

## Hiroyuki Shimada

Professor of Pathology and of Pediatrics

### CLINICAL OFFICE (PRIMARY)

- **Surgical Pathology**

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### Bio

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#### BIO

Hiroyuki Shimada, MD, PhD, FRCPA (Hon), is Professor of Pathology and of Pediatrics at the Stanford University Medical Center. He was born in Tokyo, Japan, and completed MD (1973) and PhD (1982) at the Yokohama City University School of Medicine, Yokohama, Japan, and also completed his pathology training at the Children's Hospital (now the Nationwide Children's Hospital) and the Ohio State University, Columbus, Ohio, USA (1988). Before moving to the Stanford University in 2019, he was Professor of Pathology (Clinical Scholar) at the University of Southern California Keck School of Medicine and working at the Children's Hospital Los Angeles.

Dr. Shimada was Chair of the International Neuroblastoma Pathology Committee (1999-2017) and the founder of the International Neuroblastoma Pathology Classification (INPC). As Director of the COG (Children's Oncology Group) Neuroblastoma Pathology Reference Laboratory (since 2001), he has been actively reviewing pathology samples of ~700 neuroblastoma cases per year from United States, Canada, Australia, and New Zealand. Pathology review results according to the INPC have been providing critical information for patient stratification and protocol assignment in the COG international neuroblastoma clinical trials.

#### CLINICAL FOCUS

- neuroblastoma
- Anatomic and Clinical Pathology

#### ACADEMIC APPOINTMENTS

- Professor - University Medical Line, Pathology
- Member, Maternal & Child Health Research Institute (MCHRI)

#### HONORS AND AWARDS

- Farber-Landing Lectureship, Society for Pediatric Pathology (2024)
- Lifetime Achievement Award, Advances in Neuroblastoma Research Association (2023)
- Presidential Distinguished Colleague Award, Society for Pediatric Pathology (2023)
- The Fred W. Stewart Award, Memorial Sloan Kettering Cancer Center (2022)
- Enid Gilbert-Barnes Prize, Society for Pediatric Pathology (2018)
- Honorary Fellowship, Royal College of Pathologists of Australasia (2012)
- Eleanor Humpherys Visiting Professorship, University of Chicago (2005)

- Lotte Straus Prize, Society for Pediatric Pathology (1989)

## PROFESSIONAL EDUCATION

- Residency: Nationwide Children's Hospital Pediatric Pathology (1988) OH
- Medical Education: Yokohama City University School of Medicine (1973) Japan

