



## Gerlinde Wernig

Assistant Professor of Pathology

### CLINICAL OFFICE (PRIMARY)

- **Department of Pathology**

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### Bio

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#### CLINICAL FOCUS

- Haematopathology
- Anatomic and Clinical Pathology

#### ACADEMIC APPOINTMENTS

- Assistant Professor - University Medical Line, Pathology
- Member, Bio-X
- Member, Institute for Stem Cell Biology and Regenerative Medicine

#### PROFESSIONAL EDUCATION

- Fellowship: Stanford University Hematopathology Fellowship (2012) CA
- Board Certification: Hematopathology, American Board of Pathology (2024)
- Residency: Stanford University Pathology Residency (2013) CA
- Residency: Stanford University Pathology Residency (2011) CA
- Board Certification: Anatomic Pathology, American Board of Pathology (2013)
- Board Certification: Hematology, American Board of Pathology (2013)
- Fellowship, Friedrich-Wilhelms-University Bonn, Germany , Hematology/Oncology (2004)
- Residency, Friedrich-Wilhelms-University Bonn, Germany , Internal Medicine (2001)
- Medical Education: Medical University of Vienna (1999) Austria

### Research & Scholarship

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#### CURRENT RESEARCH AND SCHOLARLY INTERESTS

Fibrotic diseases is a cover term coined by our laboratory to address complications of the excessive scarring of fibrous tissue. They occur when fibroblasts – a critical component of the structural tissue of the body – proliferate and include, but are not limited to lung fibrosis, kidney and liver fibrosis,

scleroderma, bone marrow fibrosis, wound healing and surgical adhesions. Despite fibrotic diseases being life-threatening-- the mortality rate of some are higher than that of cancer-- current treatments are ineffective and/or entirely nonexistent.

Our mission is to identify new targets for treatment through uncovering the underlying mechanisms of inflammation and fibrosis. We seek to understand how fibroblasts crosstalk with one another, with the immune system, and with epithelial and mesenchymal cells. By integrating single-cell transcriptional profiling, next-generation shotgun proteomics with mass cytometry and chromatin studies of patient-derived primary tissues in combination with in vivo modeling of fibrotic disease in mice, we gain insight into the pathophysiology of fibrotic diseases. We employ immunotherapy combined with small molecules in order to manipulate signaling pathways at the transcriptional level to disrupt pro-fibrotic cell function and fate. The transcriptional networks we study play key roles in fibrotic disease, metabolism, bone physiology, cancer, and immunology. Understanding them will provide the critical foundation to translate our findings into immunotherapies and clinical practice for fibrotic diseases.

## Teaching

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### COURSES

#### 2021-22

- Stem Cells and Human Development Laboratory: STEMREM 201B (Aut)

### STANFORD ADVISEES

#### Postdoctoral Faculty Sponsor

Marjia Afrin, Qiwen Deng

### GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Hematopathology (Fellowship Program)
- Stem Cell Biology and Regenerative Medicine (Phd Program)

## Publications

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### PUBLICATIONS

- **Innate immune cell activation causes lung fibrosis in a humanized model of long COVID.** *Proceedings of the National Academy of Sciences of the United States of America*  
Cui, L., Fang, Z., De Souza, C. M., Lerbs, T., Guan, Y., Li, I., Charu, V., Chen, S. Y., Weissman, I., Wernig, G.  
2023; 120 (10): e2217199120
- **Upregulation of PD-L1 by SARS-CoV-2 promotes immune evasion.** *Journal of medical virology*  
Huang, H., Wang, S., Fang, G., Chou, W., Liao, C., Sun, C., Jan, J., Ma, H., Ko, H., Ko, Y., Chiang, M., Liang, J., Kuo, et al  
2023
- **Targeting the Innate Immune Landscape and Pro-Fibrotic Genetic Signatures for the Effective Treatment of Myelofibrosis**  
Xu, G., De Souza, C., Liu, Y., Wernig, G.  
SPRINGER NATURE.2022: 1042-1043
- **Targeting the Innate Immune Landscape and Pro-Fibrotic Genetic Signatures for the Effective Treatment of Myelofibrosis**  
Xu, G., De Souza, C., Liu, Y., Wernig, G.  
SPRINGER NATURE.2022: 1042-1043
- **Exploring Potential Innate Immune Targets to Treat Fibrosis and Chronic Inflammation in Chronic Graft-Versus-Host Disease**  
Paulson, N., De Souza, C., Cui, L., Lerbs, T., Poyser, J., Kooshesh, M., Saleem, A., Rieger, K., Brown, R., Kwong, B., Fernandez-Po, S., Arai, S., Shizuru, et al  
SPRINGER NATURE.2022: 557

