LTL-311 datasheet

Origin	Human prostate cancer	**Histopathology**	High grade adenocarcinoma
Year of establishment	2009	**Doubling time**	10 days (subrenal capsulre graft site)
Local invasion	Yes	**Metastasis**	Yes
Hormone Sensitivity	Androgen-dependent		

The LTL-311 tumor tissue line was developed from a patient's prostate cancer biopsy (high grade prostate adenocarcinoma locally extended beyond prostatic capsule). When grafted under the renal capsules of NOD-SCID mice, the LTL-311 shows invasion into adjacent renal parenchyma (Fig. 1A) and metastases to distant organs (Fig. 1B). Growth and prostate-specific antigen (PSA) production of the LTL-311 *in vivo* is androgen-dependent (Fig. 2). Figure 3 shows the clinical course details of the patient. Viable tissues of the LTL-311 in early generations have been preserved by cryopreservation (DMSO), and can be readily resurrected for grafting.

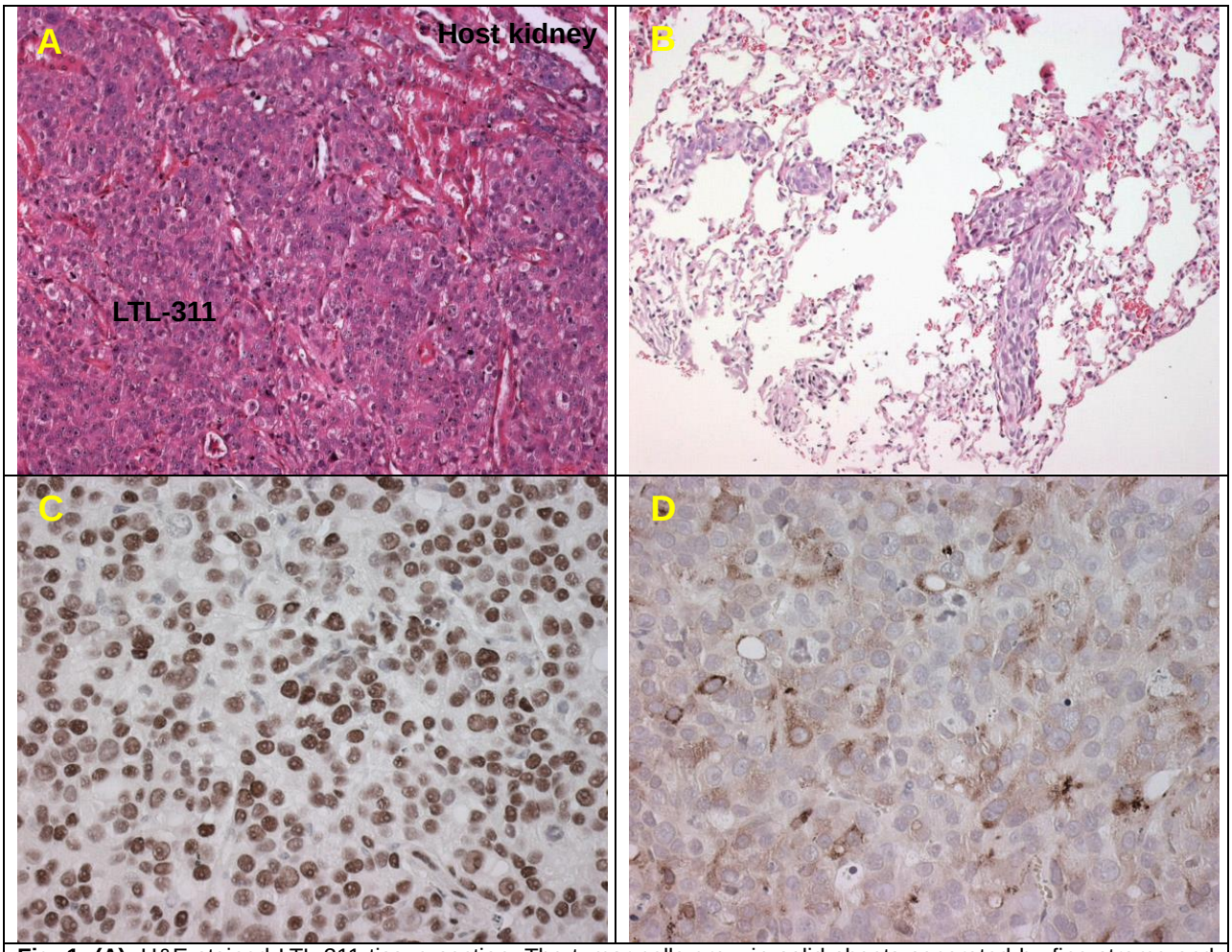

Fig. 1. (A). H&E stained LTL-311 tissue section. The tumor cells grow in solid sheets separated by fine stroma and invade renal parenchyma. X100 **(B).** Lung metastases of the LTL-311. X100 **(C-D).** The tumor cells show positive immunohistochemical stains for human-specific androgen receptor (C) and prostate-specific antigen (D). ×400

