Stanford

Claudia Katharina Petritsch

Associate Professor (Research) of Neurosurgery

NIH Biosketch available Online Curriculum Vitae available Online

Bio

BIO

Claudia earned her PhD (Dr. rer.nat) at the Institute for Molecular Pathology (IMP) in Vienna, where she trained in cancer signaling, and identified crucial regulators of growth factor receptor kinase signaling. Her postdoctoral studies on neural stem cells and asymmetric cell division in the Lab of Dr. Yuh Nung Jan at the Howard Hughes Medical Institute and University of San Francisco, California implied for the first time a minus-end directed myosin in the process of cell fate determination. During two years as an instructor and head of a research group in Munich, Germany, Dr. Petritsch and her team showed that cell fate determinants use a bimodal mechanism (diffusion and active capturing) for proper intracellular location. She returned to UCSF to conduct translational research, and apply her combined expertise in stem cells and signaling on the study of brain neoplasms and human stem and progenitor cells. Dr. Petritsch is an expert in oligodendrocyte progenitor cells, and cancer stem cells, and her team's emphasis is on intra-tumoral heterogeneity, in vitro and in vivo cancer model development, and tumor-immune interactions. Her research identified conserved mechanisms of cell fate determination in mammalian brain progenitors and led to a paradigm shift in understanding how brain progenitor cells self-renew and differentiate. She guided the generation and distribution of several immune competent mouse models for studies of the glioma immune microenvironment. A major effort of her team is to facilitate the use of fresh surgical tissue from neurosurgeries for research.

ACADEMIC APPOINTMENTS

- Associate Professor (Research), Neurosurgery
- Member, Bio-X
- Member, Maternal & Child Health Research Institute (MCHRI)
- Member, Stanford Cancer Institute
- Member, Wu Tsai Neurosciences Institute

HONORS AND AWARDS

- Cancer Research Award, Emerson Collective
- Seed Award, Women’s Health & Sex Differences in Medicine (WHSDM) (01/01/2021-12/31/2021)

BOARDS, ADVISORY COMMITTEES, PROFESSIONAL ORGANIZATIONS

- Member, Society for Neuro-Oncology (2009 - present)

LINKS

- My Lab Site: https://med.stanford.edu/petritsch-lab.html

Research & Scholarship

RESEARCH INTERESTS

- Brain and Learning Sciences
- Research Methods
- Science Education

CURRENT RESEARCH AND SCHOLARLY INTERESTS

The Petritsch lab broadly investigates underlying causes for the intra-tumoral heterogeneity and immune suppression in brain tumors from a developmental neuro-developmental perspective. Proper cell fate decisions by neuroglia stem cells are critical for growing the cell lineages that form the brain during development and to maintain adult brain homeostasis. The mechanisms for cell fate decisions in the human brain are largely unknown. By using patient-derived cells from brain surgeries, we investigate cell fate decision mechanisms in the normal brain and in brain malignancies. We think that defective cell fate decisions fuel the intra-humoral heterogeneity and plasticity that makes treatment of human brain tumors so challenging. We therefore work to gain an understanding of how brain cells control the fate of their progeny, whereby we unravel novel points of vulnerabilities in brain tumor cells, that could be exploited therapeutically.

Excessive proliferation, apoptotic evasion, and migratory spread are all hallmarks of tumorigenesis. However, these defects fail to explain the incredible heterogeneity and immune suppression observed in malignant brain tumors, two major hurdles to their treatment, which remains mostly palliative.

In the healthy brain, neuroglia stem cells generate progenitors, which in turn give rise to differentiating cells that will eventually acquire their final functional state. Cell fate decisions within these hierarchical brain cell lineages are tightly controlled and irreversible: e.g. cells in the state of differentiation will not turn into progenitor cells or stem cells. It is known that brain tumor cells, on the other hand, defy many general principles of neurobiology. This is especially true for malignant glioma cells, which simultaneously express markers of different lineages and states exhibiting incomplete differentiation. Tumor cell hierarchies are poorly understood, providing no explanation for why tumor cells with stem-like, progenitor-like, and differentiated features co-exist and interact with normal brain cells and immune-infiltrating cells within a single tumor entity, and how this heterogeneity relates to the lack of active immune infiltration.