- **Clonal Expansion of Stem/Progenitor Cells in Cancer, Fibrotic Diseases, and Atherosclerosis, and CD47 Protection of Pathogenic Cells.** *Annual review of medicine*  
Majeti, R., Jamieson, C., Pang, W. W., Jaiswal, S., Leeper, N. J., Wernig, G., Weissman, I. L.  
1800; 73: 307-320
- **Selective Targeting of Immune Modulatory Proteins to Mitigate Fibrosis and Inflammation in Sclerodermatous Graft-Vs-Host Disease**  
Cui, L., De Souza, C., Lerbs, T., Poyser, J., Kooshesh, M., Saleem, A., Rieger, K., Brown, B., Kwong, B., Fernandez-Pol, S., Arai, S., Shizuru, J. A., Mueller, et al  
AMER SOC HEMATOLOGY.2021
- **Integrated spatial multiomics reveals fibroblast fate during tissue repair.** *Proceedings of the National Academy of Sciences of the United States of America*  
Foster, D. S., Januszyk, M., Yost, K. E., Chinta, M. S., Gulati, G. S., Nguyen, A. T., Burcham, A. R., Salhotra, A., Ransom, R. C., Henn, D., Chen, K., Mascharak, S., Tolentino, et al  
2021; 118 (41)
- **JUN promotes hypertrophic skin scarring via CD36 in preclinical in vitro and in vivo models.** *Science translational medicine*  
Griffin, M. F., Borrelli, M. R., Garcia, J. T., Januszyk, M., King, M., Lerbs, T., Cui, L., Moore, A. L., Shen, A. H., Mascharak, S., Diaz Deleon, N. M., Adem, S., Taylor, et al  
2021; 13 (609): eabb3312
- **Preventing Engrailed-1 activation in fibroblasts yields wound regeneration without scarring.** *Science (New York, N.Y.)*  
Mascharak, S., desJardins-Park, H. E., Davitt, M. F., Griffin, M., Borrelli, M. R., Moore, A. L., Chen, K., Duoto, B., Chinta, M., Foster, D. S., Shen, A. H., Januszyk, M., Kwon, et al  
2021; 372 (6540)
- **Tuning MPL signaling to influence hematopoietic stem cell differentiation and inhibit essential thrombocythemia progenitors.** *Proceedings of the National Academy of Sciences of the United States of America*  
Cui, L., Moraga, I., Lerbs, T., Van Neste, C., Wilmes, S., Tsutsumi, N., Trotman-Grant, A. C., Gakovic, M., Andrews, S., Gotlib, J., Darmanis, S., Enge, M., Quake, et al  
2021; 118 (2)
- **Tuning MPL signaling to influence hematopoietic stem cell differentiation and inhibit essential thrombocythemia progenitors** *Proceedings of the National Academy of Sciences*  
Wernig, G.  
2021; 118 (2) (Jan 2021)
- **NK cell receptor and ligand composition influences the clearance of SARS-CoV-2.** *The Journal of clinical investigation*  
Hsieh, W. C., Lai, E. Y., Liu, Y. T., Wang, Y. F., Tzeng, Y. S., Cui, L., Lai, Y. J., Huang, H. C., Huang, J. H., Ni, H. C., Tsai, D. Y., Liang, J. J., Liao, et al  
2021; 131 (21)
- **Jun Activation in Dermal Fibroblasts Promotes Fibrosis and Inflammation in Sclerodermatous Graft-vs-host Disease in Mice and Humans**  
Mueller, A., Cui, L., Lerbs, T., King, M., Muscat, C., Shibata, T., Lee, J., Brown, R., Fernandez-Pol, S., Arai, S., Shizuru, J., Wernig, G.  
SPRINGER NATURE.2020: 13–14
- **Wounds Heal by Tissue-Resident Fibroblast Progenitors that Proliferate Polyclonally and Mechanoresponsively**  
Foster, D. S., Chinta, M., Salhotra, A., Nguyen, A. T., Burcham, A., Mascharak, S., Januszyk, M., Gurtner, G. C., Wernig, G., Longaker, M. T.  
ELSEVIER SCIENCE INC.2020: S236–S237
- **Detection, Scoring, and Classification of Solid Organ Fibroses with Machine Learning Analysis**  
Mascharak, S., desJardins-Park, H. E., Davitt, M., Foster, D. S., Chinta, M., Wan, D. C., Wernig, G., Longaker, M. T.  
ELSEVIER SCIENCE INC.2020: S222
- **CD47 prevents the elimination of diseased fibroblasts in scleroderma.** *JCI insight*  
Lerbs, T., Cui, L., King, M. E., Chai, T., Muscat, C., Chung, L., Brown, R., Rieger, K., Shibata, T., Wernig, G.  
2020; 5 (16)
- **Doxycycline Reduces Scar Thickness and Improves Collagen Architecture** *ANNALS OF SURGERY*  
Moore, A. L., desJardins-Park, H. E., Duoto, B. A., Mascharak, S., Murphy, M. P., Irizarry, D. M., Foster, D. S., Jones, R. E., Barnes, L. A., Marshall, C. D., Ransom, R. C., Wernig, G., Longaker, et al  
2020; 272 (1): 183–93

