Photo

Name: Tien Hsu

Current Positions: Chair Professor in the Graduate Institute of Biomedical Sciences

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Education

Institute/Location	Years	Degree/Date	Field of Study
National Taiwan University/Taiwan	1977-1981	B.S./June 1981	Agricultural Chemistry. Biochemistry
Medical University of South Carolina	1983-1988	Ph.D./Dec 1988	Molecular and Cellular Biology and Pathobiology
Harvard University	1989-1993	Postdoc	Molecular Genetics

Expertise

Cancer biology, cell and molecular biology, immunology, developmental genetics

Research Interests

Our laboratory has a long-standing interest in studying tumor progression in vivo using animal models. This stemmed from my training in developmental biology. Therefore my work has always focused on the tissue context and the importance of tumor microenvironment. My laboratory was the first to demonstrate in 2001, using the Drosophila model, the vascular abnormality in *VHL*-deficient animal. *VHL* is the tumor suppressor gene, whose mutations underlie up to 80% of a deadly cancer, clear-cell renal cell carcinoma (ccRCC). Subsequently we verified the microtubule, EMT, endocytic phenotypes in the animal models. More recently we started to dissect the inflammatory factors that contribute to the initiation and progression of ccRCC. We found, in mouse *VHL* knockout model and in clinical samples, that the metabolic imbalance in *VHL* mutant kidney cells could result in ER stress and inflammatory response, which in turn activates the vasculature and immune cells. Reciprocal signaling from the microenvironment contributes to tumor development and metastasis. We are now using single-cell analytical tools to more finely dissect the oncogenic components in the tumor microenvironment.

Selected Grants:

Name of Project	Role in project	Duration	Funding agency	Description	Budget
The role of Cellular Metabolic Abnormality and ER Stress in the Initiation	Principle investigator	Jan.1, 2019 – Dec. 31, 2021	National Health Research Institute (NHRI-EX108-10801BI)	Study the metabolic abnormalities that lead to inflammation	NTD $2.8 mil/yr (USD $90,000/yr)

of Renal Cell Carcinoma				and cancer formation	
Crosstalk between inflammatory microenvironment and tumor cells in the development of renal cell carcinoma	Principle investigator	Aug. 1, 2020-July 31, 2023	Ministry of Science and Technology (MOST 109-2320-B-008-002-MY3)	Study the cellular mechanism by which mutant epithelial cells interact with immune cells	NTD $1.98 mil/yr (USD $66,000/yr)
The active roles of dysfunctional vascular endothelium in renal cell carcinoma progression	Principle investigator	Aug. 1, 2021-July 31, 2024	Ministry of Science and Technology (MOST 110-2320-B-008-005-MY3)	Study the function of endothelial cells in ccRCC progression.	NTD $2.00 mil/yr (USD $66,000/yr)

Selected Publications

(Hsu lab members in bold: undergraduate students¶; graduate students#; postdocs†)

Hsu, T., Gogos, J.A., Kirch, S.A., and Kafatos, F.C. (1992) Multiple zinc finger forms resulting from developmentally regulated alternative splicing of a transcription factor gene. *Science* 257: 1946-1950. **[Highlighted in "This week in Science"]**

Gogos, J.A., Hsu, T., Bolton, J., and Kafatos, F.C. (1992) Sequence discrimination by alternatively spliced isoforms of a DNA binding zinc finger domain. *Science* 257: 1951-1955. **[Highlighted in "This week in Science"]**

Hsu, T., King, D.L., LaBonne, C., and Kafatos, F.C. (1993) A *Drosophila* single-stranded DNA/RNA-binding factor contains a high-mobility-group box and is enriched in the nucleolus. *Proc. Natl. Acad. Sci. (USA)* 90: 6488-6492.

Hsu, T. (corresponding author), Bagni, C., Sutherland, J.S., and Kafatos, F.C. (1996) The transcription factor CF2 is a mediator of EGF-R-activated dorsoventral patterning in *Drosophila* oogenesis. *Genes & Development* 10: 1411-1421. [**Selected for Cover Photo**].

Mantrova, E.Y.† and **Hsu, T.** (1998) Down-regulation of transcription factor CF2 by *Drosophila* Ras/MAP kinase signaling in oogenesis: cytoplasmic retention and degradation. *Genes & Development* 12: 1166-1175.

Mantrova, E.Y.†, Schulz, R.A., and **Hsu, T.** (1999) Oogenic function of the myogenic factor D MEF2: negative regulation of the Dpp type I receptor *thick veins. Proc. Natl. Acad. Sci. (USA)* 96: 11889-11894.

