ATLAS ANTIBODIES

Tumor Microenvironment and Cancer Immunity

The tumor microenvironment (TME) consists of specialized tumor vasculature and a mixture of cancer-associated fibroblasts, pericytes, endothelial cells, together with other specialized stromal cells types, like the tumor-associated macrophages producing tumor-suppressive factors. These cells are all recruited by the tumor cells to the primary tumor site.

The tumor progression is profoundly influenced by and dependent upon the tumor-TME interaction. This interaction ultimately determines whether the primary tumor becomes eradicated, metastasizes, and establishes micrometastases.

Most TMEs of solid cancers harbor specialized stromal cells that secrete factors and extracellular matrix proteins endowing the tumor cells with molecular cues that further the oncogenic phenotype.

The cellular composition of the TME influences the promotion of tumor growth and angiogenesis, the remodeling of the extracellular matrix, and directs cell-cell interactions.

The collective phenotype of the TME is decisive for tumor progression, like proliferation, migration, and multidrug resistance.

Enhanced Validation

Enhanced validation offers increased security of antibody specificity in a defined context. This is ensured by using the most relevant validation method for each combination of protein, sample, and application.

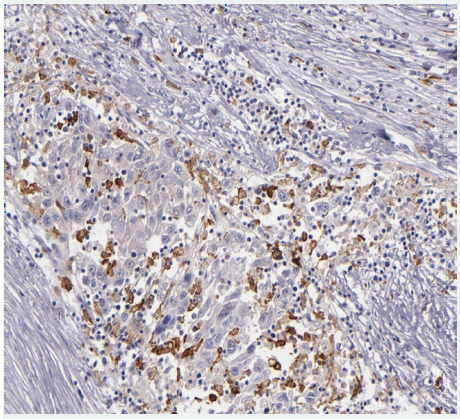

Figure 1. CD163 immunohistochemical staining of human liver cancer using the Anti-CD163 polyclonal antibody (HPA051974) showing strong immunoreactivity in brown.

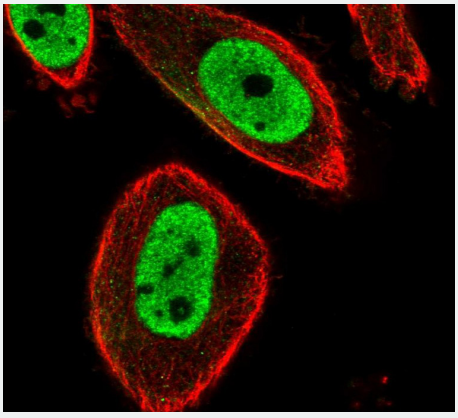

Figure 2. FOXP3 (forkhead box P3) immunofluorescent staining of human cell line PC-3 using the Anti-FOXP3 polyclonal antibody (HPA045943) showing selective localization to nucleoplasm, in green.

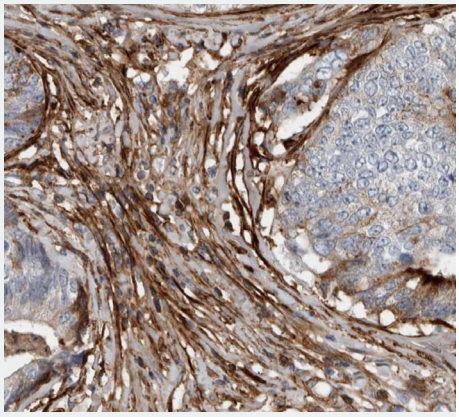

Figure 3. FN1 (fibronectin1) immunohistochemical staining of human colorectal cancer using the Anti-FN1 polyclonal antibody (HPA027066) showing strong immunoreactivity in brown.

Immunogenic tumors also host resident and tumor-infiltrating T-cells (TILs). TILs are attracted to and accumulate within the TME at the border or within the tumors due to their surface expression of altered self-antigens, i.e. neoantigens. The T-cells recognize the unique, altered-self neoantigen presented on the surface of antigen-presenting cells in a Human Leukocyte Antigen (HLA) restricted manner.

Dominant tumor neoantigens are encoded by “driver” mutations being particularly immunogenic since they are recognized by cytotoxic TILs destined to attack and eliminate cancer. The presence of immunosuppressive regulatory T-cells (T-regs) is indicative of immunotherapy resistance. Furthermore, massive stroma-formation (desmoplasia), associated with the solid tumor, provides a robust physical barrier against immune-infiltration.

Immunotherapy, using immune checkpoint inhibitors or strategies designed to harness the immune system, remains the most crucial strategy for the treatment of malignant cancers with a dismal prognosis. Hence the revolutionizing immunotherapeutic application of immune checkpoint inhibitors like anti-PD-1, anti-PD-L1, or anti-CTLA4A has opened up novel avenues for therapeutic immune checkpoint inhibitors to unleash the anti-tumor response.

Unfortunately, resistance against immune checkpoint inhibition remains a common cause of anti-tumor immunotherapy failure. The phenomenon is partly due to the expansion of anti-tumorigenic or immunosuppressive T-cells that express immune checkpoint inhibitor proteins.