Defects in cell fate control could explain many key defects present in brain tumors Of special emphasis, we study the establishment of cell fates within normal hierarchical brain lineages for comparison to the dysregulated cell-fate hierarchies seen in brain tumors. Our lab was the first to demonstrate that normal adult oligodendrocyte progenitor cells (OPCs) undergo asymmetric divisions to make cell fate decisions, i.e. to generate OPCs as well as differentiating cells each time they divide. Drawing from these data, we investigate whether brain tumors divide along hierarchical lineages and how oncogenic mutations might affect cell fate decisions within these hierarchies. A major line of investigation in our lab focuses on whether defects in asymmetric division lead to aberrant cell fate decisions that cause the paradigm mixed lineage phenotypes and the intra-tumoral heterogeneity present across tumors. We complement our work with human cells with orthotopic and genetically engineered mouse models of gliomagenesis to conduct molecular, cellular and bioinformatic analyses

Publications

PUBLICATIONS

- **LGL1 binds to Integrin #1 and inhibits downstream signaling to promote epithelial branching in the mammary gland.** *Cell reports*
  Ma, R., Gong, D., You, H., Xu, C., Lu, Y., Bergers, G., Werb, Z., Klein, O. D., Petritsch, C. K., Lu, P.
  2022; 38 (7): 110375
- **Lgl1 controls NG2 endocytic pathway to regulate oligodendrocyte differentiation and asymmetric cell division and gliomagenesis** *NATURE COMMUNICATIONS*
  Daynac, M., Chouchane, M., Collins, H. Y., Murphy, N. E., Andor, N., Niu, J., Fancy, S. J., Stallcup, W. B., Petritsch, C. K.
  2018; 9: 2862

- **Pan-cancer analysis of the extent and consequences of intratumor heterogeneity** *NATURE MEDICINE*
  Andor, N., Graham, T. A., Jansen, M., Xia, L. C., Aktipis, C. A., Petritsch, C., Ji, H. P., Maley, C. C.
  2016; 22 (1): 105-?

- **Targeting a Plk1-Controlled Polarity Checkpoint in Therapy-Resistant Glioblastoma-Propagating Cells** *CANCER RESEARCH*
  Lerner, R. G., Grossauer, S., Kadkhodaei, B., Meyers, I., Sidorov, M., Koeck, K., Hashizume, R., Ozawa, T., Phillips, J. J., Berger, M. S., Nicolaides, T., James, C., Petritsch, et al
  2015; 75 (24): 5355–66

- **Heterogeneously Expressed fezf2 Patterns Gradient Notch Activity in Balancing the Quiescence, Proliferation, and Differentiation of Adult Neural Stem Cells** *JOURNAL OF NEUROSCIENCE*
  Berberoglu, M. A., Dong, Z., Li, G., Zheng, J., Martinez, L., Peng, J., Wagle, M., Reichholf, B., Petritsch, C., Li, H., Pleasure, S. J., Guo, S.
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- **ASYMMETRIC CELL DIVISION: IMPLICATIONS FOR GLIOMA DEVELOPMENT AND TREATMENT** *TRANSLATIONAL NEUROSCIENCE*
  Lewis, K., Petritsch, C.
  2013; 4 (4): 484–503

- **Proteoglycans and their roles in brain cancer** *FEBS JOURNAL*
  Wade, A., Robinson, A. E., Engler, J. R., Petritsch, C., James, C., Phillips, J. J.
  2013; 280 (10): 2399–2417

- **Asymmetry-Defective Oligodendrocyte Progenitors Are Glioma Precursors** *CANCER CELL*
  Sugiarto, S., Persson, A. I., Munoz, E. G., Waldhuber, M., Lamagna, C., Andor, N., Hanecker, P., Ayers-Ringler, J., Phillips, J., Siu, J., Lim, D. A., Vandenberg, S., Stallcup, et al
  2011; 20 (3): 328-340

- **Dronc caspase exerts a non-apoptotic function to restrain phospho-Numb-induced ectopic neuroblast formation in Drosophila** *DEVELOPMENT*
  Ouyang, Y., Petritsch, C., Wen, H., Jan, L., Jan, Y. N., Lu, B.
  2011; 138 (11): 2185-2196

- **Non-stem cell origin for oligodendroglioma.** *Cancer cell*
  Persson, A. I., Petritsch, C., Swartling, F. J., Itsara, M., Sim, F. J., Auvergne, R., Goldenberg, D. D., Vandenberg, S. R., Nguyen, K. N., Yakovenko, S., Ayers-Ringler, J., Nishiyama, A., Stallcup, et al
  2010; 18 (6): 669-82

