## BIOGRAPHICAL SKETCH

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NAME: Nolan, Garry P.

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POSITION TITLE: Rachford and Carlota A. Harris Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Cornell University, Ithaca, NY | B.S. | 05/1983 | Biology/Genetics |
| Stanford University, Stanford, CA | Ph.D. | 06/1989 | Genetics |
| Stanford University, Stanford, CA | Postdoctoral | 06/1990 | Genetics |
| Massachusetts Institute of Technology (MIT), Cambridge, MA / Rockefeller University, New York, NY | Postdoctoral | 06/1993 | Biochemistry |

### A. Personal Statement

I am the Rachford and Carlota A. Harris Professor in the Department of Pathology at Stanford University School of Medicine. I trained with Leonard Herzenberg (for my Ph.D.) and Nobelist Dr. David Baltimore (for postdoctoral work for the first cloning/characterization of NF-kB p65/RelA and the development of 293T rapid retroviral production systems). I have published 315 peer-reviewed research papers, hold 40 US patents, and have been honored as one of the top 25 inventors at Stanford University.

I am well known for my ability to bring novel technologies to commercial fruition. My contributions to the implementation of mass cytometry (CyTOF) and its use for immuno-oncology research are a case in point, winning Nature's "Outstanding Research Achievement" for 2011. My current research is focused on the development of multiparameter, single-cell tissue imaging technologies and computational approaches for systems immuno-oncology. Two recent innovations from my lab include multiplexed ion beam imaging (MIBI) and CO-Detection by indEXing (CODEX), which allow for simultaneous spatial quantification of 50+ parameters in a single tissue section. Another focus of my lab is the development and utilization of machine learning algorithms to interpret the large, high-dimensional datasets produced by CyTOF, multiplexed ion beam imaging (MIBI), and CODEX. Collectively, our efforts are to provide a deeper understanding of normal and impaired immune function - including detailed substructures of the immune system as it relates to various cancerous states - to enable wholly new understandings that lead to improved clinical outcomes.

Additionally, I am dedicated to teaching and mentoring. I am currently mentoring 9 postdoctoral fellows and 5 graduate students, and I have taught multiple courses at Stanford and through NIH-sponsored programs. I have assisted students and colleagues in commercializing technologies via eight companies with a sum estimated present market capitalization of $800 million.

**Selected ongoing and recently completed projects I would like to highlight include:**
U54HG012723
Michael Snyder (PI), Garry Nolan (Co-PI)
09/25/2016-06/31/2026
Stanford Tissue Mapping Center – HubMAP

75F40120C00176
Garry Nolan (PI)
09/30/2020 - 12/31/2025
Pathology and Pathogenesis of Coronavirus Infections in Animal Models

209477
Garry Nolan (PI)
09/01/2020 - 10/31/2023
Center for Immune Technology

U2CCA233195
Garry Nolan (MPI)
09/24/2018 - 08/31/2023
The Cellular Geography of Therapeutic Resistance in Cancer

U19AI057229
Mark Davis (PI) Garry Nolan (Co- PI)
04/01/2019-03/31/2024
Protective Mechanisms Against Pandemic Respiratory Virus

C27165/A29073
Garry Nolan (PI)
01/01/2019 - 04/30/2025
STrOmal ReprograMing (STORMing) of Epithelial Cells: Providing New Directions to Prevent and Revert Chronic Inflammation-Associated Cancer

5U19AI100627
Richard Ulevitch (PI) Garry Nolan (Co-PI)
09/01/2017-08/31/2023
Systems Approach to Immunity and Inflammation

209477
Garry Nolan (PI)
09/01/2020 – 10/31/2023
Center for Immune Technology

**B. Positions, Scientific Appointments and Honors**

**Positions and Scientific Appointments**

2011-present Rachford and Carlota A. Harris Professor, Department of Pathology, Stanford University School of Medicine, Stanford, CA
2009-2011 Professor (Tenure), Department of Microbiology and Immunology, Stanford University School of Medicine, Stanford, CA
1999-2009 Associate Professor (Tenure), Department of Molecular Pharmacology, Stanford University School of Medicine, Stanford, CA
1995-1999 Assistant Professor, Joint Appointment, Department of Microbiology and Immunology, Stanford University School of Medicine, Stanford, CA
1993-1999 Assistant Professor, Department of Molecular Pharmacology, Stanford University School of Medicine, Stanford, CA

**Other Professional Appointments and Activities**

Present Editorial Boards: *Gene Therapy & Molecular Biology*, *Genes to Cells*, *Molecular Therapy* (American Cancer Society), *Molecular Systems Biology*, and *Open Network Biology*
2016-present Co-director (with Sylvia Plevritis, PhD), Stanford Center for Cancer Systems Biology
2011-2015 NCI-Frederick Advisory Committee, National Cancer Institute (NCI) of the NIH

