

**Table S1.** Antibody details for immunohistochemistry.

<b>Antibody</b>	<b>Supplier</b>	<b>Cat. no.</b>
D2-40	DAKO; Agilent Technologies, Inc.	D2-40
WT-1	Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.	ZM-0269
AE1/AE3	Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.	ZM-0067/68
CR	Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.	ZM-0036
CDX-2	Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.	ZA-0520
PAX8	Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.	ZM-0468
OCT3/4	Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.	ZM-0233
HBME-1 (MC)	Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.	ZM-0386
SATB2	Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.	ZM-0163
P63	Fuzhou Maixin Biotechnology Development Co., Ltd.	4A4
P40	Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.	ZM-0472
CK5/6	Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.	ZM-0313
TTF-1	Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.	ZM-0250
GATA3	Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.	ZA-0661
ER	Roche Tissue Diagnostics	SP1
PR	Roche Tissue Diagnostics	1E2
HER-2	Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.	ZM-0065
CHRA	Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.	ZM-0076
SYNO	Fuzhou Maixin Biotechnology Development Co., Ltd.	MAB-0742
MELAN-A	Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.	ZM-0398
CEA	Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.	ZM-0062

CK7	Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.	OV-TL12/30
CK18	Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.	DC-10
Ki67	Fuzhou Maixin Biotechnology Development Co., Ltd.	MIB-1
PD-L1	Fuzhou Maixin Biotechnology Development Co., Ltd.	RMA-0732
PD-L1 (22C3)	DAKO; Agilent Technologies, Inc.	SK006
DAKO real envision detection system	DAKO; Agilent Technologies, Inc.	K5007

CR, calretinin; CK, cytokeratin; WT-1, Wilms' tumor-1 protein; PD-L1, programmed cell death ligand 1; ER, estrogen receptor; PR, progesterone receptor; CDX-2, caudal-type homeobox transcription factor 2; PAX8, paired-box gene 8; HBME-1, human bone marrow endothelial cell marker-1; SATB2, special AT-rich sequence-binding protein 2; TTF-1, thyroid transcription factor 1; HER2, human epidermal growth factor receptor 2; ChrA, chromogranin A; SYNO, synaptophysin.

**Table SII.** Known pathogenesis that provides significant insights for potential therapeutic targets.

Author, year	(Ref.)	Pathogenesis/targets	Evidence source
Attanoos, 1997	(1)	Asbestos-induced neoplasia: Active oxygen free-radicals liberated by macrophages and polymorph neutrophils following asbestos phagocytosis; arachidonic acid metabolism in neutrophils to generate active oxygen species via the cyclooxygenase and lipoxygenase pathways; physical interaction of asbestos fibres with phagocytic cells; oncogene/oncosuppressor gene expression and function modulated by free radical-induced genotoxicity and lipid peroxidation; deletional changes in chromosomes 1p, 3p and 22q; inappropriate stimulation of a proliferating cell fraction with PDGF- $\alpha$ , EGF, TGF- $\alpha$ and IGF-1; extracellular matrix synthesis and hyaluronic acid production regulated by PDGF and FGF; tumour cell invasiveness and metastasis formation regulated by CD44H and TGF- $\beta$ ; oncogenes c-fos and c-jun. Non-asbestos-associated mesothelioma: Therapeutic irradiation; exposure to thorium dioxide (thorotrast), heavy metals like nickel and beryllium, and diethylstilboestrol; Simian virus-40; chronic inflammation like peritonitis; familial factors	Clinical, preclinical
Carbone, 2002	(2)	T-antigen to bind and inhibit cellular p53 and Rb-family proteins regulated by SV40; asbestos exposure; EGFR-MAPK-AP-1; p16/p14ARF-MDM2-p53/pRB; mutagenic ROS related genetic damage; 239PuO <sub>2</sub> exposure; loss and/or inactivation of TSGs residing in recurrent sites of chromosomal deletion; loss of p16 <sup>INK4a</sup> ; NF2, p16 and p14 <sup>ARF</sup> mutation/loss	Clinical, preclinical
Hassan, 2006	(3)	Antibody response following recombinant SV40 Tag immunization with a CD8+CTL response following plasmid DNA immunization	<i>Preclinical</i>
Ranieri, 2006	(4)	Angiogenesis; VEGF	Clinical
Borczuk, 2007	(5)	ubiquitin-proteasome pathway; UBE2D2 and PSMD8	Clinical, preclinical
Miselis, 2008	(6)	M2-polarized, TAM-mediated immunosuppressive microenvironment; suppression of T lymphocyte-mediated TH1 responses	Preclinical
Palumbo, 2008	(7)	EGFR, PDGFR, Src, Flt-1, KDR, Flt-4, Raf, VEGF, mTOR, proteasome, HDACs, mesothelin	Clinical, preclinical