Adryan, B.#, Decker, H.-J., Papas, T.S., and **Hsu, T.** (2000) Tracheal development and the von Hippel-Lindau tumor suppressor homolog in *Drosophila*. *Oncogene* 19: 2803-2811.

Hsu, T. (corresponding author) and Schulz, R.A. (2000) Sequence and functional properties of *Ets* genes in the model organism *Drosophila*. *Oncogene* 19: 6409-6416. **[Review]**

Hsu, T. (corresponding author), **McRackan, D¶**, Vincent, T.S. and de Couet, H.G. (2001) The *Drosophila* Pin1 prolyl isomerase Dodo is a MAP kinase signal responder during oogenesis. *Nature Cell Biology* 3: 538-543. **[Accompanied by News and Views. *Nature Cell Biology* 3: E136-E137.]**

Dammai, V.†, **Adryan, B.#**, **Lavenburg, K.R.†** and **Hsu, T.** (2003) *Drosophila awd*, the homolog of human *nm23*, regulates FGF receptor levels and functions synergistically with *shi/dynamin* during tracheal development. *Genes & Dev.* 17: 2812-2824.

Hsu, T., Trojanowska, M. and Watson, D.K. (2004) Ets proteins in biological control and cancer. *J. Cell. Biochem.* 91: 896-903. **[Review]**

Adereth, Y.#, **Dammai, V.**, **Kose, N.**, Li, R. and **Hsu, T.** (2005) RNA-dependent integrin 3 protein localisation regulated by the Muscleblind-like protein MLP1. *Nature Cell Biology* 7: 1240-1247 **[Accompanied by News and Views *Nature Cell Biology* 7: 1155-1156] [Highlighted in Nature Cell Migration Gateway, Dec. 2005]**

Hsu, T. (co-corresponding author), Adereth, Y.†, Kose, N. and Dammai, V. (2006) Endocytic function of Von Hippel-Lindau tumor suppressor protein regulates surface localization of FGF receptor 1 and cell motility. *J. Biol. Chem.* 281: 12069-12080. **[Editor's Choice, Cancer, Science's STKE, May 2006]**

Nallamothu, G.†, Woolworth, J.A.#, Dammai, V. **and Hsu, T.** (2008) *awd*, the homolog of metastasis suppressor gene *Nm23*, regulates *Drosophila* epithelial cell invasion. *Mol. Cell. Biol.* 28: 1964–1973.

Chintalapudi, M. R.†, Markiewicz, M., **Kose, N,** Dammai, V., **Championl, K.J**.#, Hoda, R. S., Trojanowska, M. and **Hsu, T.** (2008) Cyr61/CCN1 and CTGF/CCN2 mediate the pro-angiogenic activity of *VHL* mutant renal carcinoma cells. *Carcinogenesis* 29: 696-703.

Champion, K.J.#, Guinea, M.†, Dammai, V. and **Hsu, T.** (2008) Endothelial function of von Hippel-Lindau tumor suppressor gene: control of FGF receptor signaling. *Cancer Research* 68: 4649-4657. [IF: 12.7; 16/211, Cancer Research]

Nallamothu, G.†, Dammai, V. and **Hsu, T.** (2009) Developmental Function of *Nm23/awd* - A Mediator of Endocytosis. *Mol. Cell. Biochm*. 329: 35-44. **[Review]**

Woolworth, J.A.#, Nallamothu, G.†, and **Hsu, T.** (2009) The *Drosophila* metastasis suppressor *Nm23* homolog, *awd*, regulates epithelial integrity during oogenesis. *Mol. Cell. Biol*. 29: 4679-4690. **[Selected for cover photo]**

Duchi, S.#, Fagnocchi, L., Cavaliere, V., **Hsouna, A.†**, Gargiulo, G. and **Hsu, T.** (2010) *Drosophila VHL* tumor suppressor gene regulates epithelial morphogenesis by promoting microtubule stability. *Development* 137:1493-1503. **[Featured "In This Issue"]**

Hsouna, A.†, **Kose, N.**, **Guinea, M.†**, Dammai, V. and **Hsu, T.** (2010) *Drosophila* von Hippel-Lindau tumor suppressor gene regulates epithelial tubule migration and lumen formation by promoting endocytosis. *Mol. Cell. Biol*. 30:3779-3794. **[Featured in "Spotlight"][Selected for cover photo]**

Hsu, T. (2012) Complex cellular functions of the von Hippel-Lindau tumor suppressor gene: Insights from model organisms. *Oncogene* 31: 2247-2257. **[Invited Review]**

Bader, H. L.† and **Hsu, T.** (2012) Systemic *VHL* gene functions and the VHL disease. *FEBS Lett.* 586:1562-1569. **[Invited Review]**

Bader, H. L.†, Pritchett, T.L.†, and **Hsu, T.** (2012) Hematopoietic Functions of the Tumor Suppressor Von Hippel Lindau (VHL) in the Etiology of Hemangioblastoma. *Blood* 120: 2425-2425.

