BIOGRAPHICAL SKETCH

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NAME: Stephen P. Hunger, MD

eRA COMMONS USER NAME (credential, e.g., agency login): HUNGESP

POSITION TITLE: Chief, Division of Oncology; Director, Center for Childhood Cancer Research

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	Completion Date	FIELD OF STUDY
Massachusetts Institute of Technology	B.S.	05/1981	Applied Biology
University of Connecticut School of Medicine	M.D.	05/1985	Medicine
Johns Hopkins Hospital		06/1988	Intern/Resident, Pediatrics
Stanford University School of Medicine		06/1991	Fellow, Pediatric Hematology/Oncology
Stanford University School of Medicine		07/1994	Postdoctoral Scholar, Pathology

A. Personal Statement

My research is focused on improving understanding of the molecular genetics of childhood acute lymphoblastic leukemia (ALL) and translating new discoveries into improved outcomes via clinical trials and linked translational research studies. As Vice Chair (2002-07) and Chair of the Children's Oncology Group (COG) ALL committee (2008-15), I was responsible for oversight of the design and conduct of clinical trials and translational research studies that enroll over 70% of US children with ALL. Since 2006, I have been the Principal Investigator of the COG High Risk ALL TARGET (Therapeutically Applicable Research to Generate Effective Targets) Project, a multi-institutional collaborative effort that has discovered new sentinel genetic lesions in childhood ALL (*IKZF1* deletions/mutations, *JAK* mutations, *CRLF2* alterations), identified the Ph-like ALL high risk ALL subtype, and defined its genomic landscape. This has allowed us to develop new clinical trials to test molecularly targeted therapies in high risk ALL subsets with kinase activating lesions. I have been an author on 272 peer-reviewed manuscripts, including over 150 since 2010.

B. Positions and Honors

Positions and Employment

1994-2001 **Assistant and Associate Professor,** Dept. of Pediatrics, Univ. of Colorado Health Sciences Center, Denver CO

2001-2007 **Associate Professor, Associate Professor with Tenure and Professor with Tenure,** Dept. of Pediatrics, and Dept. of Molecular Genetics and Microbiology, Univ. of Florida College of Medicine, Gainesville FL

2001-2007 **Chief, Division of Pediatric Hematology/Oncology**, Univ. of Florida College of Medicine, Gainesville FL

2007-2014 **Professor with Tenure and Ergen Family Chair in Pediatric Cancer**, Dept. of Pediatrics, Univ. of Colorado School of Medicine, Aurora CO

2007-2014 **Chief, Section of Pediatric Hematology/Oncology/BMT and Director, Center for Cancer and Blood Disorders**, Children's Hospital Colorado, Aurora, CO

2014- **Chief, Division of Pediatric Oncology, Director, Center for Childhood Cancer Research, and Jeffrey E. Perelman Distinguished Chair in the Department of Pediatrics**, Children's Hospital of Philadelphia, Philadelphia, PA

2015- **Professor (with tenure)**, Department of Pediatrics, Perelman School of Medicine at the University of Pennsylvania; Philadelphia, PA