Villa, 2008	(8)	Telomerase activity and alternative lengthening of telomeres	Clinical
Chua, 2009	(9)	TNF $\alpha$ -NF $\kappa$ B translocation and activation pathway; disruption of the mitotic spindles; the ferritin heavy chain in iron; extracellular signal-regulated kinases 1/2 and elevates expression of early response proto-oncogenes (FOS or JUN or activator protein 1 family members); SV 40	Clinical, preclinical
Perrone, 2010	(10)	PI3K-AKT-TSC1/2-mTOR-S6/4EBP1; PTEN; KRAS-BRAF-ERK1/2	Preclinical
Varghese, 2010	(11)	PI3K, mTOR	Preclinical
Mossman, 2013	(12)	RTK/Ras/ERK1/2, PI3K-AKT; EGF and other growth factors; Rac/PAK/NF2/E2F2; p16 <sup>Ink4a</sup> /p19 <sup>Arf</sup> ; ROS and mitogenic signaling; redox-regulated transcription factors (i.e., FOXM150), redox-sensitive proteins (i.e., thioredoxins)	Clinical, preclinical
Guo, 2014	(13)	Tsc1-Tp53 loss	Preclinical
Marcq, 2015	(14)	CTLA-4, PD-1, TIM-3 and LAG-3	Clinical, preclinical
Sheffield, 2015	(15)	CDKN2A, NF2	Clinical
Singhi, 2016	(16)	BAP1, NF2 and CDKN2A	Clinical
Ugurluer, 2016	(17)	BAP1, CDKN2A/B and NF2	Clinical
Dolly, 2017	(18)	PI3K-mTOR	Clinical
El Bezawy, 2017	(19)	miR-34a/c-MET/AXL; ERK and AKT signaling	Clinical
Joseph, 2017	(20)	BAP1, SETD2, and DDX3X	Clinical
Boussios, 2018	(21)	Paired box gene 8, BAP1, SETD2 and DDX3X; PI3K-mTOR	Clinical
Hung, 2018	(22)	ALK Rearrangement	Clinical
Sementino, 2018	(23)	CDKN2A-Tp53, RB (p16INK4A) pathways, BAP1, and NF2; PI3K-PTEN-AKT-mTOR	Clinical
Belfiore, 2019	(24)	EGFR activation associated with HER2, HER3, Axl, and MET co-activation	Clinical
Hamaidia, 2019	(25)	EZH2/PD-1	Preclinical
Sciarrillo, 2019	(26)	Spliceosomal genes SF3b	Clinical
Hung, 2020	(27)	BAP1, ARID1B, PRDM1, PBRM1, SETD2, NF2, CDKN2A, SUZ12, ALK rearrangement, TP53, CHEK2, TRAF7	Clinical

Shrestha, 2020	(28)	EHD1, ATM, FBXO10, SH2D2A, CDH5, MAGED1, and TP73; BAP1, SETD2, NF2, CDKN2A/B, LASTS1/2, PBRM1, and SMARCC1	Clinical
White, 2020	(29)	PD-L1	Clinical
Miyagawa, 2021	(30)	STRN-ALK fusion	Clinical
Offin, 2021	(31)	CDKN2A/B, BAP1, NF2, TP53, SETD2, LATS2	Clinical
Raghav, 2021	(32)	PD-1	Clinical
El Bezawy, 2022	(33)	miR-550a-3p/HSP90AA1	Clinical, preclinical
Hiltbrunner, 2022	(34)	BAP1, CDKN2A, CDKN2B, NF2, MTAP, TP53 and SETD2; PTCH1/2 and SUFU; KRAS, EGFR, PDGFRA/B, ERBB2 and FGFR3	Clinical
Malpica, 2022	(35)	CDKN2A, NF2, ALK rearrangements and EWSR1/FUS-ATF1 fusions	Clinical
Panagopoulos, 2023	(36)	CDKN2A, NF2, EWSR1, FUS, ALK, MAP3K8, ABLIM1	Clinical

---

PDGF- $\alpha$ , platelet-derived growth factor  $\alpha$ ; EGFR, epidermal growth factor receptor; TGF- $\alpha$ , transforming growth factor  $\alpha$ ; IGF-1, insulin-like growth factor; FGF, fibroblast growth factor; Rb, retinoblastoma; SV40, Simian virus 40; VEGF, vascular endothelial growth factor; UBE2D2, ubiquitin-conjugating enzyme E2D 2; PSMD8, proteasome 26S subunit, nonATPase, 8; TAMs; tumor-associated macrophages; HDACs, histone deacetylases; RTK, canonical receptor tyrosine kinase; CTLA-4, cytotoxic T lymphocyte antigen-4; TIM-3, T-cell immunoglobulin mucin-3; LAG-3, lymphocyte activation gene-3; PD-1, programmed death-1; PD-L1, programmed death-ligand 1; BAP1, BRCA1-associated protein-1; NF2, Hippo pathway-related gene; ATM, ataxia-telangiectasia mutated serine/threonine kinase.