary Site

PHOX2B, RMab (EP312)



PHOX2 gene over-expression in Neuroblastoma (NB) tumors and cell lines suggests these genes may be widely involved in Neuroblastoma development through either a direct mechanism of up-regulation or a failure in maintaining proper transcript levels after embryonic development. The PHOX2B expression has been observed in all peripheral neuroblastic tumors, paragangliomas, and pheochromocytomas tested but in no other pediatric tumors among the 388 cases studied by expression microarray and the 109 cases studied by immunohistochemical analysis. PHOX2B and CD57 have been found to be useful markers of Neuroblastoma. PHOX2B is specific for Neuroblastoma in its differential diagnosis with other small round cell tumors, and its nuclear staining may be helpful for accurate bone marrow tumor quantification.

Application: Neural & Neuroendocrine Cancer

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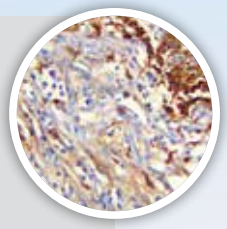
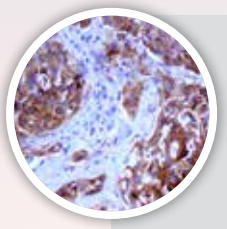
Prealbumin / Transthyretin, MMab (BSB-125)



TTR mutations are associated with amyloid deposition, predominantly affecting peripheral nerves or the heart. TTR misfolding and aggregation is known to be associated with the Amyloid Diseases, Senile Systemic Amyloidosis (SSA), Familial Amyloid Polyneuropathy (FAP), and Familial Amyloid Cardiomyopathy (FAC). Transthyretin amyloidosis is a slowly progressive condition characterized by the buildup of abnormal deposits amyloid (Amyloidosis) in the body's organs and tissues. It has been reported that TTR can be used as an immunohistochemical marker for choroid plexus papillomas, as well as carcinomas. The TTR gene has been found to be suppressed in Hepatic Carcinoma, where the TTR gene was found to be defective in its gene structure, which may have a relevance in its pathogenesis.

Application: Neural & Neuroendocrine Cancer, Liver Cancer

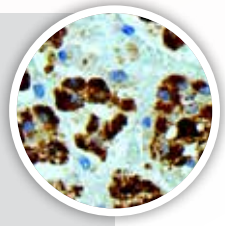


ROS-1, RMab (EP282)

Gene rearrangements involving the ROS1 gene were first detected in glioblastoma tumors and cell lines. ROS1 fusion partners include CD74, SLC34A2 and SDC4, leading to oncogenic transformation. ROS1 rearrangement was identified in a cell line derived from a lung adenocarcinoma patient and multiple studies have demonstrated its incidence in lung cancers. While ROS1 is undetectable in the normal lung, studies have described ROS1 rearrangements in 1-2% of NSCLC by FISH. Recent reports have demonstrated strong correlation between ROS1 IHC with FISH positivity. ROS1 fusions have been detected in multiple other tumors, including glioblastoma, non-small cell lung cancer (NSCLC), cholangiocarcinoma, ovarian cancer, gastric adenocarcinoma, colorectal cancer, inflammatory myofibroblastic tumor, angiosarcoma, and epithelioid hemangioendothelioma.

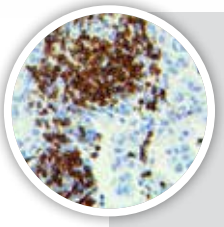
Application: Lung Cancer, Neural and Neuroendocrine Cancer, Ovarian Cancer, Colon & GI Cancer

STAR, RMab (EP226)



STAR is primarily present in steroid-producing cells, including Leydig cells in the testis, theca cells and luteal cells in the ovary and adrenal cells in the adrenal cortex. Low level of STAR expression in other tissues that produce steroid hormones for local use have been reported. STAR is a sensitive and specific marker for Leydig cell tumor. It is useful for differential diagnosis of sex-cord stromal tumor (SCST). Mutations in this gene are a cause of congenital lipoid adrenal hyperplasia (CLAH), also called lipoid CAH.