Other Experience and Professional Memberships

1998-2000	Chairman, Young Investigators Committee, Children's Cancer Group
1999-2001	Co-Chairman, Young Investigators Committee, Children's Oncology Group (COG)
2001-2010	Member, NCI Intergroup Specimen Banking Committee
2002-2007	Vice Chairman (Laboratory Biology), COG ALL Disease Committee
2005-2010	Faculty Member and Small Group Leader, ASH Clinical Research Training Institute
2008-2015	Chairman, COG ALL Disease Committee
2009-2012	Member, ASH Committee on Training Programs
2011-12	Track Leader (Pediatric Oncology), ASCO Scientific Program Committee
2011-12	Member, ASCO Cancer Education Committee (Pediatric Oncology)
2012-	Member, External Advisory Board, Dan L. Duncan Cancer Center at Baylor College of Medicine
2012-	Member, External Scientific Advisory Board, Medical College of Wisconsin Cancer Center
2012	Co-Chair, FDA Workshop on Minimal Residual Disease as a Surrogate Endpoint in ALL
2012-15	Member, American Society of Pediatric Hematology Oncology Board Review Course Committee
2012-	Member, Board of Directors, World Child Cancer
2013-16	Member, ASCO Special Awards Selection Committee
2013-	Member (elected), Scientific Committee, International Society of Pediatric Oncology
2014-16	Member, Cancer Communications Committee, American Society of Clinical Oncology
2014-	Chair, External Advisory Committee, Center for Cancer and Blood Disorders at Children's Medical Center at University of Texas Southwester Medical Center
2015-17	Member, Scientific Advisory Council, CureSearch
2016	Member, NCI Blue Ribbon Panel Working Group on Pediatric Cancer
2016-19	Chair, Scientific Committee; Member Executive Board, International Society of Pediatric Oncology
2018-present	Associate Director for Pediatric Research, Abramson Cancer Center
2018-present	Member, Executive Committee, Abramson Cancer Center

Honors

1977-1981	National Merit Scholar
1995-1997	BLOOD/American Society of Hematology (ASH) Scholar Award
2001-2007	STOP! Children's Cancer Endowed Chair in Pediatric Oncology
2002-present	Listed in *The Best Doctors In America* (Woodward/White)
2007-2014	Ergen Family Endowed Chair in Pediatric Cancer
2009	International Society for Pediatric Oncology (SIOP) Award for Basic Science Abstract

C. Contribution to Science

1. An initial major theme of my research focused on identifying genes involved in chromosome translocations in ALL and characterizing their functional products, with a major focus on translocations targeting *TCF3* (*E2A*). This work began when I was a post-doctoral fellow with Michael Cleary and continued for 20 years.
   a. **Hunger SP**, Galili N, Carroll AJ, Crist WM, Link M, Cleary ML. The t(1;19)(q23;p13) results in consistent fusion of *E2A* and *PBX1* coding sequences in acute lymphoblastic leukemias. *Blood* 77: 687-693, 1991. PMID: 1671560
   b. **Hunger SP**, Ohyashiki K, Toyama K, Cleary ML: HLF, a novel hepatic bZIP protein, shows altered DNA-binding properties following fusion to E2A in t(17;19) acute lymphoblastic leukemia. *Genes and Development* 6: 1608-1620, 1992. PMID: 1516826
   c. Prima V, Gore L, Caires A, Boomer T, Yoshinari M, Imaizumi M, Varella-Garcia M, **Hunger SP**. Cloning and functional characterization of MEF2D/DAZAP1 and DAZAP1/MEF2D fusion proteins created by a variant t(1;19)(q23;p13.3) in acute lymphoblastic leukemia. *Leukemia* 19: 806-813, 2005. PMID: 15744350
   d. Zhong C-h, Prima V, Liang X, Frye C, McGavran L, Meltesen L, Wei Q, Boomer T, Varella-Garcia M, Gump J, **Hunger SP**. *E2A-NMP4* and *P120-E2A* fusion created by a cryptic t(12;19) in acute leukemia. *Leukemia* 22: 723-729, 2008. PMID: 18185522
2. As a direct offshoot of these basic studies, I developed an interest in using molecular diagnostics in treatment stratification and detection of minimal residual disease (MRD). I initially led studies testing PCR amplification of *E2A-PBX1* and *BCR-ABL1* fusion transcripts for MRD detection, but then played a lead role in cooperative group studies of more universal techniques to measure MRD in large-scale clinical trials. As

Vice Chair and Chair of the COG ALL Committee, I led efforts to incorporate real time MRD testing into the first generation of COG ALL trials that started in 2004 and helped to adjust the MRD threshold used to assign patients to intensified treatment in the second generation of COG ALL trials that started in 2010. These studies have helped define MRD to be the single strongest prognostic factor in pediatric ALL and have been used in risk-stratified treatment assignment of over 20,000 children, adolescents, and young adults enrolled in COG ALL trials in the past decade.

