LTL-352 datasheet

Origin	Human prostate cancer	**Histopatho-logy**	Poorly differentiated neuroendo-crine carcinoma of the prostate
Year of establishment	2009	**Doubling time**	11 days (subrenal capsule graft site)
Local invasion	Yes	**Metastasis**	Yes
Hormone sensitivity	Androgen-independent		

The LTL-352 tumor tissue line (Fig. 1) was developed from a patient's metastatic prostate carcinoma (Fig. 2, poorly differentiated neuroendo-crine carcinoma of the prostate, urethra metastasis). When grafted under the renal capsules of NOD-SCID mice, LTL-352 xenografts show invasion into adjacent host kidney parenchyma and metastases to distant organs. Growth of the LTL-352 *in vivo* is androgen-independent. Viable tissues of the LTL-352 in early generations have been preserved following by cryopreservation (DMSO), and can be readily resurrected for grafting.

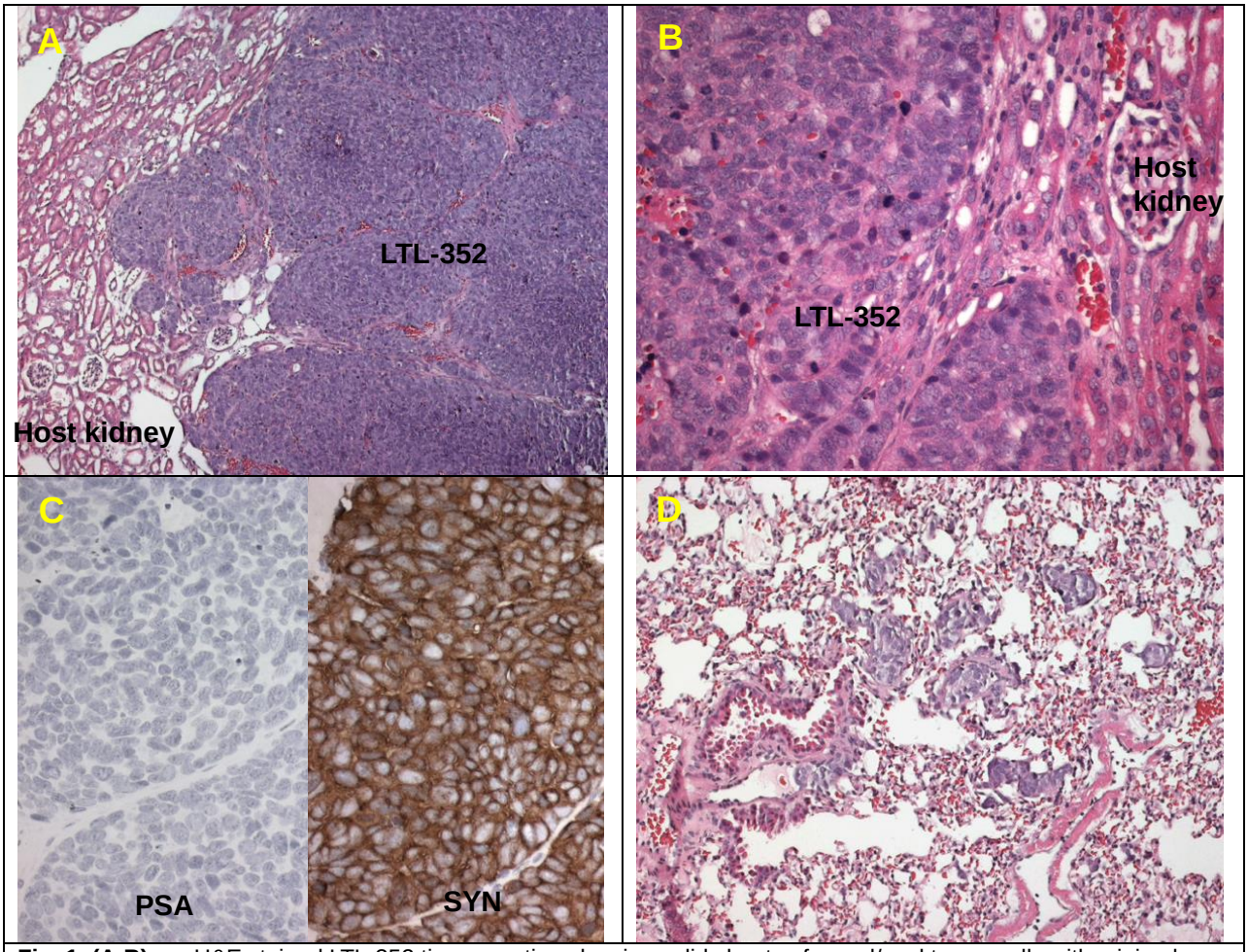

Fig. 1. (A-B), an H&E stained LTL-352 tissue section showing solid sheets of round/oval tumor cells with minimal cytoplasm and frequent mitotic figures, invading adjacent host kidney. **(C),** the tumor cells stain strongly with antibodies to neuroendocrine marker, synaptophysin (SYN, positive location: cytoplasm) but are negative for prostate- specific antigen (PSA) ×400 **(D)** Lung metastases of the LTL-352. (x200)