Application: Pituitary, Ovarian Cancer, Kidney and Urothelial Cancer, Testicular Cancer



TCR Alpha, MMab (BSB-126)

T-cell receptor alpha locus is a protein that in humans is encoded by the TRA gene, also known as TCRA or TRAα; It contributes the alpha chain to the larger TCR protein (T-cell receptor). The T cell receptor or TCR is a molecule found on the surface of T lymphocytes (or T cells) that is responsible for recognizing antigens bound to major histocompatibility complex (MHC) molecules. The TCR is composed of two different protein chains (that is, it is a heterodimer). In 95% of T cells, this consists of an alpha (α) and beta (β) chain, whereas in 5% of T cells this consists of gamma and delta (γ/δ) chains. This ratio changes during ontogeny and in cancers, such as Leukemia.

Application: Lymphoma, Leukemia & Histiocytic

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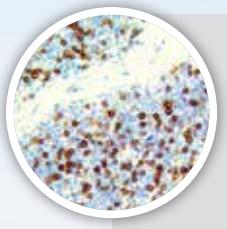
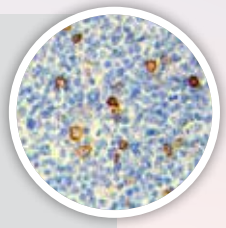


TCR Beta, MMab (BSB-117)

The T cell receptor or TCR is a molecule found on the surface of T lymphocytes (or T cells) that is responsible for recognizing antigens bound to major histocompatibility complex (MHC) molecules. The TCR is composed of two different protein chains (that is, it is a heterodimer). In 95% of T cells, this consists of an alpha (α) and beta (β) chain, whereas in 5% of T cells this consists of gamma and delta (γ/δ) chains. TCR Beta is a member of the immunoglobin super family and a component of the CD3/TCR complex (along with TCR Alpha). TCR Beta is expressed by thymocytes and a majority of peripheral (α-β TCR-bearing) T-cells. TCR recognition of self-peptides has been linked to autoimmune disease. Mutant self-peptides have been associated with tumors.

Application: Lymphoma, Leukemia & Histiocytic

TCR Delta, MMab (BSB-127)



Deletions and mutations of the TRG and TRD gene have been implicated in a variety of cancers. Specifically, γδ T cells may contribute to the immune response against several tumor types (lymphoma, myeloma, breast, colon, lung, ovary, and others). They act directly through mediation of cytotoxic activity and indirectly through the regulation of other cell types responsible for the anti-tumor response. The presence of γδ T cells in the tumor microenvironment has been associated with poor prognosis in some cancers. While γδ T cells have been implicated in T cell lymphomas, there is also a specific subtype known as γδ T-cell lymphoma, characterized by the proliferation of those cells exclusively. This lymphoma can be quite aggressive with ulcerative plaques and subcutaneous nodules. In adenocarcinoma, polyclonal rearrangement of the TCR γ chain gene was significantly greater in N1 and N2 patients (using the TNM cancer staging system) than in N0 patients. Apart from carcinomas, TRG has also been correlated with heptatis B virus (HBV). Specifically, Vδ2+ T cell levels and TCR γδ T cell cytotoxicity were significantly lower was in patients with chronic HBV infections.

Application: Lymphoma, Leukemia & Histiocytic

Antibody Presentations

Tinto Prediluted Antibodies	Concentrated Antibodies
3 mL Tinto Predilute (30 tests) 7 mL Tinto Predilute (70 tests) 15 mL Tinto Predilute (150 tests)	0.1 mL Concentrate 0.5 mL Concentrate 1 mL Concentrate
• *No need for optimization.* • *Compatible with biotin or micro-polymer based detection systems.* • *Tinto Predilutes diluted in proprietary protein blocker/stabilizer.*	• *Cost effective solution.* • *Compatible with biotin or micro-polymer based detection systems.* • *Can be optimized to meet the needs of each laboratory.*

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