- **miR-124 and miR-137 inhibit proliferation of glioblastoma multiforme cells and induce differentiation of brain tumor stem cells** *BMC MEDICINE*
  Silber, J., Lim, D. A., Petritsch, C., Persson, A. I., Maunakea, A. K., Yu, M., Vandenberg, S. R., Ginzinger, D. G., James, D., Costello, J. F., Bergers, G., Weiss, W. A., Alvarez-Buylla, et al
  2008; 6: 14

- **HIF1 alpha induces the recruitment of bone marrow-derived vascular modulatory cells to regulate tumor angiogenesis and invasion** *CANCER CELL*
  Du, R., Lu, K. V., Petritsch, C., Liu, P., Ganss, R., Passegue, E., Song, H., VandenBerg, S., Johnson, R. S., Werb, Z., Bergers, G.
  2008; 13 (3): 206–20

- **TGF beta inhibits p70 S6 kinase via protein phosphatase 2A to induce G1 arrest**
  Petritsch, C., Beug, H., Balmain, A., Oft, M.
  AMER SOC CELL BIOLOGY.2000: 289A

- **Clinically relevant MAPK pathway inhibition reverses stem cell fate defects and sensitize BRAF mutant glioma to immune modulatory therapies.**
  Petritsch, C. K., Grossauer, S., Wang, W., Barrette, A., Park, J.
  AMER ASSOC CANCER RESEARCH.2021

- **MAPK PATHWAY INHIBITION SENSITIZES TO IMMUNOTHERAPY IN BRAF-MUTANT GLIOMAS**
  Park, J., Barrette, A., Wang, W., Grossauer, S., Grant, G., Lau, K., Pitteri, S., Monje, M., Petritsch, C.
  OXFORD UNIV PRESS INC.2021: 3-4

- **GENERATION OF NOVEL MOUSE MODELS FOR BRAF V600E MUTANT GLIOMAGENESIS TO GAIN MECHANISTIC INSIGHTS INTO TUMOR FORMATION AND PROGRESSION**
  Petritsch, C. K., Barrette, A., Park, J.

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- **THE IMMUNE MICROENVIRONMENT IN LOWER GRADE GLIOMAS**
  Kumar, A., Chen, K., Petritsch, C., Nicolaides, T., Santi-Vicini, M., Perry, A., Bollen, A., Solomon, D., Molinaro, A. M., Phillips, J.
  OXFORD UNIV PRESS INC.2020: 214

- **A NOVEL BRAF V600E LOW-GRADE GLIOMA MOUSE MODEL HIGHLIGHTS EXOMIC AND TUMOR IMMUNE ALTERATIONS AND DIFFERING THERAPEUTIC RESPONSES IN LOW- AND HIGH-GRADE GLIOMAS**
  Barrette, A., Meyer, L., Hirata, Y., Grossauer, S., Lu, E., Tamaki, W., Petritsch, C., Wang, W.
  OXFORD UNIV PRESS INC.2020: 232–33

- **DETERMINING THE NEUROANAFOMICAL AND CELLULAR ORIGIN OF BRAEV600E MUTANT CDKN2A DELETED GLIOMAS AND MECHANISMS OF TRANSFORMATION BY BRAEV600E EXPRESSION IN "FRANSGENIC MICE**
  Sugiarto, S., Lerner, R. G., Reichholf, B., McMahon, M., James, C., Petritsch, C. K.
  OXFORD UNIV PRESS INC.2019: 122

- **GAINING A MECHANISTIC UNDERSTANDING OF THERAPY EVASION FROM DUAL MAPK PATHWAY INHIBITION IN A SYNGENEIC BRAFV600E MUTANT CDKN2A DELETED MOUSE MODEL'TO PREEMPT RESISTANCE IN PATIENTS WITH BRAFV600E MUTANT E PEDIATRIC CIIOMA**
  Wang, W., Grossauer, S., Koeck, K., Simonds, E., Lu, E., Bergers, G., Weiss, W., Petritsch, C.
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- **Impaired neural stem cell expansion and hypersensitivity to epileptic seizures in mice lacking the EGFR in the brain** *FEBS JOURNAL*
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  2018; 285 (17): 3175–96