a. **Hunger SP**, Fall MZ, Camitta BM, Carroll AJ, Link MP, Lauer SJ, Mahoney DH, Pullen DJ, Shuster JJ, Steuber CP, Cleary ML. *E2A-PBX1* chimeric transcript status at end of consolidation does not predict treatment outcome in childhood acute lymphoblastic leukemias with a t(1;19)(q23;p13): A Pediatric Oncology Group study. *Blood* 91: 1021-1028, 1998. PMID: 9446665
b. Schultz KR, Pullen JK, Sather HN, Shuster JJ, Devidas M, Borowitz MJ, Carroll AJ, Heerema NA, Rubnitz JE, Loh ML, Raetz ER, Winick NJ, **Hunger SP**, Carroll WL, Gaynon PS, Camitta BM. Risk and response-based classification of childhood B-precursor acute lymphoblastic leukemia: A combined analysis of prognostic markers from the pediatric oncology group (POG) and Children's Cancer Group (CCG). *Blood* 109: 926-935, 2007. PMC1785141
c. Borowitz MJ, Devidas M, **Hunger SP**, Bowman WP, Carroll AJ, Carroll WL, Linda S, Martin PL, Pullen DJ, Viswanatha D, Willman CL, Winick N, Camitta BM. Clinical significance of minimal residual disease in childhood acute lymphoblastic leukemia and its relationship to other prognostic factors. A Children's Oncology Group study. *Blood*, 111: 5477-5485, 2008. PMC2424148
d. Borowitz MJ, Wood BL, Devidas M, Loh ML, Raetz EA, Salzer WL, Nachman JB, Carroll AJ, Heerema NA, Gastier-Foster JM, Willman CL, Dai Y, Winick NJ, **Hunger SP**, Carroll WL, Larsen E. Minimal Residual Disease In High Risk Pediatric All Retains Prognostic Significance Even With More Effective Therapy. A Report From Children's Oncology Group Study AALL0232. *Blood*, 26:964-971, 2015. PMC4543229

3. I have played a lead role in the design and conduct of COG ALL trials since 2002. This is highly interactive and collaborative team science that has helped to steadily improve survival of children, adolescents and young adults with ALL. In 2012 we published the largest cohort of pediatric ALL outcomes with over 22,000 patients treated on COG ALL trials 1990-2005. Five-year survival rates increased from 83.7% in 1990-1994 to 90.4% in 2000-2005 and have continued to increase to 92.0% in 2006-09. Key findings included our seminal observation that imatinib could be added safely to intensive chemotherapy in Philadelphia chromosome positive ALL and dramatically improved survival rates. This fundamentally changed treatment options for Ph^+ ALL and defined a new paradigm for addition of targeted therapy to chemotherapy, which we have pursued in TARGET studies that led to identification of Ph-like ALL.
   a. **Hunger SP**, Lu X, Devidas M, Camitta BM, Gaynon PS, Winick NJ, Reaman GH, Carroll WL. Improved survival for children and adolescents with acute lymphoblastic leukemia from 1990-2005: A report from the Children's Oncology Group. *Journal of Clinical Oncology,* 30:1663-1669, 2012. PMC3383113.
   b. Larsen EC, Devidas M, Chen S, Salzer WL, Nachman JB, Raetz EA, Loh ML, Mattano LA Jr., Cole C, Eicher A, Haugan M, Sorenson M, Heerema NA, Carroll AJ, Gastier-Foster JM, Borowitz MJ, Wood BL, Willman CL, Winick* NJ, **Hunger* SP**, Carroll* WL. Dexamethasone and High Dose Methotrexate Improve Outcome for Children and Young Adults with High-Risk B-Acute Lymphoblastic Leukemia: A Report From Children's Oncology Group Study AALL0232. *NJW, **SPH** and WLC contributed equally. *Journal of Clinical Oncology,* 34: 2380-2388, 2016. PMC4981974
   c. Slayton WB, Schultz KR, Kiarella JA, Devidas M, Mi X, Pulsipher MA, Chang BH, Mullighan C, Iacobucci I, Silverman LB, Borowitz MJ, Carroll AJ, Heerema NA, Gastier-Foster JM, Wood BL, Mizrahy SL, Merchant T, Brown VL, Sieger L, Siegel M, Raetz EA, Winick NJ, Loh ML, Carroll WL, **Hunger SP**. Dasatinib plus intensive chemotherapy in children, adolescents and young adults with Philadelphia chromosome positive acute lymphoblastic leukemia: Results of Children's Oncology Group trial AALL0622. *Journal of Clinical Oncology*, in Press.
   d. Winter SS*, Dunsmore KP*, Devidas M, Wood BL, Esiashvili N, Chen Z, Eisenberg N, Briegel N, Hayashi RJ, Gastier-Foster JM, Carroll AJ, Heerema NA, Asselin B, Gaynon P, Borowitz M, Loh ML, Rabin KR, Raetz EA, Zweidler-Mckay PA, Winick NJ**, Carroll WL**, **Hunger SP**. Improved Survival for Children and Young Adults with T-lineage ALL: Results from the Children's Oncology Group AALL0434 Methotrexate Randomization. *contributed equally as 1st authors; **contributed equally as senior authors. *Journal of Clinical Oncology*, in press.