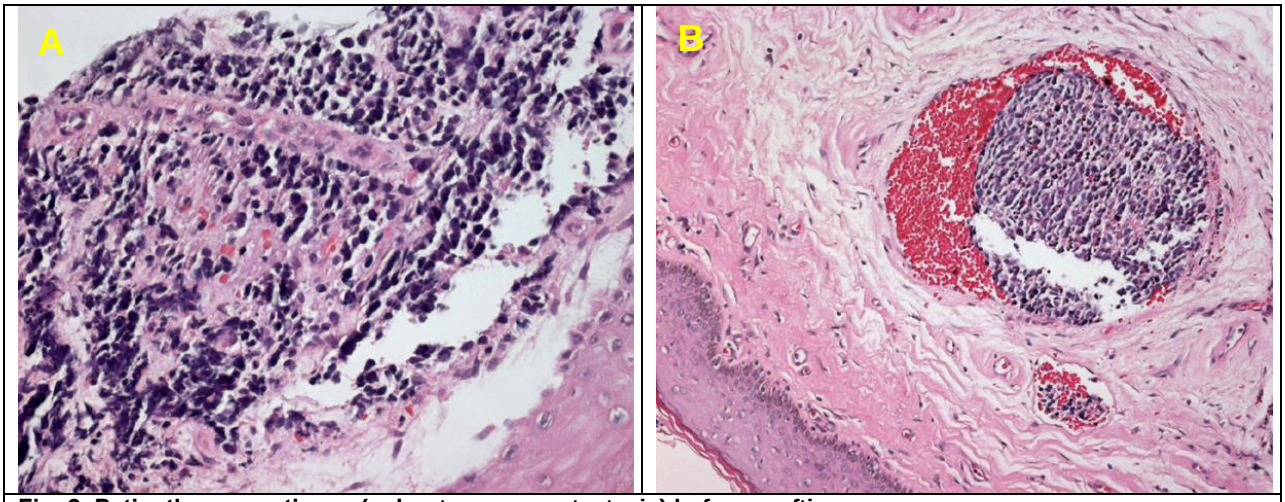

Fig. 2. Patient's cancer tissue (subcutaneous metastasis) before grafting.
H&E stained sections of a penile biopsy revealed small cell carcinoma in the dermis. **(A).** The tumor cells have the usual features of small cell carcinoma including nuclear hyperchromasia, nuclear molding, small punctate nucleoli, and brisk mitotic activity. **(B).** Showing a vessel partially occluded by tumor emboli.

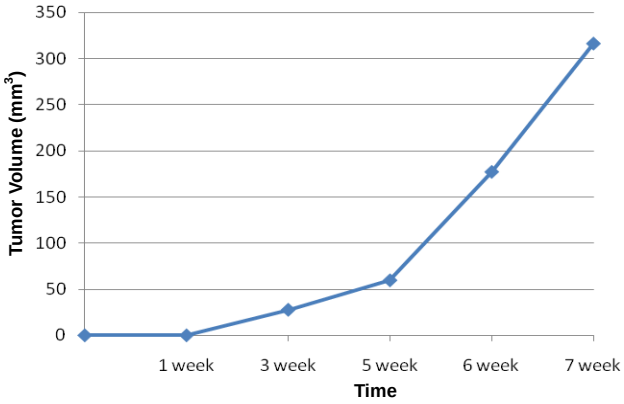

Fig. 3. Growth curve of LTL-352 (subcutaneous graft site)

The LTL-352 tumor line has been characterized using array comparative genomic hybridization (aCGH) and next generation sequencing (NGS). Some of the genes with potential therapeutic application are listed below.

Targets	aCGH	NGS	IHC*
AKT1	Gain	29207	++++
AKT2		22005	+++
PTEN		11575	
P53	Neutral	12418	+++
mTOR	Neutral	7898	+
IGF		298	-
IGF-R		4867	
VEGF	Gain	67648	+++++
PDGFRA	Loss	3328	
FGF-R	Gain	22402	+++
MEK1(MAP2K1)		8394	
MEK2(MAP2K2)		28562	
CHK1	loss	4271	

Aurora kinase A	Gain	6407	+++
Aurora kinase B		8494	+++
ERBB2	Neutral	6656	
ANG-2	Gain	4420	
EZH2	Neutral	8841	++
PARP1	Gain	24836	++++
BRCA1	Neutral	3675	+/-
BRCA2	LOH	1589	-
MTAP	Homozygous loss	1588	-

*IHC: immunohistochemical staining

Applications

1. Preclinical evaluation of established and potential anticancer drugs. Examination of drug efficacy on tumor growth, cell death (apoptosis, necrosis), tissue invasion, metastasis and angiogenesis.

2. Discovery of potential therapeutic targets and/or biomarkers for drug sensitivity.

3. Study of genetic and cellular mechanisms underlying castration resistance, chemoresistance, tumor growth and progression/metastasis.

References

1. Collins CC, Volik SV, Lapuk AV, Wang Y, Gout PW, Wu C, Xue H, Cheng H, Haegert A, Bell RH, Brahmbhatt S, Anderson S, Fazli L, Hurtado-Coll A, Rubin MA, Demichelis F, Beltran H, Hirst M, Marra M, Maher CA, Chinnaiyan AM, Gleave M, Bertino JR, Lubin M, Wang Y. *Next generation sequencing of prostate cancer from a patient identifies a deficiency of methylthioadenosine phosphorylase, an exploitable tumor target.* Mol Cancer Ther. 2012 Mar;11(3):775-83.

2. Beltran H, Rickman DS, Park K, Chae SS, Sboner A, Macdonald TY, Wang Y, Sheikh KL, Terry S, Tagawa ST, Dhir R, Nelson JB, de la Taille A, Allory Y, Gerstein MB, Perner S, Pienta KJ, Chinnaiyan AM, Wang Y, Collins CC, Gleave ME, Demichelis F, Nanus DM, Rubin MA. *Molecular Characterization of Neuroendocrine Prostate Cancer and Identification of New Drug Targets.* Cancer Discov. 2011 Nov;1(6):487-495.

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Note

The LTL-352 and LTL-370 were derived from the same donor cancer.

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