2010-2015 Director, Stanford NHLBI Proteomics Center for Systems Immunology, supported by National Heart, Lung, and Blood Institute of the NIH
2007-present Board of External Experts, National Heart, Lung, and Blood Institute of the NIH
2000-present Reviewers for various NIH study sections
1997-1999 Editorial Board: *Chemistry and Biology*

**Selected Honors and Awards**

2022 Keio University Medical Science Prize
2022 M.D. Anderson Award
2020-2023 HOPE foundation award
2019-2023 Cancer grand challenge award from Cancer Research UK
2017-2018 Celgene award
2017-2018 Silicon Valley Community Foundation award
2016-2019 Inaugural "Bio-agent protection" Award, FDA
2012-2018 Inaugural Teal Innovator Award, Department of Defense
2021 Hans Sigrist Prize, Hans Sigrist Foundation at the University of Bern in Switzerland
2015 Ernest Cotlove Award, Academy of Clinical Laboratory Physicians & Scientists
2015 Fellow of the American Institute for Medical and Biological Engineering
2011 "Outstanding Research Achievement in 2011" for Mass Cytometry & CyTOF, Nature Publishing Group
2000 Stohlman Scholar, Leukemia and Lymphoma Society
1997-1998 Howard Hughes Medical Institute Junior Faculty Scholar Award, Stanford University
1996-2000 Burroughs Wellcome Fund New Investigator Award
1995-2000 Leukemia Society Scholar Award
1995-1998 Board of Trustees, Leukemia Society of America, Northern California
1993-1998 Hume Faculty Scholar
1992-1995 Leukemia Society Special Fellow
1990-1992 National Institutes of Health Fellowship
1988 National Science Foundation Fellowship. Organization and Function of the Eukaryotic Genome. Spetsai, Greece.

**C. Contributions to Science**

Dr. Garry P. Nolan has undertaken research at the interface of biology, bioinformatics and electrical engineering, and developed transformative technologies and equipment, such as CyTOF, three-dimensional MIBI, and CODEX. His contributions include development of the 293T-cell based retroviral production systems in David Baltimore's lab and later at Stanford, the phospho-flow approach for single cell phosphorylation in immune and other cells, CyTOF mass spectrometry for immune system monitoring, and more lately MIBI and CODEX imaging systems for multiparameter tissue analysis. His contributions to science have been recognized by many awards, including the prestigious Hans Sigrist Prize (2021). He has published over 300 peer reviewed papers, holds 40 patents, and has spun eight companies out of his lab—two of which were sold to Roche, two have gone public on NASDAQ, and the remainder are still private, but VC funded in the $20 million and above range. The latter underscores the translation of public investment to utility towards health and patient care.

**1. Immunogenetics, and individualized cell gene expression**

Dr. Nolan received his Ph.D. in Genetics at Stanford University under the mentorship of Leonard and Leonore Herzenberg (co-developers of the Fluorescence Activated Cell Sorter) where he worked on the cloning of CD8, and heritability of transcription states. Here, he also developed the FACS-Gal assay for in vivo measure of transcription, a highly influential and widely used reporter system to study gene expression. These studies led to two last-author papers published in *Proc Natl Acad Sci* and *Science* during his graduate work.

a. Nakauchi H, **Nolan GP**, Hsu C, Huang HS, Kavathas P, and Herzenberg LA. Molecular cloning of Lyt-2, a membrane glycoprotein marking a subset of mouse T lymphocytes: molecular homology to its human counterpart, Leu-2/T8, and to immunoglobulin variable regions. *Proc Natl Acad Sci USA* 1985; 82(15): 5126-5130. PMCID: PMC390512.

b. Tagawa M, Nakauchi H, Herzenberg LA, and **Nolan GP**. Formal proof that different-size Lyt-2 polypeptides arise from differential splicing and post-transcriptional regulation. *Proc Natl Acad Sci USA* 1986; 83(10):3422-3426. PMCID: PMC323526.
c. **Nolan GP**, Fiering S, Nicolas JF, and Herzenberg LA. Fluorescence-activated cell analysis and sorting of viable mammalian cells based on beta-D-galactosidase activity after transduction of Escherichia coli lacZ. *Proc Natl Acad Sci USA* 1988; 85(8):2603-2607. PMCID: PMC280046. (**cited by 621**)
d. Krasnow MA, Cumberledge S, Manning G, Herzenberg LA, and **Nolan GP**. Whole animal cell sorting of *Drosophila* embryos. *Science* 1991; 251(4989):81-85.