Pritchett, T.L.†, Bader, H.L.†, Henderson, J. and **Hsu, T.** (2015) Conditional inactivation of the mouse *von Hippel–Lindau* tumor suppressor gene results in wide-spread hyperplastic, inflammatory, and fibrotic lesions in the kidney. *Oncogene*, 34: 2631-2639. [IF: 8.56; 19/196, Oncology]

Hsu, T., Steeg, P. S., Zollo, M. and Wieland, T (2015) Progress on *Nme* (NDP kinase/Nm23/Awd) gene family-related functions derived from animal model systems: studies on development, cardiovascular disease, and cancer metastasis exemplified (Editorial) *Naunyn-Schmiedeberg Arch. Pharm.* 388: 109-117. [IF: 2.38; 204/773, Pharmacology]

Bader, H.L.† and Hsu, T. (2016) Inactivation of the tumor suppressor gene von Hippel-Lindau (VHL) in granulocytes contributes to development of liver hemangiomas in a mouse model. *BMC Cancer.* 16: 797. [IF: 3.36; 63/322, Oncology]

Kuo, C.Y.,† Lin, C.H.,# and Hsu, T. (2017) VHL inactivation in precancerous kidney cells induces an inflammatory response via ER stress-activated IRE1α signaling. *Cancer Research*. 77: 3406-3416. [9.12; 9/344, Oncology] [This paper won the Ministry of Science and Technology, Taiwan, Outstanding Postdoctoral Research Paper Award, 2017].

Chen, H.Y., Hsiao, Y.T., **Liu, S.C.,† Hsu, T.**, Woon, W.Y., and I, L. (2018) Enhancing Cancer Cell Collective Motion and Speeding up Confluent Endothelial Dynamics through Cancer Cell Invasion and Aggregation. *Physical Rev. Lett.* 121:018101. [IF: 8.84; 7/268, Physics and Astronomy]

Liu, S.C., **Hsu, T.,** Chang, Y.S., Chung, A.K., Jiang, S.S, OuYang, C.N., Hsueh, C., Liu, Y.P., Yuh, C.H., and Tsang, N.M. (2018) Cytoplasmic LIF reprograms invasive mode to enhance NPC dissemination through YAP1-FAK/PXN signaling. *Nature Communications.* 9: 5105. [IF: 12.35; 3/64, Multidisciplinary Sciences]

Hsu, T., Nguyen-Tran, Hieu-Huy[#], and Trojanowska, M.E. (2019) Active roles of dysfunctional vascular endothelium in fibrosis and cancer. *J. Biomed. Sci.* 26: 86. **[Invited review]** [IF: 5.20; 80/277, Cancer Research]

Pan, S.-Y., Tsai, P.-Z., Chou, Y.-H., Chang, Y.-T., Chang, F.-C., Chiu, Y.-L., Chiang, W.-C., **Hsu, T.**, Wu, M.-., Chen, Y.-M., Chu, T.-S., and Lin, S.-L. (2021) Kidney pericyte hypoxia-inducible factor regulates erythropoiesis but not kidney fibrosis. *Kidney International* 99, 1354–1368. [IF: 8.945; 3/66 Medicine-Nephrology]

Nguyen-Tran, H.-H.,[#] Nguyen, T.-N.,[#] Chen, C.-Y. † and **Hsu, T.** (2021). Endothelial reprograming stimulated by oncostatin M promotes inflammation and tumorigenesis in VHL-deficient kidney tissue. *Cancer Res., in press* [IF: 12.7; 16/211, Cancer Research]

Kuo, C.Y., Chiu, V., Hsieh, P.C., **Hsu, T.** and Lin, T.-Y. (2021) Loss of function of von Hippel-Lindau triggers lipocalin 2-dependent inflammatory responses in cultured and primary renal tubular cells.
Oxidative Medicine and Cellular Longevity, in press [IF: 5.076; 10/35, Aging]

Selected Patents