## Teaching

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### STANFORD ADVISEES

#### Postdoctoral Faculty Sponsor

Yuichi Shibui

## Publications

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### PUBLICATIONS

- **Artificial intelligence-based morphologic classification and molecular characterization of neuroblastic tumors from digital histopathology.** *Research square*  
Applebaum, M., Ramesh, S., Dyer, E., Pomaville, M., Doytcheva, K., Dolezal, J., Kochanny, S., Terhaar, R., Mehrhoff, C., Patel, K., Brewer, J., Kusswurm, B., Naranjo, et al  
2024
- **A Perspective on the CD47-SIRPA Axis in High-Risk Neuroblastoma.** *Current oncology (Toronto, Ont.)*  
Tang, X. X., Shimada, H., Ikegaki, N.  
2024; 31 (6): 3212-3226
- **Mitochondrial uncoupler and retinoic acid synergistically induce differentiation and inhibit proliferation in neuroblastoma.** *bioRxiv : the preprint server for biology*  
Jiang, H., Tiche, S. J., He, C. J., Jedoui, M., Forgo, B., Zhao, M., He, B., Li, Y., Li, A. M., Truong, A. T., Ho, J., Simmermaker, C., Yang, et al  
2024
- **Differences Between Male and Female Patients with Pilonidal Disease**  
Chiu, B., Abrajano, C., Yousefi, R., Shimada, H., Dalusag, K., Su, W. T., Hui, T. T., Mueller, C. M., Fuchs, J. R., Dunn, J. C.  
LIPPINCOTT WILLIAMS & WILKINS.2023: S349
- **Concurrent application of interferon-gamma and vincristine inhibits tumor growth in an orthotopic neuroblastoma mouse model.** *Pediatric surgery international*  
Zeki, J., Yavuz, B., Wood, L., Shimada, H., Kaplan, D. L., Chiu, B.  
2023; 39 (1): 241
- **The capture of extracellular vesicles endogenously released by xenotransplanted tumours induces an inflammatory reaction in the premetastatic niche.** *Journal of extracellular vesicles*  
Blavier, L., Nakata, R., Neviani, P., Sharma, K., Shimada, H., Benedicto, A., Matei, I., Lyden, D., DeClerck, Y. A.  
2023; 12 (5): e12326
- **Lorlatinib with or without chemotherapy in ALK-driven refractory/relapsed neuroblastoma: phase 1 trial results.** *Nature medicine*  
Goldsmith, K. C., Park, J. R., Kayser, K., Malvar, J., Chi, Y. Y., Groshen, S. G., Villablanca, J. G., Krytska, K., Lai, L. M., Acharya, P. T., Goodarzian, F., Pawel, B., Shimada, et al  
2023
- **Fibroblasts and macrophages cooperate to create a pro-tumorigenic and immune resistant environment via activation of TGF- $\beta$ /IL-6 pathway in neuroblastoma.** *Oncoimmunology*  
Louault, K., Porras, T., Lee, M. H., Muthugounder, S., Kennedy, R. J., Blavier, L., Sarte, E., Fernandez, G. E., Yang, F., Pawel, B. R., Shimada, H., Asgharzadeh, S., DeClerck, et al  
2022; 11 (1): 2146860
- **Mitochondrial uncoupling induces epigenome remodeling and promotes differentiation in neuroblastoma.** *Cancer research*  
Jiang, H., Greathouse, R. L., Tiche, S. J., Zhao, M., He, B., Li, Y., Li, A. M., Forgo, B., Yip, M., Li, A., Shih, M., Banuelos, S., Zhou, et al

2022

- **Use of Niclosamide Ethanolamine as a Mitochondrial Decoupler in Neuroblastoma**  
Rafeeqi, T., Jiang, H., Greathouse, R., He, B., Li, A., Shimada, H., Ye, J., Chiu, B.  
LIPPINCOTT WILLIAMS & WILKINS.2022: S194-S195