- **Expansion of Bone Precursors through Jun as a Novel Treatment for Osteoporosis-Associated Fractures.** *Stem cell reports*  
Lerbs, T., Cui, L., Muscat, C., Saleem, A., van Neste, C., Domizi, P., Chan, C., Wernig, G.  
2020
- **Activation of JUN in fibroblasts promotes pro-fibrotic programme and modulates protective immunity.** *Nature communications*  
Cui, L. n., Chen, S. Y., Lerbs, T. n., Lee, J. W., Domizi, P. n., Gordon, S. n., Kim, Y. H., Nolan, G. n., Betancur, P. n., Wernig, G. n.  
2020; 11 (1): 2795
- **Elucidating the fundamental fibrotic processes driving abdominal adhesion formation.** *Nature communications*  
Foster, D. S., Marshall, C. D., Gulati, G. S., Chinta, M. S., Nguyen, A. n., Salhotra, A. n., Jones, R. E., Burcham, A. n., Lerbs, T. n., Cui, L. n., King, M. E., Titan, A. L., Ransom, et al  
2020; 11 (1): 4061
- **JUN Drives Pathologic Scarring by Activating Key Fibroproliferative Pathways in Fibroblast Subpopulations**  
Borrelli, M. R., Garcia, J. T., Moore, A. L., Patel, R. A., Mascharak, S., Duoto, B., Cui, L., Wan, D. C., Wernig, G., Longaker, M. T.  
ELSEVIER SCIENCE INC.2019: E215–E216
- **Selective hematopoietic stem cell ablation using CD117-antibody-drug-conjugates enables safe and effective transplantation with immunity preservation** *NATURE COMMUNICATIONS*  
Czechowicz, A., Palchaudhuri, R., Scheck, A., Hu, Y., Hoggatt, J., Saez, B., Pang, W. W., Mansour, M. K., Tate, T. A., Chan, Y., Walck, E., Wernig, G., Shizuru, et al  
2019; 10
- **Direct targeting of the mouse optic nerve for therapeutic delivery** *JOURNAL OF NEUROSCIENCE METHODS*  
Mesentier-Louro, L. A., Dodd, R., Domizi, P., Nobuta, H., Wernig, M., Wernig, G., Liao, Y.  
2019; 313: 1–5
- **DOXYCYCLINE REDUCES SCARRING BY MODULATING COLLAGEN ARCHITECTURE**  
desJardins-Park, H. E., Moore, A. L., Duoto, B. A., Mascharak, S., Murphy, M. P., Irizarry, D. M., Wernig, G., Longaker, M. T.  
BMJ PUBLISHING GROUP.2019: 157–58
- **Modeling chronic Graft-vs-Host disease in MHC-matched mouse strains: genetics, graft composition and tissue targets.** *Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation*  
Müller, A. M., Min, D. n., Wernig, G. n., Levy, R. B., Perez, V. L., Herretes, S. n., Florek, M. n., Burnett, C. n., Weinberg, K. n., Shizuru, J. A.  
2019
- **Doxycycline Reduces Scar Thickness and Improves Collagen Architecture.** *Annals of surgery*  
Moore, A. L., desJardins-Park, H. E., Duoto, B. A., Mascharak, S., Murphy, M. P., Irizarry, D. M., Foster, D. S., Jones, R. E., Barnes, L. A., Marshall, C. D., Ransom, R. C., Wernig, G., Longaker, et al  
2018
- **Surgical adhesions in mice are derived from mesothelial cells and can be targeted by antibodies against mesothelial markers.** *Science translational medicine*  
Tsai, J. M., Sinha, R., Seita, J., Fernhoff, N., Christ, S., Koopmans, T., Krampitz, G. W., McKenna, K. M., Xing, L., Sandholzer, M., Sales, J. H., Shoham, M., McCracken, et al  
2018; 10 (469)
- **Reduced Scar Thickness Achieved by Topical Doxycycline Is Mediated by Specific Skin Fibroblast Populations and Not Immune Cell Infiltrate**  
Moore, A. L., Murphy, M. P., Irizarry, D. M., Des Jardins-Park, H. E., Duoto, B. A., Mascharak, S., Foster, D. S., Jones, R., Wernig, G., Longaker, M. T.  
ELSEVIER SCIENCE INC.2018: S210–S211
- **Mouse Model with cJUN Over-Expression Eludes to Deep Dermal Fibroblast Expansion and Immune Cell Recruitment as the Biologic Mechanism of Hypertrophic Scarring**  
Moore, A. L., Duoto, B. A., Des Jardins-Park, H. E., Mascharak, S., Wernig, G., Longaker, M. T.  
ELSEVIER SCIENCE INC.2018: S208
- **Stem cell therapy for treatment of ischemic optic neuropathy**  
Mesentier-Louro, L., Yang, N., Shariati, A., Domizi, P., Dodd, R., Wernig, G., Wernig, M., Liao, Y.  
ASSOC RESEARCH VISION OPHTHALMOLOGY INC.2018

