Stanford

Crystal Mackall

Ernest and Amelia Gallo Family Professor and Professor of Pediatrics and of Medicine

Pediatrics - Hematology & Oncology

NIH Biosketch available Online Curriculum Vitae available Online

CLINICAL OFFICES

- **Pediatric Oncology**

  725 Welch Rd

  Clinic D

  Palo Alto, CA 94304

  Tel (650) 497-8953 **Fax** (650) 724-1164

ACADEMIC CONTACT INFORMATION

- **Administrative Contact**

  Carol Sinoben - Executive Asst.

  Email csinoben@stanford.edu

  Tel 650-725-9670

Bio

BIO

Crystal L Mackall MD is the Ernest and Amelia Gallo Family Professor of Pediatrics and Internal Medicine at Stanford University. She serves as Founding Director of the Stanford Center for Cancer Cell Therapy, Associate Director of Stanford Cancer Institute, Leader of the Cancer Immunology and Immunotherapy Program and Director of the Parker Institute for Cancer Immunotherapy at Stanford. During a 27 year tenure culminating as Chief of the Pediatric Oncology Branch, NCI, and now at Stanford, she has led an internationally recognized translational research program spanning basic studies of T cell homeostasis and tumor immunology, and clinical trials of immune based therapies for cancer. Her work is credited with identifying an essential role for the thymus in human T cell regeneration and discovering IL-7 as the master regulator of T cell homeostasis. She has led numerous first-in-human and first-in-child clinical trials spanning dendritic cell vaccines, cytokines, and adoptive immunotherapy using NK cells and genetically modified T cells. Her group was among the first to demonstrate impressive activity of CD19-CAR in pediatric leukemia, recently demonstrated impressive activity of CD22-CARs for leukemia and has identified T cell exhaustion as a major feature limiting the activity of CAR T cells.. Dr. Mackall’s clinical trials are notable for the incorporation of deep biologic endpoints that further our understanding of the basis for success and failure of novel immunotherapeutics. She has published over 185 manuscripts and serves in numerous leadership positions, including co-PI on the NCI Pediatric Cancer Immunotherapy Network (U54), Leader of the NCI Pediatric Cancer Immunotherapy Trials Network, and co-Leader of the St. Baldrick’s-StandUp2Cancer Pediatric Dream Team. She is Board Certified in Pediatrics, Pediatric Hematology-Oncology and Internal Medicine.

CLINICAL FOCUS

- Pediatric Hematology-Oncology

ACADEMIC APPOINTMENTS

- Professor, Pediatrics - Hematology & Oncology
- Professor, Medicine - Blood & Marrow Transplantation
- Member, Bio-X
- Member, Maternal & Child Health Research Institute (MCHRI)
- Member, Stanford Cancer Institute

ADMINISTRATIVE APPOINTMENTS

- Founding Director, Stanford Center for Cancer Cell Therapy, (2017- present)
- Director, Parker Institute for Cancer Immunotherapy at Stanford, (2016- present)
- Associate Director, Stanford Cancer Institute, (2016- present)
- Leader, Cancer Immunology and Immunotherapy Program, Stanford Cancer Institute, (2016- present)
- Director, Cancer Immunotherapy Program, Department of Pediatrics, (2016- present)

HONORS AND AWARDS

- Lila and Murray Gruber Memorial Cancer Research Award and Lectureship, American Academy of Dermatology (March 2018)
- BJ Kennedy Keynote Lecturer, Masonic Cancer Center, Minneapolis, MN (2018)
- Top 10 Clinical Research Award for New CAR-T Cell Therapy for Relapsed Leukemia, Top 10 Clinical Research Award (2018)
- Chair, Pediatric Cancer Working Group, American Association for Cancer Research (2017-18)
- Stephen Max Memorial Lectureship, University of Maryland (2017)

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BOARDS, ADVISORY COMMITTEES, PROFESSIONAL ORGANIZATIONS

- Executive Board, Federation of Clinical Immunology Societies (FOCIS) (2001 - 2002)
- Member, Biologic Response Modifiers Advisory Committee, Food and Drug Administration (2002 - 2003)
- Member, NIH Central Tenure Committee (2004 - 2008)
- Education Committee, American Society of Clinical Oncology (2006 - 2009)
- Member, DNA Advisory Committee, US Food and Drug Administration (2008 - 2008)
- Advisory Board for Clinical Research, NIH Clinical Center (2008 - 2012)

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PROFESSIONAL EDUCATION

- Board Certification: Pediatric Hematology-Oncology, American Board of Pediatrics (1992)
- Fellowship: National Cancer Institute - Center Cancer Research (1992) MD
- Board Certification: Pediatrics, American Board of Pediatrics (1989)
- Board Certification: Internal Medicine, American Board of Internal Medicine (1989)
- Residency: Akron General Hospital (1988) OH

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PATENTS

- Rimas Orentas, Ira Pastan, Crystal Mackall. "United States Patent 61/549,516 Anti-CD22 Chimeric Antigen Receptors, patent pending", National Cancer Institute
- Rimas Orentas, Ira Pastan, Crystal Mackall, Dimiter Dimitrov. "United States Patent 61/717,960 M971 Chimeric Antigen Receptors, patent pending", National Cancer Institute
- Dimiter Dimitrov, Rimas Orentas, Crystal Mackall. "United States Patent 61/805001 Anti-CD276 polypeptides, proteins and chimeric antigen receptors, patent pending", National Cancer Institute
- Rimas Orentas, Dimiter Dimitrov, Crystal Mackall. "United States Patent 61/900,906 ALK Antibodies, Conjugates and Chimeric Antigen Receptors, patent pending", National Cancer Institute
- Terry Fry, Haiying Qin, Crystal Mackall, Rimas Orentas. "United States Patent 62/135,442 Dual Specific Anti-CD22-Anti-CD19-Chimeric Antigen Receptors, patent pending", National Cancer Institute