**2. Cloning P65/RelA and retroviral transfer technologies**

For his postdoctoral training, Dr. Nolan worked in the laboratory of Nobelist Dr. David Baltimore at MIT, where he cloned and characterized the p65/RelA subunit of NFκB, a central molecule in inflammation and cancer biology. Nolan's work was a seminal contribution to the NFκB field, and thousands of subsequent publications from others focus directly on p65/RelA. Dr. Nolan is also the originator of the idea, co-creator (with Dr. Warren Pear) of the 293T-based retroviral production systems in the Baltimore lab, and developer of the subsequent Phoenix packaging systems at Stanford in the Nolan lab. Dr. Nolan's research created retroviral vector and library production system for the field of gene therapy, and paved the way for others to rapidly produce lentiviral vectors for safe gene therapy.

a. Ghosh S, Gifford AM, Riviere LR, Tempst P, **Nolan GP**, and D. Baltimore. Cloning of the p50 DNA binding subunit of NF-kappa B: homology to rel and dorsal. *Cell* 1990; 62(5):1019-1029. (**cited by 1,019**)
b. **Nolan GP**, Ghosh S, Liou HC, Tempst P, and Baltimore D. DNA binding and I kappa B inhibition of the cloned p65 subunit of NF-kappa B, a rel-related polypeptide. *Cell* 1991; 64(5):961-969. (**cited by 729**)
c. Pear WS., **Nolan GP**, Scott ML, and Baltimore D. Production of high-titer helper-free retroviruses by transient transfection. *Proc Natl Acad Sci USA* 1993; 90(18):8392-8396. PMCID: PMC47362. (**cited by 3,142**)
d. Kitamura T, Onishi M, Kinoshita S, Shibuya A, Miyajima A, and **Nolan GP**. Efficient screening of retroviral cDNA expression libraries. *Proc Natl Acad Sci USA* 1995; 92(20):9146-9150. (**cited by 293**)

**3. Creating the phospho-flow cytometry approach for single-cell mapping of cell signaling networks**

As a professor at Stanford University, Dr. Nolan's lab began pioneering techniques in "phospho-flow cytometry", the use of flow cytometry combined with phospho-specific antibodies to map signaling pathways in single cells. These pathways were delineated through perturbation of specimens with environmental cues, such as cytokines or drugs. This technique was used to derive causal protein-signaling networks from multiparameter single-cell data, a breakthrough and now highly cited technique. This technique is now commonly used in flow cytometry and the newly developed mass cytometry (described below) for interrogation of healthy and disease cell specimens.

a. Irish JM, Hovland R, Krutzik PO, Perez OD, Bruserud O, Gjertsen BT, and **Nolan GP**. Single cell profiling of potentiated phospho-protein networks in cancer cells. *Cell* 2004; 118(2):217-228. (**cited by 796**)
b. Sachs K, Perez O, Pe'er D, Lauffenburger DA, and **Nolan GP**. Causal protein-signaling networks derived from multiparameter single-cell data. *Science* 2005; 308(5721):523-529. (**cited by 1,728**)
c. O'Gorman WE, Sampath P, Simonds EF, Sikorski R, O'Malley M, Krutzik PO, Chen H, Panchanathan V, Chaudhri G, Karupiah G, Lewis DB, Thorne SH, and **Nolan GP**. Alternate mechanisms of initial pattern recognition drive differential immune responses to related poxviruses. *Cell Host Microbe* 2010; 8(2):174-185. PMCID: PMC2940993.

**4. Developing mass cytometry for highly multiplexed cell analysis and MIBI and CODEX imaging systems for a tissue atlas of spatially-resolved, multiplexed single-cell mapping**

In collaboration with DVS Sciences (Toronto, Ontario), Dr. Nolan introduced assays based on next-generation single-cell "mass cytometry" (CyTOF) to simultaneously measure 45 (theoretically up to 100) markers per cell. Previously, fluorescence flow cytometry could not provide such a measurement because of spectral overlap existing between each fluorophore being measured. Early work using this technology revealed a previously hidden layer of hematopoietic organization and provided a reference point for studies of immune cell dysfunction and hematological malignancies. This technology is now being applied to single cell analysis of signaling proteins, cell types, epigenetic states, and mRNA expression patterns to delineate and understand cancer lineage and stem cell structures. Based on Dr. Nolan's pioneering work, CyTOF is poised to be the next revolution in single cell analysis, and is currently being adopted by major research institutions and industry. Dr.