- **Tumor suppression by regulator of asymmetric cell division in glioma**
  Daynac, M., Chouchane, M., Valenzuela, A., Petritsch, C. K.
  AMER ASSOC CANCER RESEARCH.2018

- **MAPK pathway blockade effects on glioma stem cells and immunotherapy in BRAF(V600E) mutant gliomas**
  Grossauer, S., Koeck, K., Chouchane, M., Phillips, J. J., Petritsch, C. K., Nicolaides, T.
  AMER ASSOC CANCER RESEARCH.2018

- **Regulation of Asymmetric Cell Division in Mammalian Neural Stem and Cancer Precursor Cells** *ASYMMETRIC CELL DIVISION IN DEVELOPMENT, DIFFERENTIATION AND CANCER*
  Daynac, M., Petritsch, C. K., Tassan, J. P., Kubiak, J. Z.
  2017; 61: 375–99

- **MAPK PATHWAY BLOCKADE PRIMES BRAFV600E MUTANT GLIOMA FOR IMMUNOTHERAPY**
  Grossauer, S., Koeck, K., Murphy, N., Phillips, J., Wrainwright, D., Okada, H., Mueller, S., James, C., Nicolaides, T., Petritsch, C. K.
  OXFORD UNIV PRESS INC.2016: 90

- **Pan-cancer analysis of the etiology and consequences of intra-tumor heterogeneity**
  Andor, N., Graham, T. A., Petritsch, C., Ji, H. P., Maley, C. C.
  AMER ASSOC CANCER RESEARCH.2015

- **Pan-cancer analysis of the causes and consequences of Intra-tumor heterogeneity**
  Andor, N., Graham, T. A., Aktipis, A. C., Petritsch, C., Ji, H. P., Maley, C. C.
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- **Divergent effects of BRAF activation in neural stem and progenitor-like glioblastoma cells**
  Lerner, R. G., Ihara, Y., Lewis, K., Griveau, A., Reichhold, B., Qu, D., McMahon, M., Rowitch, D., James, C. D., Petritsch, C.
  AMER ASSOC CANCER RESEARCH.2014

- **TREATMENT EFFECTS ON STEM AND PROGENITOR SUBPOPULATIONS IN A MODEL OF GLIOBLASTOMA**
  Harness, J., Lerner, R., Ihara, Y., Santos, R., De La Torre, J., Lu, A., Ozawa, T., Nicolaides, T., James, D., Petritsch, C.
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- **CLONAL EXPANSIONS AND EVOLVING SUBPOPULATIONS IN GLIOBLASTOMA MULTIFORME**
  Andor, N., Harness, J., Lopez, S., Fung, T., Mewes, H. W., Petritsch, C.

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  Lerner, R. G., Loan Nguyen, Petritsch, C.
  AMER ASSOC CANCER RESEARCH.2013

- **ANALYSIS OF CELLULAR AND MOLECULAR CHANGES ACCOMPANYING BRaf(V600E) - TARGETED TREATMENT IN A MODEL OF PEDIATRIC ASTROCYTOMA**
  Lerner, R., Harness, J., Yoshida, Y., Santos, R., De La Torre, J., Nicolaides, T., Ozawa, T., James, D., Petritsch, C.
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- **GENE EXPRESSION AND METHYLATION ANALYSES OF ATYPICAL TERATOID/RHABDOID TUMORS AND MEDULLOBLASTOMAS**
  Kolkowitz, I., Andor, N., Jensen, T., Banerjee, A., Gupta, N., Petritsch, C., Taylor, M., Hashizume, R., Tom, M., Haas-Kogan, D., Mueller, S.
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- **Deregulation of asymmetry genes in oligodendrogliomas and glioblastomas**
  Andor, N., Petritsch, C.
  AMER ASSOC CANCER RESEARCH.2012

- **ASYMMETRY-DEFECTIVE OLIGODENDROCYTE PROGENITORS ARE GLIOMA PRECURSORS**
  Sugiarto, S., Persson, A., Munoz, E., Waldhuber, M., Vandenberg, S., Stallcup, W., Philips, J., Berger, M. S., Bergers, G., Weiss, W. A., Petritsch, C.
  OXFORD UNIV PRESS INC.2011: 25

- **The divergent caspase DRONC processes Notch and regulates neurogenesis.**
  Petritsch, C., Wang, S. W., Jan, L. Y., Jan, Y. N.
  AMER SOC CELL BIOLOGY.2000: 290A