- **Time to resolution of iodine-123 metaiodobenzylguanidine (123 I-MIBG) avidity and local control outcomes for high-risk neuroblastoma following radiation therapy.** *Journal of medical imaging and radiation oncology*  
Oh, J., Gutkin, P., Wang, Y. P., Sandhu, N., Majzner, R. G., Nadel, H., Shimada, H., Lansinger, O., von Eyben, R., Donaldson, S., Bruzoni, M., Sodji, Q. H., Hiniker, et al  
2022
- **Outcomes Following GD2-Directed Postconsolidation Therapy for Neuroblastoma After Cessation of Random Assignment on ANBL0032: A Report From the Children's Oncology Group.** *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*  
Desai, A. V., Gilman, A. L., Ozkaynak, M. F., Naranjo, A., London, W. B., Tenney, S. C., Diccianni, M., Hank, J. A., Parisi, M. T., Shulkin, B. L., Smith, M., Moscow, J. A., Shimada, et al  
2022: JCO2102478
- **Deciphering the Warburg effect: Redox is the key to tumor differentiation**  
Jiang Haowen, Greathouse, R. L., He, B., Li, Y., Li, A. M., Forgo, B., Banuelos, S., Gruber, J., Shimada, H., Chiu, B., Ye, J.  
AMER ASSOC CANCER RESEARCH.2022
- **Cancer-associated fibroblasts and tumor-associated macrophages cooperate to promote TGF-beta 1-dependent NFkB activation and IL6 production and immune escape**  
Louault, K., Porras, T., Lee, M., Muthugounder, S., Kennedy, R., Sarte, L., Fernandez, G. E., Pawel, B., Shimada, H., Asgharzadeh, S., Declerck, Y. A.  
AMER ASSOC CANCER RESEARCH.2022
- **A pilot induction regimen incorporating dinutuximab and sargramostim for the treatment of newly diagnosed high-risk neuroblastoma: A report from the Children's Oncology Group.**  
Federico, S., Naranjo, A., Zhang, F., Marachelian, A., Desai, A., Shimada, H., Braunstein, S. E., Tinkle, C. L., Yanik, G. A., Asgharzadeh, S., Sondel, P. M., Yu, A. L., Acord, et al  
LIPPINCOTT WILLIAMS & WILKINS.2022
- **Macrophage-mediated anti-tumor immunity against high-risk neuroblastoma.** *Genes and immunity*  
Tang, X. X., Shimada, H., Ikegaki, N.  
2022
- **Genetic and Histopathological Heterogeneity of Neuroblastoma and Precision Therapeutic Approaches for Extremely Unfavorable Histology Subgroups.** *Biomolecules*  
Shimada, H., Ikegaki, N.  
1800; 12 (1)
- **Composite Neuroblastoma Metastatic to a Lymph Node: The Novel Histopathologic Diagnosis of a Unique Multiclonal Neoplasm.** *Annals of clinical and laboratory science*  
Kurtz, J. L., Shimada, H., Hazard, F. K.  
2021; 51 (4): 573-579
- **Composite Neuroblastoma Metastatic to a Lymph Node: The Novel Histopathologic Diagnosis of a Unique Multiclonal Neoplasm** *ANNALS OF CLINICAL AND LABORATORY SCIENCE*  
Kurtz, J. L., Shimada, H., Hazard, F. K.  
2021; 51 (4): 573-579
- **Combining inhibitors of Brd4 and cyclin-dependent kinase can decrease tumor growth in neuroblastoma with MYCN amplification.** *Journal of pediatric surgery*  
Wood, L., Huang, M., Zeki, J., Gong, M., Taylor, J., Shimada, H., Chiu, B.  
2021: 60215
- **A unique composite tumour of the adrenal gland in a paediatric patient, with adrenal cortical and neural crest cell-like components.** *Pathology*  
Taege, L., Shimada, H.  
2021