- **Doxycycline Improves Wound Healing via Nonantibiotic Associated Mechanisms**  
Moore, A. L., Murphy, M. P., Irizarry, D. M., Brett, E. A., Wernig, G., Longaker, M. T.  
ELSEVIER SCIENCE INC.2017: S162–S163
- **Unifying mechanism for different fibrotic diseases** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
Wernig, G., Chen, S., Cui, L., Van Neste, C., Tsai, J. M., Kambham, N., Vogel, H., Natkunam, Y., Gilliland, D. G., Nolan, G., Weissman, I. L.  
2017; 114 (18): 4757-4762
- **Unifying Mechanism of fibrotic diseases** *Proceedings of the National Academy of Science*  
Wernig, G., Weissman, I. L.  
2017; 114 (18): 4757-4762
- **Mapping the Pairwise Choices Leading from Pluripotency to Human Bone, Heart, and Other Mesoderm Cell Types** *CELL*  
Loh, K. M., Chen, A., Koh, P. W., Deng, T. Z., Sinha, R., Tsai, J. M., Barkal, A. A., Shen, K. Y., Jain, R., Morganti, R. M., Shyh-Chang, N., Fernhoff, N. B., George, et al  
2016; 166 (2): 451-467
- **Tuning Cytokine Receptor Signaling by Re-orienting Dimer Geometry with Surrogate Ligands** *CELL*  
Moraga, I., Wernig, G., Wilmes, S., Gryshkova, V., Richter, C. P., Hong, W., Sinha, R., Guo, F., Fabionar, H., Wehrman, T. S., Krutzik, P., Demharter, S., Plo, et al  
2015; 160 (6): 1196-1208
- **STAT5 Is Crucial to Maintain Leukemic Stem Cells in Acute Myelogenous Leukemias Induced by MOZ-TIF2** *CANCER RESEARCH*  
Tam, W. F., Haehnel, P. S., Schueler, A., Lee, B. H., Okabe, R., Zhu, N., Pante, S. V., Raffel, G., Mercher, T., Wernig, G., Bockamp, E., Sasca, D., Kreft, et al  
2013; 73 (1): 373-384
- **Anti-CD47 antibodies promote phagocytosis and inhibit the growth of human myeloma cells** *LEUKEMIA*  
Kim, D., Wang, J., Willingham, S. B., Martin, R., Wernig, G., Weissman, I. L.  
2012; 26 (12): 2538-2545
- **EXEL-8232, a small-molecule JAK2 inhibitor, effectively treats thrombocytosis and extramedullary hematopoiesis in a murine model of myeloproliferative neoplasm induced by MPLW515L** *LEUKEMIA*  
Wernig, G., Kharas, M. G., Mullally, A., Leeman, D. S., Okabe, R., George, T., Clary, D. O., Gilliland, D. G.  
2012; 26 (4): 720-727
- **Physiological Jak2V617F Expression Causes a Lethal Myeloproliferative Neoplasm with Differential Effects on Hematopoietic Stem and Progenitor Cells** *CANCER CELL*  
Mullally, A., Lane, S. W., Ball, B., Megerdichian, C., Okabe, R., Al-Shahrour, F., Paktinat, M., Haydu, J. E., Housman, E., Lord, A. M., Wernig, G., Kharas, M. G., Mercher, et al  
2010; 17 (6): 584-596
- **High-throughput sequence analysis of the tyrosine kinome in acute myeloid leukemia** *BLOOD*  
Loriaux, M. M., Levine, R. L., Tyner, J. W., Froehling, S., Scholl, C., Stoffregen, E. P., Wernig, G., Erickson, H., Eide, C. A., Berger, R., Bernard, O. A., Griffin, J. D., Stone, et al  
2008; 111 (9): 4788-4796
- **The Jak2V617F oncogene associated with myeloproliferative diseases requires a functional FERM domain for transformation and for expression of the Myc and Pim proto-oncogenes** *BLOOD*  
Wernig, G., Gonneville, J. R., Crowley, B. J., Rodrigues, M. S., Reddy, M. M., Hudon, H. E., Walz, C., Reiter, A., Podar, K., Royer, Y., Constantinescu, S. N., Tomasson, M. H., Griffin, et al  
2008; 111 (7): 3751-3759
- **Efficacy of TG101348, a selective JAK2 inhibitor, in treatment of a murine model of JAK2V617F-induced polycythemia vera** *CANCER CELL*  
Wernig, G., Kharas, M. G., Okabe, R., Moore, S. A., Leeman, D. S., Cullen, D. E., Gozo, M., McDowell, E. P., Levine, R. L., Doukas, J., Mak, C. C., Noronha, G., Martin, et al  
2008; 13 (4): 311-320
- **JAK2T875N is a novel activating mutation that results in myeloproliferative disease with features of megakaryoblastic leukemia in a murine bone marrow transplantation model** *BLOOD*