4. I have led the COG ALL High Risk TARGET Project since its inception in 2006. This pediatric analog of The Cancer Genome Atlas (TCGA) is a large team science project that has made a number of seminal observations regarding the genomic landscape of ALL. Most of our initial publications utilized high throughput characterization of gene expression profiles and copy number alterations and targeted sequencing. In 2015 we started to publish a series of papers derived from whole exome and whole genome sequencing.
    a. Zhang J*, Mullighan CG*, Harvey RC, Wu G, Chen X, Edmonson M, Buetow KE, Carroll WL, Chen I-M, Devidas M, Gerhard DS, Loh ML, Reaman GH, Relling MV, Camitta BM, Bowman WP, Smith M, Willman CL#, Downing JR#, **Hunger SP#**. Key pathways are frequently mutated in high risk childhood acute lymphoblastic leukemia: A report from the Children's Oncology Group TARGET Project. *JZ and CGM contributed equally. #CLW, JRD and **SPH** contributed equally and are corresponding authors. *Blood* 118: 3080-3087, 2011. PMC3175785
    b. Loh* ML, Zhang* J, Harvey RC, Roberts K, Payne-Turner D, Kang H, Wu G, Chen X, Becksfort J, Edmonson M, Buetow KH, Carroll WL, Chen I-M, Wood B, Borowitz MJ, Devidas M, Gerhard DS, Bowman WP, Larsen E, Winick, N, Raetz E, Smith M, Downing JR, Willman CL#, Mullighan# CG, **Hunger# SP**. Tyrosine Kinome Sequencing of Pediatric Acute Lymphoblastic Leukemia: A Report from The Children's Oncology Group TARGET Project. MLL and JZ contributed equally. CLW, CGM and **SPH** are corresponding authors. *Blood*, 121: 485-488, 2013. PMC3548168
    c. Ma X, Edmonson M, Yergeau D, Muzny DM, Vardhan Doddapaneni D, Rusch M, Song G, Easton J, Harvey RC, Wheeler DA, Ma J, Hampton OA, Vadodaria B, Wu G, Nagahawatte P, Carroll WL, Chen I-M, Gastier-Foster JM, Relling MV, Smith MA, Devidas M, Guidry Auvil JM, Downing JR, Loh ML, Willman CL, Gerhard DS, Mullighan* CG, **Hunger* SP**, Zhang* J. The Rise and Fall of Subclones from Diagnosis to Relapse in Pediatric B-Acute Lymphoblastic Leukemia (B-ALL). *Nature Communications*, 6: 6604, 2015. PMC4377644. *CGM, **SPH** and JZ are corresponding authors.
    d. Liu Y, Easton J, Shao Y, Wang Z, Wilkinson MR, Maciaszek J, McCastlain K, Edmonson M, Zhou X, Ma X, Li Y, Rusch M, Gupta P, Pei D, Cheng C, Smith MA, Guidry Auvil J, Gerhard DS, Relling MV, Winick NJ, Carroll AJ, Heerema NA, Raetz E, Devidas M, Willman CL, Harvey RC, Carroll WL, Dunsmore KP, Winter SS, Wood BL, Sorrentino B, Downing JR, Loh ML, **Hunger SP***, Zhang J*, Mullighan CG*. The Genomic Landscape of Pediatric and Young Adult T-lineage Acute Lymphoblastic Leukemia. *Nature Genetics*, 49:1211-1218, 2017. PMCID 5535770. *corresponding authors.
