

Curriculum Vitae

Date Prepared: April 15, 2016
Name: Rameen Beroukhim
Office Address: Dana-Farber Cancer Institute
450 Brookline Avenue SM1022C
Boston, MA 02215
Home Address: 204 Aspinwall Avenue
Brookline, MA 02446
Work Phone: 617-582-7941
Work Email: rameen_beroukhim@dfci.harvard.edu
Work FAX: 617-632-4393
Place of Birth: Brooklyn, NY

Education

1991	AB with High Honors	Physics and Philosophy	University of California, Berkeley, CA
1992	MPhil	Molecular Biology	University of Cambridge, England, UK
1996	PhD	Molecular Biology (advisor Nigel Unwin, PhD)	University of Cambridge, England
2000	MD	Medicine	University of California, San Francisco, CA

Postdoctoral Training

06/00-06/01	Intern	Internal Medicine	University of California, San Francisco
06/00-06/02	Fellow	Molecular Medicine	University of California, San Francisco
06/01-06/02	Resident	Internal Medicine	University of California, San Francisco
07/02-06/03	Clinical Fellow	Medical Oncology	Dana-Farber Cancer Institute, Boston, MA
07/03-06/06	Postdoctoral Fellow	Medical Oncology	Dana-Farber Cancer Institute
05/05-	Visiting Postdoctoral Scientist	Cancer Program	Broad Institute, Cambridge, MA

Faculty Academic Appointments

07/06-01/10	Instructor	Medicine	Harvard Medical School, Boston, MA
02/10-	Assistant Professor	Medicine	Harvard Medical School

Appointments at Hospitals/Affiliated Institutions

07/06-01/10	Instructor	Medical Oncology	Dana-Farber Cancer Institute
07/06-	Attending Staff Oncologist	Medical Oncology	Dana-Farber Cancer Institute
07/06-	Associate Physician	Medicine	Brigham and Women's Hospital, Boston, MA
01/09-01/10		Cancer Biology	Dana-Farber Cancer Institute
02/10-		Medical Oncology	Dana-Farber Cancer Institute
02/10-		Cancer Biology	Dana-Farber Cancer Institute

Other Professional Positions

2009-	Consultant	Novartis Institutes for Biomedical Research, Cambridge, MA
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Major Administrative Leadership Positions

Local

2011-13	CB 399: Cancer Genomics – Principles and Applications (Course Director) Graduate students, postdoctoral fellows, and faculty	Harvard Medical School Two 4-hr sessions every two years
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Committee Service

Local

2010-	Ethics Advisory Committee	Dana-Farber Cancer Institute Member
2010-	MD-PhD Admissions Committee	Harvard Medical School Member
2013	Research Computing Strategic Planning Committee	Dana-Farber Cancer Institute Member
2013-	Broad Institute Cancer Program Steering Committee	Broad Institute Member
2014-	Bioinformatics and Integrative Genomics Program Admissions Committee	Harvard Medical School Member
2014	Faculty Model Workgroup	Dana-Farber Cancer Institute Member
2014-	Massachusetts General Hospital/Dana-Farber Neurooncology Fellowship Admissions Committee	Massachusetts General Hospital and Dana-Farber Cancer Institute Member

National and International

2007-2011	CNS Disease Working Group	The Cancer Genome Atlas Project, National
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		Institutes of Health (NIH), Bethesda, MD Member
2009-	Genitourinary Disease Working Group	The Cancer Genome Atlas Project, NIH Member
2011-	Glioblastoma Analysis Working Group	The Cancer Genome Atlas Project NIH Member
2011-	Kidney Clear Cell Carcinoma Analysis Working Group	The Cancer Genome Atlas Project, NIH Member
2011-	Endometrial Adenocarcinoma Analysis Working Group	The Cancer Genome Atlas Project, NIH Member
2012-	Translational Research Program Executive Committee	Alliance for Clinical Trials Chicago, IL Member
2013-	Genomics Committee	Adult Brain Tumor Consortium Baltimore, MD Co-Chair
2014-	Pan-Cancer Structural Rearrangements Working Group	International Cancer Genome Consortium Co-Chair
2015-	PanCanAtlas Telomeres Analysis Group	The Cancer Genome Atlas Project, NIH Co-Chair
2015	PanCanAtlas Aneuploidy Analysis Group	The Cancer Genome Atlas Project, NIH Co-Chair

Professional Societies

2002-2006	American Medical Association	Member
2003-2006	Massachusetts Medical Society	Member

Grant Review Activities

2008-2009	Barts and The London Charity Special Purpose Fund	Peer Reviewer Proforma
2010-2011	Cancer Research UK Training & Career Development Board	Ad hoc Reviewer
2011-2012	Dutch Cancer Society Scientific Advisory Board	Independent Referee
2012-	Wellcome Trust Strategic Awards Committee	External Advisor
2013	Netherlands Organisation for Scientific Research	External Referee
2013	Breakthrough Breast Cancer	