Nolan's lab also applied key concepts used in mass cytometry to develop multiparametric tissue imaging platforms: 1) multiplexed ion beam imaging" (MIBI) and 2) CO-detection by inDEXing (CODEX). Both techniques bring high-parameter antibody staining to the field of microscopy, where dimensions such as subcellular localization and cell-type "neighborhoods" can be used in the machine learning algorithms the Nolan lab has developed to analyze these high-parameter datasets (see following section). Dr. Nolan's lab has also worked with the Deisseroth lab to develop technology for 3D intact-tissue RNA sequencing (STARmap), which was recently applied to define cell types and circuit states in the mouse brain.

a. Bendall SC, Simonds EF, Qiu P, Amir el-AD, Krutzik PO, Finck R, Bruggner RV, Melamed R, Trejo A, Ornatsky OI, Balderas RS, Plevritis SK, Sachs K, Pe'er D, Tanner SD, **Nolan GP**. Single-cell mass cytometry of differential immune and drug responses across a human hematopoietic continuum. *Science* 2011; 332(6030):687-696. (**cited by 2,590**)
b. Angelo M, Bendall SC, Finck R, Hale M, Hitzman C, Borowsky A, Levenson R, Lowe J, Liu S, Zhao S, Natkunam Y, **Nolan GP**. Multiplexed ion beam imaging of human breast tumors. *Nat Med* 2014; 20(4):436-442. PMCID: PMC4110905. (**cited by 656**)
c. Goltsev Y, Samusik N, Kennedy-Darling J, Bhate S, Hale M, Vazquez G, Black S, **Nolan, GP**. Deep profiling of mouse splenic architecture with CODEX multiplexed imaging. *Cell* 2018; 174(4):968-981. PMCID: PMC6086938. (**cited by 459**)
d. Wang X, Allen WE, Wright MA, Sylwestrak EL, Samusik N, Vesuna S, Evans K, Liu C, Ramakrishnan C, Liu J, **Nolan GP***, Bava F-A*, and Deisseroth K*. Three-dimensional intact-tissue sequencing of single-cell transcriptional states. *Science* 2018; 361(6400):eaat5691. *co-corresponding authors. (**cited by 483**)

## 5. Designing machine learning programs for automated mass cytometry data analysis

The datasets acquired by 45+ parameter mass cytometry are too overwhelming for humans to analyze through manual gating. Thus, Dr. Nolan's lab began developing algorithms to characterize these multiple cell subsets. Programs such as SPADE use clustering to visually represent 45 dimensional datasets in a two-dimensional minimum spanning tree. Another example is a program developed in the Nolan lab called Citrus, which utilizes a clustering and regression-based approach with both CyTOF data and additional patient information to make high-resolution predictions about the given patients. For example, Citrus successfully identified phospho-proteins within specific immune cell subsets that predicted whether patients undergoing major hip surgery would have good or poor recoveries. A publication of ours in *Science* sets up a framework for merging all immune system data into a unified format much like the genome reference map. Similarly, a recent publication of ours in *Nature Medicine* provides a framework for predicting relapse in acute leukemia.

a. Gaudilliere B, Fragiadakis GK, Bruggner RV, Nicolau M, Finck R, Tingle M, Silva J, Ganio EA, Yeh CG, Maloney WJ, Huddleston JI, Goodman SB, Davis MM, Bendall SC, Fantl WJ, Angst MS, and **Nolan GP**. Clinical recovery from surgery correlates with single-cell immune signatures. *Sci Transl Med* 2014; 6(255):255ra131. PMCID: PMC4334126. (**cited by 243**)
b. Spitzer MH, Gherardini PF, Fragiadakis GK, Bhattacharya N, Yuan RT, Hotson AN, Finck R, Carmi Y, Zunder ER, Fantl WJ, Bendall SC, Engleman EG, and **Nolan GP**. An interactive reference framework for modeling a dynamic immune system. *Science* 2015; 349(6244):1259425. PMCID: PMC4537647. (**cited by 201**)
c. Spitzer MH, Carmi Y, Reticker-Flynn NE, Kwek SS, Madhireddy D, Martins MM, Gherardini PF, Prestwood TR, Chabon J, Bendall SC, Fong L, **Nolan GP***, and Engleman EG*. Systemic Immunity Is Required for Effective Cancer Immunotherapy. *Cell* 2017; 168(3):487-502. PMCID: PMC5312823. *co-corresponding authors. (**cited by 546**)
d. Good Z, Sarno J, Jager A, Samusik N, Aghaeepour N, Simonds EF, White L, Lacayo NJ, Fantl W, Fazio G, Gaipa G, Biondi A, Tibshirani R, Bendall SC, **Nolan GP***, and Davis KL*. Single-cell developmental classification of B-cell precursor acute lymphoblastic leukemia at diagnosis reveals predictors of relapse. *Nat Med* 2018; 24(4):474-483. PMCID: PMC5953207. *These authors jointly directed this work.

**Garry P. Nolan, Ph.D. has published 315 peer-reviewed research papers and holds 40 issued patents. Total citations by others: 52,918.**

**Complete List of Published Work in**: **http://www.ncbi.nlm.nih.gov/pubmed/?term=nolan+g+p**