5. The most exciting finding of the TARGET project has been our initial identification of the high risk Ph-like ALL subset, based upon its shared gene expression profile with *BCR-ABL1*$^+$ ALL that is reminiscent of activated kinase signaling. Our studies have showed that about 30% of Ph-like ALL cases have gene fusions involving *ABL1*, *ABL2*, *CSF1R*, *PDGFRB*, and *JAK2*. We have published preclinical data and anecdotal human data that these kinase fusions can be targeted by ABL class and JAK2 class tyrosine kinase inhibitors analogous to the use of imatinib/dasatinib in Ph$^+$ ALL and have obtained a number of grants to develop clinical trials testing this approach, which started to enroll patients in late 2016.
    a. Roberts KG*, Morin RD*, Zhang J, Hirst M, Zhao Y, Su X, Chen SC, Payne-Turner D, Churchman ML, Harvey RC, Chen X, Kasap C, Yan C, Becksfort J, Finney RP, Teachey DT, Maude SL, Tse K, Moore R, Jones S, Mungall K, Birol I, Edmonson MN, Hu Y, Buetow KE, Chen IM, Carroll WL, Wei L, Ma J, Kleppe M, Levine RL, Garcia-Manero G, Larsen E, Shah NP, Devidas M, Reaman G, Smith M, Paugh SW, Evans WE, Grupp SA, Jeha S, Pui CH, Gerhard DS, Downing JR, Willman CL, Loh M, **Hunger SP#,** Marra M#, Mullighan CG#. Genetic alterations activating kinase and cytokine receptor signaling in high-risk acute lymphoblastic leukemia**. *****RD and KGR contributed equally. #**SPH,** MM and CGM are corresponding authors. *Cancer Cell*, 22: 153-166, 2012. PMC3422513.
    b. Roberts* KG, Li* Y, Payne-Turner D, Harvey RC, Yang YL, Pei D, McCastlain K, Ding L, Lu C, Song G, Ma J, Becksfort J, Rusch M, Chen S-C, Easton J, Cheng J, Boggs K, Santiago-Morales N, Iacobucci I, Fulton RS, Wen J, Valentine M, Cheng C, Paugh SW, Devidas M, Chen I-M, Reshmi S, Smith A, Hedlund E, Gupta P, Nagahawatte P, Wu G, Chen X, Yergeau D, Vadodaria B, Mulder H, Winick NJ, Larsen EC, Carroll WL, Heerema NA, Carroll AJ, Grayson G Tasian SK, Moore AS, Keller F, Frei-Jones M, Whitlock J, Raetz EA, White D, Hughes TP, Guidry Auvil JM, Smith MA, Marcucci G, Bloomfield CD, Mrózek K, Kohlschmidt J, Stock W, Kornblau SM, Konopleva M, Paietta E, Pui C-H, Jeha S, Relling MV, Evans WE, Gerhard DS, Gastier-Foster JM, Mardis E, Wilson RK, Loh ML, Downing^ JR, **Hunger^ SP,** Willman^ C, Zhang^ J, Mullighan^ CG. Targetable kinase activating lesions in Ph-like acute lymphoblastic leukemia. *New England Journal of Medicine*; 371:1005-1015,

