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TGF β signaling in cancer progression

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Abbreviations

ABP	Activity-based probe
AKT	Protein kinase B
AMSH	Associated molecule with SH3 domain proteases
ATCC	American Type Culture Collection
ATXN3	Ataxin-3
BGG	Globulins from bovine blood
BLI	Bioluminescent imaging
BMP	Bone morphogenetic protein
BRCC36	BRCA1/BRCA2-containing complex subunit 36
CHIP	Carboxy terminus of Hsc70-interacting protein
CHT	Caudal hematopoietic tissue
CSN5	COP9 signalosome subunit 5
CuAAC	Copper(I)-catalyzed azide alkyne cycloaddition
DoC	Duct of Cuvier
dpf	Days post-fertilization
dpi	Days post-injection
DUB	Deubiquitinase
E1	Ubiquitin-activating enzyme
E2	Ubiquitin-conjugating enzyme
E3	Ubiquitin ligase enzyme
Ecto	Ectoderm
ELISA	Enzyme-linked immunosorbent assay
EMT	Epithelial-to-mesenchymal transition
ER	Estrogen receptor
FBS	Fetal bovine serum
GATD3B	Glutamine amidotransferase-like class-1 domain-containing protein 3B
GSR	Glutathione reductase
HECT	Homologous to the E6AP carboxyl terminus
HER2	Human epidermal growth factor receptor 2
HIF1 α	Hypoxia-inducible factor 1 α
HNSCC	Head and neck squamous cell carcinoma
hpf	Hours post-fertilization
hpi	Hours post-injection
IB	Immunoblotting
IC ₅₀	Half-maximum inhibitory concentration
IF	Immunofluorescence
IGF-I	Insulin-like growth factor 1
IKK	I κ B kinase
IP	Immunoprecipitation
ISOC2	Isochorismatase domain-containing protein 2
JAB1	Jun activating binding protein
JAMMs	JAB1/MPN/MOV34 proteases
JNK	C-Jun NH2-terminal kinase
JOSD1	Josephin domain containing 1

Appendix

LC/MS	Liquid chromatography-tandem mass spectrometry
LFQ	Label-free quantification
LPS	Lipopolysaccharide
MAPKs	Mitogen-activated protein kinases
MITF	Microphthalmia associated transcription factor
MJDs	Machado-Joseph disease proteases
MPN	Mpr1-Pad1-N-terminal
MPND	MPN domain-containing protein
MYSM1	Myb-like with SWIRM and MPN domains 1
NEM	<i>N</i> -ethylmaleimide
NSCLC	Non-small cell lung cancer
NTA	Nanoparticle tracking analysis
OUT	Ovarian tumor protease
PARK5	Parkinson disease 5
PARK7	Parkinson disease 7
PFA	Paraformaldehyde
PGP9.5	Neuron-specific protein PGP9.5
PI	Proteasome inhibitor
PI3K	Phosphoinositide 3 kinase
PLA	Proximity ligation assay
POH1	Proteasome-associated PAD1 homolog1
PR	Progesterone receptor
PSMD14	Proteasome 26S Subunit Non-ATPase 14
Rh-Ub-PA	Rhodamine-Ubiquitin-propargylamide
RING	Really interesting new gene
RPMI	Roswell Park Memorial Institute
RTK	Receptor tyrosine kinase
Smad	Sma and Mad related proteins
Smurf	Smad ubiquitin regulatory factor
TAK1	Transforming growth factor- β -activated kinase 1
TAMRA	5-carboxytetramethylrhodamine
TCEP	Tris(2-carboxyethyl)phosphine
TEM	Transmission electron microscopy
TGFBR	TGF β receptor
TGF β	Transforming growth factor- β
TNBC	Triple-negative breast cancer
TNF α	Tumor necrosis factor- α
TRAFs	Tumor necrosis factor receptor-associated factors
Tregs	T cells
Ub	Ubiquitin
UBA	Ubiquitin-associated domain
UCHL1	Ubiquitin Carboxy-terminal Hydrolase L1
UIM	Ubiquitin-interacting motif
USP	Ubiquitin specific protease
VME	Vinyl methyl ester

List of Publications

Deubiquitinase activity profiling identifies UCHL1 as a candidate oncoprotein that promotes TGF β -induced breast cancer metastasis.