- Mercher, T., Wernig, G., Moore, S. A., Levine, R. L., Gu, T., Frohling, S., Cullen, D., Polakiewicz, R. D., Bernard, O. A., Boggon, T. J., Lee, B. H., Gilliland, D. G.  
2006; 108 (8): 2770-2779
- **MPLW515L is anovel somatic activating mutation in myelofibrosis with myeloid metaplasia** *PLOS MEDICINE*  
Pikman, Y., Lee, B. H., Mercher, T., McDowell, E., Ebert, B. L., Gozo, M., Cuker, A., Wernig, G., Moore, S., Galinsky, I., DeAngelo, D. J., Clark, J. J., Lee, et al  
2006; 3 (7): 1140-1151
  - **Expression of Jak2V617F causes a polycythemia vera-like disease with associated myelofibrosis in a murine bone marrow transplant model** *BLOOD*  
Wernig, G., Mercher, T., Okabe, R., Levine, R. L., Lee, B. H., Gilliland, D. G.  
2006; 107 (11): 4274-4281
  - **Role of JAK-STAT signaling in the pathogenesis of myeloproliferative disorders.** *Hematology / the Education Program of the American Society of Hematology. American Society of Hematology. Education Program*  
Levine, R. L., Wernig, G.  
2006: 233-?
  - **Expression of a homodimeric type I cytokine receptor is required for JAK2V617F-mediated transformation** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
Lu, X. H., Levine, R., Tong, W., Wernig, G., Pikman, Y., Zarnegar, S., Gilliland, D. G., Lodish, H.  
2005; 102 (52): 18962-18967
  - **The vast majority of bone-marrow-derived cells integrated into mdx muscle fibers are silent despite long-term engraftment** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
Wernig, G., Janzen, V., SCHAFFER, R., Zweyer, M., Knauf, U., Hoegemeier, O., Mundegar, R. R., Garbe, S., Stier, S., Franz, T., Wernig, M., Wernig, A.  
2005; 102 (33): 11852-11857
  - **Activating mutation in the tyrosine kinase JAK2 in polycythemia vera, essential thrombocythemia, and myeloid metaplasia with myelofibrosis** *CANCER CELL*  
Levine, R. L., Wadleigh, M., Cools, J., Ebert, B. L., Wernig, G., Huntly, B. J., Boggon, T. J., Wlodarska, L., Clark, J. J., Moore, S., Adelsperger, J., Koo, S., Lee, et al  
2005; 7 (4): 387-397
  - **Correction of CFTR malfunction and stimulation of Ca<sup>2+</sup>- activated Cl<sup>-</sup> channels restore HCO<sub>3</sub><sup>-</sup> secretion in cystic fibrosis bile ductular cells** *HEPATOLOGY*  
Zsembery, A., Jessner, W., Sitter, G., Spirli, C., Strazzabosco, M., Graf, J.  
2002; 35 (1): 95-104