2014. PMC4191900. ^JRD, **SPH**, CLW, JZ and CGM contributed equally and are corresponding authors.

c. Reshmi* SC, Harvey* RC, Roberts* KG, Stonerock E, Smith A, Jenkins H, Chen I-M, Valentine M, Liu Y, Li Y, Shao Y, Easton J, Payne-Turner D, Gu Z, Tran TH, Nguyen JV, Devidas M, Dai Y, Heerema NA, Carroll AJ, Raetz EA, Borowitz MJ, Wood BL, Angiolillo AL, Burke MJ, Salzer WL, Zweidler-McKay PA, Rabin KR, Carroll WL, Zhang J, Loh** ML, Mullighan** CG, Willman** CL, Gastier-Foster** JM, **Hunger** SP**. Targetable Kinase Gene Fusions in Children, Adolescents, and Young Adults with High Risk B-ALL: A Study from the Children's Oncology Group. *Blood,* 129: 3352-3361, 2017. PMC5482101 **contributed equally as senior authors.

d. Roberts* KG, Reshmi* SC, Harvey* RC, Chen I-M, Patel K, Stonerock E, Jenkins H, Dai Y, Valentine M, Gu Z, Zhao Y, Liu Y, Li Y, Zhang J, Payne-Turner D, Devidas M, Heerema NA, Carroll AJ, Raetz EA, Borowitz MJ, Wood BL, Angiolillo AL, Burke MJ, Salzer WL, Zweidler-McKay PA, Rabin KR, Mattano L, Maloney KW, Carroll WL, Loh** ML, Mullighan** CG, Willman** CL, Gastier-Foster** JM, **Hunger** SP**. Genomic and Outcome Analyses of Philadelphia chromosome-like ALL in NCI Standard-risk Patients: A Report from the Children's Oncology Group. Submitted. *contributed equally as 1st authors; **contributed equally as senior authors. *Blood*, in press.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/stephen.hunger.1/bibliography/54036430/public/?sort=date&direction=ascending

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D. Research Support

Ongoing Research Support

1 P50 GM115279-01 Relling/Loh (Multi PI) 07/01/2015-06/30/2020 1.32 calendar
Center for Precision Medicine in Leukemia
Dr. Hunger is co-Leader of Project #1 *Genome-wide Studies of ALL Response* (Hunger/Mullighan). This Project aims to perform a large-scale, integrated genomic, transcriptomic and epigenomic analysis of childhood and adult ALL, to comprehensively define the genomic landscape of ALL and identify features associated with treatment response (MRD) and outcome.

U2C CA233285 Tan/Hunger (Multi PI) 09/30/2018-08/31/2023 1.20 calendar
Center for Pediatric Tumor Cell Atlas
This collaborative project aims to produce a pediatric tumor cell atlas focused on high-grade glioma, neuroblastoma, and very high-risk B-cell-precursor acute lymphoblastic leukemia.

T32 CA009615-29 Hunger/Schuchter (Multi PI) 07/01/2004-06/30/2020 0.3 calendar
Cancer Center Research Training Program
This Cancer Center Training Grant is focused on preparing post-doctoral fellows for careers as translational cancer researchers.

P30 CA016520-43 Vonderheide 12/01/2015-11/30/2020 1.2 calendar
Abramson Cancer Center Support Grant
This Center grant supports the cancer research mission of the Abramson Cancer Center of the University of Pennsylvania. Dr. Hunger is the Associate Director for Pediatric Research at the Abramson Cancer Center.

K12 CA076931 Schuchter/Hunger (Multi PI) 04/01/2014-03/31/2019 0.6 Calendar
Cellular Molecular Biologics in Clinical Cancer Research
An institutional training grant focused on post-fellowship instructors and faculty, which is designed to prepare the next generation of translational cancer researchers.