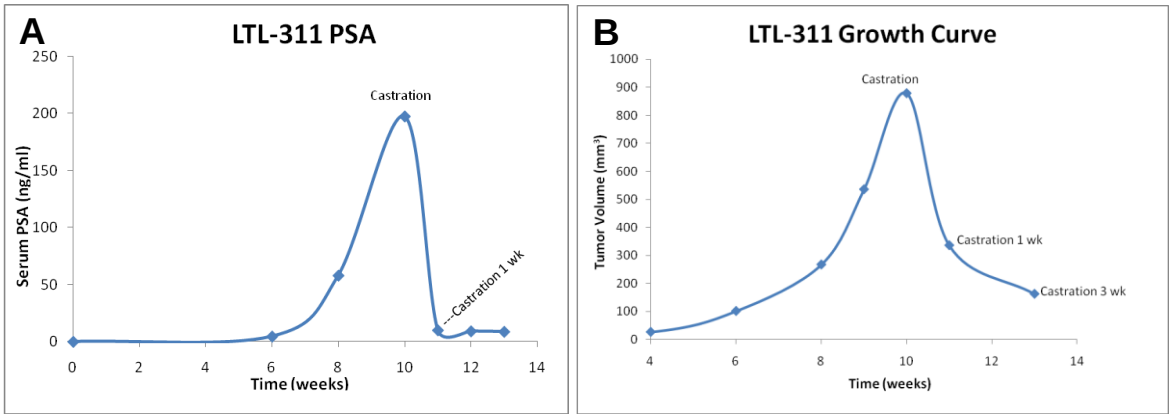

Fig. 2. LTL-311 shows androgen-dependent PSA production and growth *in vivo*: **(A)** Serum PSA levels increase in intact mice following implantation of LTL-311 xenografts under the renal capsules. Castration quickly decreases the level of serum PSA to very low concentrations. **(B)** Castration leads to major tumor shrinkage.

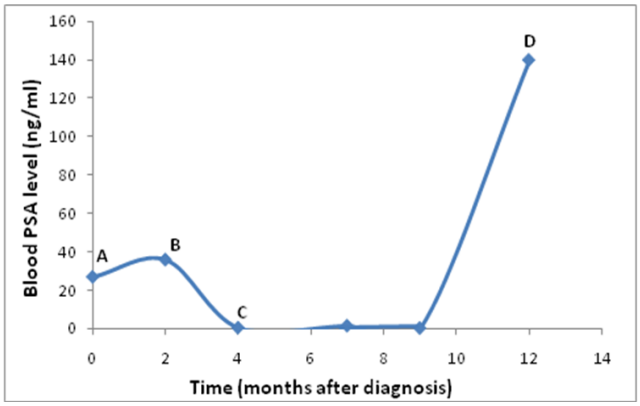

Fig. 3. Clinical course details of the patient. **(A)**, hematuria presented in the patient. Detection of elevated blood PSA leves. **B)**, biopsy of tumor tissue used for LTL-311 development and initiation of androgen deprivation. **(C)**, initiation of complete androgen blockade and pelvic radiotherapy. **(D)**, rapid clinical deterioration. Poorly differentiated metastatic carcinoma was identified in liver.

The LTL- 311 tumor tissue 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*
AR		10798	+++
AKT1		124363	+++
AKT2		1329	-
PTEN	Loss	845	-
mTOR	Neutral	8783	+
IGF1	Neutral	4875	+
IGF-R		22285	+++
VEGF		14787	
VEGFR1(FLT1)		322	-
VEGFR2(KDR)		40	-
VEGFR3(FLT4)		100	-
PDGFA		6708	
PDGFB		2518	
PDGFRA		543	-

PDGFRB	Homozygous loss	60	-
FGF-R	loss	1551	-
MEK1(MAP2K1)	NA	12792	
MEK2(MAP2K2)	NA	17003	
CHK1	NA	1430	
Aurora kinase A	Gain	2780	+/-
Aurora kinase B	NA	2880	
ERBB2	NA	17890	+++
ANG-2	Homozygous loss	2054	-
EZH2	Gain	10798	+++
PARP1	Neutral	9448	+++
BRCA1	Loss	1752	-
BRCA2	Neutral	664	-

*IHC: immunohistochemical staining

Applications

1. Pre-clinical 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 mechanisms underlying tumor growth, progression and metatasis.

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