- **Clinical Relevance of CD4 Cytotoxic T Cells in High-Risk Neuroblastoma.** *Frontiers in immunology*  
Tang, X. X., Shimada, H., Ikegaki, N.  
2021; 12: 650427
- **Revised Neuroblastoma Risk Classification System: A Report From the Children's Oncology Group.** *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*  
Irwin, M. S., Naranjo, A., Zhang, F. F., Cohn, S. L., London, W. B., Gastier-Foster, J. M., Ramirez, N. C., Pfau, R., Reshmi, S., Wagner, E., Nuchtern, J., Asgharzadeh, S., Shimada, et al  
2021: JCO2100278
- **Randomized Phase II Trial of MIBG Versus MIBG, Vincristine, and Irinotecan Versus MIBG and Vorinostat for Patients With Relapsed or Refractory Neuroblastoma: A Report From NANT Consortium.** *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*  
DuBois, S. G., Granger, M. M., Groshen, S., Tsao-Wei, D., Ji, L., Shamirian, A., Czarnecki, S., Goodarzian, F., Berkovich, R., Shimada, H., Villablanca, J. G., Vo, K. T., Pinto, et al  
2021: JCO2100703
- **Stage 4S Neuroblastoma: Molecular, Histologic, and Immunohistochemical Characteristics and Presence of 2 Distinct Patterns of MYCN Protein Overexpression-A Report From the Children's Oncology Group.** *The American journal of surgical pathology*  
Kawano, A., Hazard, F. K., Chiu, B., Naranjo, A., LaBarre, B., London, W. B., Hogarty, M. D., Cohn, S. L., Maris, J. M., Park, J. R., Gastier-Foster, J. M., Ikegaki, N., Shimada, et al  
2020
- **Peripheral Neuroblastic Tumors - History and Perspective: A Report from Pathologist**  
Shimada, H.  
WILEY.2020
- **Gene Expression Signature in Human Neuroblastoma with TERT Overexpression Can Be Identified by Gene Set Enrichment Analysis and Epigenetically Targeted in an Orthotopic Mouse Xenograft Model**  
Huang, M., Wood, L., Zeki, J. C., Diyaolu, M., Gong, M., Taylor, J. S., Shimada, H., Chiu, B.  
ELSEVIER SCIENCE INC.2020: S199
- **MYC transcription activation mediated by OCT4 as a mechanism of resistance to 13-cisRA-mediated differentiation in neuroblastoma**  
Wei, S., Nguyen, T. H., Mook, D. G., Makena, M. R., Verlekar, D., Hindle, A., Martinez, G., Yang, S., Shimada, H., Reynolds, C., Kang, M. H.  
AMER ASSOC CANCER RESEARCH.2020
- **Outcomes and toxicities in patients (pts) non-randomly assigned to immunotherapy Children's Oncology Group (COG) ANBL0032.**  
Desai, A., Gilman, A., Ozkaynak, M., Naranjo, A., London, W. B., Tenney, S., Smith, M., Seibel, N., Shimada, H., Matthay, K. K., Cohn, S., Maris, J. M., Bagatell, et al  
AMER SOC CLINICAL ONCOLOGY.2020
- **Randomized phase II trial of MIBG versus MIBG/vincristine/irinotecan versus MIBG/vorinostat for relapsed/refractory neuroblastoma: A report from the New Approaches to Neuroblastoma Therapy Consortium.**  
DuBois, S. G., Granger, M., Groshen, S. G., Tsao-Wei, D., Shamirian, A., Czarnecki, S., Goodarzian, F., Berkovich, R., Shimada, H., Mosse, Y. P., Shusterman, S., Cohn, S., Goldsmith, et al  
AMER SOC CLINICAL ONCOLOGY.2020
- **The Role of the Clinical Laboratory in the Diagnosis of Neuroblastoma** *JOURNAL OF APPLIED LABORATORY MEDICINE*  
Hazard, F. K., Shimada, H.  
2020; 5 (2): 254-56
- **The Role of the Clinical Laboratory in the Diagnosis of Neuroblastoma.** *The journal of applied laboratory medicine*  
Hazard, F. K., Shimada, H.  
2020; 5 (2): 254-256
- **Enhancing sustained-release local therapy: Single versus dual chemotherapy for the treatment of neuroblastoma.** *Surgery*  
Taylor, J. S., Yavuz, B., Zeki, J., Wood, L., Ikegaki, N., Coburn, J., Harrington, K., Shimada, H., Kaplan, D. L., Chiu, B.  
2020
- **Local delivery of dinutuximab from lyophilized silk fibroin foams for treatment of an orthotopic neuroblastoma model.** *Cancer medicine*  
Ornell, K. J., Taylor, J. S., Zeki, J., Ikegaki, N., Shimada, H., Coburn, J. M., Chiu, B.  
2020