Liu S, González-Prieto R, Zhang M, Geurink PP, Kooij R, Iyengar PV, van Dinther M, Bos E, Zhang X, Le Dévédec SE, van de Water B, Koning RI, Zhu HJ, Mesker WE, Vertegaal ACO, Ovaa H, Zhang L, Martens JWM, Ten Dijke P.
Clin Cancer Res. 2020 Mar 15;26(6):1460-1473.

Invasive Behavior of Human Breast Cancer Cells in Embryonic Zebrafish.

Ren J*, Liu S*, Cui C, Ten Dijke P.
J Vis Exp. 2017 Apr 25;(122).

Mutational activation of BRAF confers sensitivity to transforming growth factor β inhibitors in human cancer cells.

Spender LC, Ferguson GJ, Liu S, Cui C, Girotti MR, Sibbet G, Higgs EB, Shuttleworth MK, Hamilton T, Lorigan P, Weller M, Vincent DF, Sansom OJ, Frame M, ten Dijke P, Marais R, Inman GJ.
Oncotarget. 2016 Dec 13;7(50):81995-82012.

Regulation of the TGF- β pathway by deubiquitinases in cancer.

Liu S, de Boeck M, van Dam H, Ten Dijke P.
Int J Biochem Cell Biol. 2016 Jul;76:135-45.

Electroneutralized Amphiphilic Triblock Copolymer with a Peptide Dendron for Efficient Muscular Gene Delivery.

Pu L, Geng Y, Liu S, Chen J, Luo K, Wang G, Gu Z.
ACS Appl Mater Interfaces. 2014 Sep 10;6(17):15344-51.

Pluronic L64-mediated stable HIF-1 α expression in muscle for therapeutic angiogenesis in mouse ischemic limb.

Song H, Liu S, Li C, Geng Y, Wang G, Gu Z.
Int J Nanomedicine. 2014 Jul 21;9:3439-52.

Safe and efficient local gene delivery into skeletal muscle via a combination of Pluronic L64 and modified electrotransfer.

Liu S, Ma L, Tan R, Lu Q, Geng Y, Wang G, Gu Z.
Gene Ther. 2014 Jun;21(6):558-65.

* Equal contribution

Curriculum Vitae

Sijia Liu was born on the 14th of July 1988 in Chengde, China. From 10th September 2007, she started her bachelor study in biotechnology at Southwest University for Nationality, Chengdu, China. During her bachelor internship, she joined the lab of Prof. Yongli Wen and worked on bioinformatic analysis of alternative spliceosome for melatonin synthetase gene HO1MT. She obtained her bachelor degree on the 16th of June 2011. From 1st September 2011, Sijia started her master study in chemical biology at Sichuan University, Chengdu, China. During her master internship, she investigated high-efficient and safe muscular gene delivery of HIF-1 α for therapeutic angiogenesis with the supervision of Prof. Gang Wang in the lab of National Engineering Research Center for Biomaterials. She obtained her master degree on the 19th of June 2014. From 4th September 2014, Sijia started her PhD study in cell biology at Leiden University Medical Center, Leiden, The Netherlands. During her PhD, she studied TGF β signaling in cancer progression with the supervision of Prof. Peter ten Dijke. She focused on understanding of the underlying mechanisms driving metastatic progression of triple-negative breast cancer (TNBC) and identified UCHL1 as a candidate oncoprotein that promotes TGF β -induced breast cancer metastasis. From 1st September 2018 till now, Sijia continued her research in ten Dijke's lab with the support from Cancer Genomics Center Netherlands. Her work focused on investigating UCHL1 activity inhibitor as a potential drug for TNBC therapy and developed cell permeable fluorescent activity-based probe for UCHL1.

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