Many anti-cancer immunotherapies did fail due to the escape of transformed cells from T-cell mediated killing. This escape is, among other things, caused by shedding of tumor antigens from tumor cells surfaces and/or a subthreshold antigen exposure unable to trigger or sustain an immunological response.

Readings

Bashar Emon et al. (2018) Biophysics of Tumor Microenvironment and Cancer Metastasis - A Mini Review *Computational and Structural Biotechnology Journal* 16: 279-287

Frances R. et al., (2012) The tumor microenvironment at a glance. *Journal of Cell Science* 125: 5591-5596

Gregory L. et al. (2015) Immune Escape Mechanisms as a Guide for Cancer Immunotherapy. *Clin Cancer Res*. 21(4):687-692

Ribatti D. (2017) The concept of immune surveillance against tumors: The first theories. *Oncotarget* 8(4):7175–7180.

Wang M. et al. (2017) Role of tumor microenvironment in tumorigenesis. *J Cancer*. 8(5): 761–773

Yin Z. et al. (2019) Targeting T cell metabolism in the tumor microenvironment: an anti-cancer therapeutic strategy. *J Exp&Clin Cancer Res* 38:403

Yuan Y. et al. (2016) Role of the tumor microenvironment in tumor progression and the clinical applications (Review) *Oncology Reports* 35(5): 2499-2515

Table 1. Suggested **PrecisA Monoclonal™** markers from Atlas Antibodies

Product Name	Catalog No	Application	Sequence Identity Mouse/Rat	Clone ID / Isotype
Anti-ARG1	AMAb90545	IHC, WB	82% / 81%	CL0186 / IgG1
Anti-CD68	AMAb90874	IHC, WB*	76% / 76%	CL1346 / IgG1
Anti-DES	AMAb91302	WB, ICC-IF	100% / 100%	CL4501 / IgG1
Anti-FN1	AMAb91223	IHC, WB	95% / 95%	CL3730 / IgG1
Anti-HDAC1	AMAb90781	IHC, WB*, ICC-IF	98% / 98%	CL0510 / IgG1
Anti-KIT	AMAb90904	IHC, WB	66% / 72%	CL1667 / IgG2a
Anti-LAMP/CD107a	AMAb91298	IHC, WB	65% / 70%	CL4463 / IgG3
Anti-PDCD1/PD1	AMAb91197	IHC, WB	82% / 81%	CL3624 / IgG1
Anti-PROM1/CD133	AMAb91494	IHC, WB	84% / 62%	CL7971 / IgG1
Anti-RGS5	AMAb91377	WB	89% / 89%	CL5568 / IgG1
Anti-TNFRSF18	AMAb91487	WB	66% / 80%	CL7787 / IgG2a
Anti-VIM	AMAb90516	IHC, WB*	99% / 99%	CL0157 / IgG1

* Products with enhanced validation for indicated application

Table 2. Suggested **Triple A Polyclonals™** markers from Atlas Antibodies

Product Name	Catalog No	Application	Sequence Identity Mouse/Rat
Anti-CA9	HPA055207	IHC*	80% / 80%
Anti-CD34	HPA036722	IHC	63% / 56%
Anti-CD44	HPA005785	IHC, WB*, ICC-IF	51% / 47%
Anti-CD163	HPA051974	IHC*	75% / 83%
Anti-CD248	HPA051856	IHC*, ICC-IF	67% / 67%
Anti-CSPG4	HPA002951	IHC, WB*	87% / 83%
Anti-FOXP3	HPA045943	WB, ICC-IF	87% / 86%
Anti-HDAC1	HPA029693	IHC*, WB*, ICC-IF	98% / 98%
Anti-HDAC6	HPA026321	IHC, ICC-IF	47% / 49%
Anti-IDO1	HPA023072	IHC*, WB*	58% / 57%
Anti-LAG3	HPA013967	IHC*	69% / 64%
Anti-NR4A1	HPA059742	WB*, ICC-IF	82% / 81%
Anti-PDCD1LG2/PDL2	HPA013411	IHC, ICC-IF	77% / 77%
Anti-PDGFRA	HPA004947	ICC-IF	83% / 83%
Anti-PDGFRB	HPA028499	WB, ICC-IF	76% / 76%
Anti-PDPN	HPA007534	IHC*, WB	25% / 25%
Anti-TOX	HPA018322	IHC*, WB	98% / 98%
Anti-TOX2	HPA049900	IHC*, ICC-IF	88% / 80%
Anti-VIM	HPA001762	IHC*, WB*, ICC-IF	99% / 99%
Anti-VHL	HPA031631	ICC-IF	49% / 43%

* Products with enhanced validation for indicated application

PrecisA Monoclonals™ are mouse monoclonal primary antibodies developed against a number of carefully selected targets. Clones are selected to recognize only unique non-overlapping epitopes and isotypes.

Triple A Polyclonals™ are rabbit polyclonal primary antibodies developed within the Human Protein Atlas project. IHC characterization data from 44 normal tissues and 20 cancers is available on the Human Protein Atlas portal.

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