- **MYC transcription activation mediated by OCT4 as a mechanism of resistance to 13-cisRA-mediated differentiation in neuroblastoma.** *Cell death & disease*  
Wei, S. J., Nguyen, T. H., Yang, I. H., Mook, D. G., Makena, M. R., Verlekar, D. n., Hindle, A. n., Martinez, G. M., Yang, S. n., Shimada, H. n., Reynolds, C. P., Kang, M. H.  
2020; 11 (5): 368
- **Age Inherently Links to Histology to Define Histoprognostic Classification of Peripheral Neuroblastic Tumors.** *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*  
Beiske, K. n., Ikegaki, N. n., Shimada, H. n.  
2020: JCO2001839
- **Association of heterogeneous MYCN amplification with clinical features, biological characteristics and outcomes in neuroblastoma: A report from the Children's Oncology Group.** *European journal of cancer (Oxford, England : 1990)*  
Campbell, K. n., Naranjo, A. n., Hibbitts, E. n., Gastier-Foster, J. M., Bagatell, R. n., Irwin, M. S., Shimada, H. n., Hogarty, M. n., Park, J. R., DuBois, S. G.  
2020; 133: 112–19
- **Pathology of Peripheral Neuroblastic Tumors: An Update**  
Shimada, H.  
WILEY.2019: S1–S2
- **Optimizing Sustained Release Local Therapy: Single vs Dual Chemotherapy for the Treatment of Neuroblastoma**  
Taylor, J. S., Yavuz, B., Zeki, J., Ikegaki, N., Coburn, J. M., Harrington, K., Shimada, H., Kaplan, D. L., Chiu, B.  
ELSEVIER SCIENCE INC.2019: S210–S211
- **Replicating and identifying large cell neuroblastoma using high-dose intra-tumoral chemotherapy and automated digital analysis.** *Journal of pediatric surgery*  
Taylor, J. S., Sha, L., Ikegaki, N., Zeki, J., Deaton, R., Harris, J., Coburn, J., Yavuz, B., Sethi, A., Shimada, H., Kaplan, D. L., Gann, P., Chiu, et al  
2019
- **Anti-CD105 Antibody Eliminates Tumor Microenvironment Cells and Enhances Anti-GD2 Antibody Immunotherapy of Neuroblastoma with Activated Natural Killer Cells.** *Clinical cancer research : an official journal of the American Association for Cancer Research*  
Wu, H. W., Sheard, M. A., Malvar, J., Fernandez, G. E., DeClerck, Y. A., Blavier, L., Shimada, H., Theuer, C. P., Sposto, R., Seeger, R. C.  
2019; 25 (15): 4761-4774
- **Down-regulation of MYCN protein by CX-5461 leads to neuroblastoma tumor growth suppression**  
Taylor, J. S., Zeki, J., Ornell, K., Coburn, J., Shimada, H., Ikegaki, N., Chiu, B.  
W B SAUNDERS CO-ELSEVIER INC.2019: 1192–97
- **Down-regulation of MYCN protein by CX-5461 leads to neuroblastoma tumor growth suppression.** *Journal of pediatric surgery*  
Taylor, J. S., Zeki, J., Ornell, K., Coburn, J., Shimada, H., Ikegaki, N., Chiu, B.  
2019
- **MYC-family protein overexpression and prominent nucleolar formation represent prognostic indicators and potential therapeutic targets for aggressive high-MKI neuroblastomas: a report from the children's oncology group.** *Oncotarget*  
Niemas-Teshiba, R., Matsuno, R., Wang, L. L., Tang, X. X., Chiu, B., Zeki, J., Coburn, J., Ornell, K., Naranjo, A., Van Ryn, C., London, W. B., Hogarty, M. D., Gastier-Foster, et al  
2018; 9 (5): 6416-6432
- **Dose Escalation Study of No-Carrier-Added I-131-Metaiodobenzylguanidine for Relapsed or Refractory Neuroblastoma: New Approaches to Neuroblastoma Therapy Consortium Trial** *JOURNAL OF NUCLEAR MEDICINE*  
Matthay, K. K., Weiss, B., Villablanca, J. G., Maris, J. M., Yanik, G. A., DuBois, S. G., Stubbs, J., Groshen, S., Tsao-Wei, D., Hawkins, R., Jackson, H., Goodarzi, F., Daldrop-Link, et al  
2012; 53 (7): 1155-1163
- **Outcome analysis of non-high-risk neuroblastoma patients enrolled on Children's Oncology Group trials P9641 and A3961**  
Meany, H., Attiyeh, E. F., Naranjo, A., Twist, C., London, W. B., Villablanca, J., Schmidt, M., Baker, D., Strother, D. R., Shimada, H., Matthay, K. K., Cohn, S., Maris, et al  
AMER SOC CLINICAL ONCOLOGY.2012
- **Current Treatment Protocols Have Eliminated the Prognostic Advantage of Type 1 Fusions in Ewing Sarcoma: A Report From the Children's Oncology Group** *JOURNAL OF CLINICAL ONCOLOGY*

van Doorninck, J. A., Ji, L., Schaub, B., Shimada, H., Wing, M. R., Krailo, M. D., Lessnick, S. L., Marina, N., Triche, T. J., Sposto, R., Womer, R. B., Lawlor, E. R.

2010; 28 (12): 1989-1994

- **Mouse mesenchymal stem cells expressing PAX-FKHR form alveolar rhabdomyosarcomas by cooperating with secondary mutations** *CANCER RESEARCH*

Ren, Y., Finckenstein, F., Abdueva, D. A., Shahbazian, V., Chung, B., Weinberg, K. I., Triche, T. J., Shimada, H., Anderson, M. J.

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- **Primary and metastatic rhabdomyosarcoma in the breast: Neoplasms of adolescent females, a report from the intergroup rhabdomyosarcoma study** *MEDICAL AND PEDIATRIC ONCOLOGY*

Hays, D. M., Donaldson, S. S., Shimada, H., Crist, W. M., Newton, W. A., Andrassy, R. J., Wiener, E., Green, J., Triche, T., Maurer, H. M.

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