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Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

We are impressed by the potency of T cell immune responses for the treatment of cancer and our work focuses on enhancing the effectiveness of T cell based immunotherapies for cancer. Our approach is to simultaneously conduct basic studies alongside clinical trials, leveraging an iterative bench-to-bedside-bench rotation to efficiently optimize clinically relevant cancer immunotherapies. Our laboratory seeks to develop novel therapies for early phase testing in clinical trials, and also conducts intensive studies on clinical samples obtained from patients treated on immunotherapy trials. We also seek to enhance fundamental understanding of human T cell biology.

We focus primarily on using genetically engineered T cells to treat cancer, with an emphasis on chimeric antigen receptors (CARs). CARs are non-natural receptors, created using synthetic biology, that endow T cells with the capacity for antigen-specific, MHC-unrestricted killing. Some clinical results using CAR based therapies have been impressive, but we believe that further progress will emerge as a result of focus on these three major areas:

1. T cell exhaustion, a state whereby continued T cell activation leads to diminished functionality, is a fundamental barrier limiting the efficacy of many cancer immunotherapies. Our laboratory is focused on using high dimensional, single cell analyses to better define human T cell exhaustion and to enhance understanding of the biological mechanisms responsible for this phenomena. We believe that enhanced understanding of T cell exhaustion will give rise to novel approaches to prevent or reverse this phenomenon in the context of cancer immunotherapy.

2. Effective immunotherapies require a therapeutic window which allows the immune cell to preferentially or exclusively attack the neoplastic cell while sparing non-neoplastic, vital tissues. Our laboratory is focused on identifying novel targets for T cell based immunotherapies and for enhancing our understanding of the basis for differential antigen recognition using CAR T cells for cancer therapy. We are also interested in using novel approaches for combinatorial recognition, both to diminish the risk for tumor escape due to loss of antigen expression, and to allow targeting of tumor antigens that pose a risk due to co-expression on healthy, vital tissues.

3. The tumor microenvironment is potently immunosuppressive and can prevent potent antigen specific immune responses from effectively mediating antitumor effects. Our laboratory focuses on enhancing understanding of the immunosuppressive tumor microenvironment and on developing novel approaches to diminish the ability of the tumor microenvironment to limit the efficacy of T cell based immunotherapies.

CLINICAL TRIALS

- Anti-CD22 Chimeric Receptor T Cells in Pediatric and Young Adults With Recurrent or Refractory CD22-expressing B Cell Malignancies, Recruiting
- Axicabtagene Ciloleucel Expanded Access Study, Recruiting
- CD19/CD22 Chimeric Antigen Receptor T Cells and Chemotherapy in Treating Children or Young Adults With Recurrent or Refractory CD19 Positive B Acute Lymphoblastic Leukemia, Recruiting
- CD19/CD22 Chimeric Antigen Receptor T Cells and Chemotherapy in Treating Patients With Recurrent or Refractory CD19 Positive Diffuse Large B-Cell Lymphoma or B Acute Lymphoblastic Leukemia, Recruiting
- Nivolumab With or Without Ipilimumab in Treating Younger Patients With Recurrent or Refractory Solid Tumors or Sarcomas, Recruiting
- Screening Protocol for Tumor Antigen Expression Profiling and HLA Typing for Eligibility Determination, Recruiting

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Teaching

STANFORD ADVISEES

Postdoctoral Faculty Sponsor

Hima Anbunathan, Zina Good, Dorota Klysz, Amaury Leruste, Johanna Lena Theruvath, Evan Weber

Postdoctoral Research Mentor

Dorota Klysz, Amaury Leruste, Johanna Lena Theruvath, Diane Tseng, Evan Weber

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Cancer Biology (Phd Program)
- Immunology (Phd Program)
- Pediatric Hem/Onc (Fellowship Program)

Publications

PUBLICATIONS

- **Pharmacologic control of CAR-T cell function using dasatinib.** *Blood advances*
  Weber, E. W., Lynn, R. C., Sotillo, E., Lattin, J., Xu, P., Mackall, C. L.
  2019; 3 (5): 711–17

- **Driving CAR T cell translation forward.** *Science translational medicine*
  Schultz, L., Mackall, C.
  2019; 11 (481)

- **CAR T cells targeting B7-H3, a Pan-Cancer Antigen, Demonstrate Potent Preclinical Activity Against Pediatric Solid Tumors and Brain Tumors.** *Clinical cancer research : an official journal of the American Association for Cancer Research*
  Majzner, R. G., Theruvath, J. L., Nellan, A., Heitzeneder, S., Cui, Y., Mount, C. W., Rietberg, S. P., Linde, M. H., Xu, P., Rota, C., Sotillo, E., Labanieh, L., Lee, et al
  2019

- **CAR T cell therapy: inroads to response and resistance.** *Nature reviews. Immunology*
  Brown, C. E., Mackall, C. L.
  2019

- **Pregnancy-Associated Plasma Protein-A (PAPP-A) in Ewing Sarcoma: Role in Tumor Growth and Immune Evasion.** *Journal of the National Cancer Institute*
  Heitzeneder, S., Sotillo, E., Shern, J. F., Sindiri, S., Xu, P., Jones, R., Pollak, M., Noer, P. R., Lorette, J., Fazli, L., Alag, A., Meltzer, P., Lau, et al
  2019

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