External Referee

2014-15 V Foundation

External Referee

Editorial Activities

***Ad hoc* Reviewer:**

Bioinformatics
BMC Bioinformatics
BMC Genomics
Cancer Cell
Cancer Discovery
Cancer Research
Cell Systems
Clinical Cancer Research
EMBO Molecular Medicine
Genome Biology
Genome Medicine
Human Molecular Genetics
Journal of Clinical Oncology
Journal of Medical Genetics
Molecular Cancer Research
Molecular Cancer Therapeutics
Nature
Nature Biotechnology
Nature Communications
Nature Genetics
Nature Medicine
Neurooncology
New England Journal of Medicine
Nucleic Acids Research
Oncogene
PLoS Computational Biology
PloS One
Proceedings of the National Academy of Sciences
Science
Science Translational Medicine
Trends in Genetics

Editorial Review Board:

Neurooncology 2013-

Other Editorial Roles:

Elsevier

Honors and Prizes

1987	Chancellor's Scholar	University of California, Berkeley	Academic
1990	Phi Beta Kappa	Phi Beta Kappa Society	Academic
1991	Winston Churchill Scholarship	Winston Churchill Foundation of the United States of America	Academic
1992	Glaxo Dorothy Hodgkin Scholarship	Glaxo	Molecular/Structural Biology
1992	Overseas Research Studentship	British Government	Molecular/Structural Biology
1996	Max Perutz Prize	Medical Research Council Laboratory of Molecular Biology	Structural Biology
2007	Physician Research Training Award (declined)	Department of Defense	Prostate Cancer Genomics
2009	V Scholar Award	V Foundation	Genomics research
2012	Distinguished Scientist Award	Sontag Foundation	Neurooncology research

Report of Funded and Unfunded Projects

Funding Information

Past

2004-2006	High-resolution mapping of structural mutations in prostate cancer with SNP arrays Department of Defense Postdoctoral Award PI The main goal of this proposal was to identify chromosomal alterations related to prostate cancer progression from primary to metastatic cancer.
2006-2008	High-resolution genome-wide mapping of structural mutations in prostate cancer Dana-Farber/Harvard Cancer Center (DF/HCC) Prostate Specialized Programs of Research Excellence (SPORE) Career Development Award PI The main goal of this proposal was to identify chromosomal alterations enriched among primary and metastatic prostate cancers.
2009-2010	Evaluation of MCL1 amplification and overexpression as predictors of MCL1 dependency in multiple tumor types DFCI/Novartis Drug Discovery Program PI The main goal of this proposal was to determine whether amplification or overexpression of MCL1 predicts MCL1 dependency in multiple cancer types.
2007-2011	Translational studies based on tumor suppressor proteins Doris Duke Charitable Foundation Co-Investigator (William Kaelin, MD– PI) The main goal of this award was to identify and validate new kidney cancer drug targets and biomarkers.
2007-2012	High-resolution genome-wide mapping of structural mutations in prostate cancer National Cancer Institute (NCI)/K08CA122833 PI The goal of this proposal was to identify chromosomal aberrations in prostate cancer and

- determine the oncogene and tumor suppressor targets through a combination of sequencing and functional experiments in model systems.
- 2010-2012 Reconstructing the meningioma genome
Brain Science Foundation
PI
The objective of this award was to identify somatic genetic events in typical meningiomas through whole-genome sequencing
- 2011-2012 The Somatic Genetics of Lung Adenocarcinoma Metastases To Brain
DFCI/Novartis Drug Discovery Program (DDP 08004-03)
PI
The goal of this project was the identification of somatic genetic events that drive lung adenocarcinoma metastasis to the brain.
- 2010-2013 Comprehensive genetic characterization of grade II pediatric astrocytomas
PLGA Foundation
PI
The goal of this project is to use ultra-deep shotgun sequencing of DNA from pediatric low-grade gliomas to completely characterize the somatic mutations that lead to pediatric astrocytomas.
- 2012-2013 Comprehensive characterization of the anaplastic meningioma genome
Voices against Brain Cancer
PI
The overarching hypothesis of this application is that comprehensive characterization of anaplastic meningioma genomes will reveal the somatic genetic events responsible for anaplastic meningioma development.
- 2011-2013 Genomic characterization of pituitary tumors
Brain Science Foundation
Co-Investigator (Ian Dunn, MD—PI)
The goal of these studies is to determine the important oncogenes and tumor suppressor genes that drive pituitary tumor development and in doing so will guide the development of rational therapeutics for this disease.
- 2009-2014 Developing a robust method for genotyping copy-number alteration in clinical samples of low tumor purity
The V Foundation for Cancer Research Scholarship
PI
The main goal of this project is to identify the most significant copy-number changes across a range of cancer types and develop a sequencing-based assay to robustly measure these in FFPE samples of low tumor purity.
- 2010-2014 PS-OC: Evolutionary dynamics of brain, lung, and hematopoietic tumors – Project 1
NIH (U54CA143798, Michor)
PI
The main goal of this proposal was to study tumorigenesis and the development of resistance as an evolutionary process with techniques borrowed from the physical sciences, and to propose an interdisciplinary approach to predict and prevent the evolution of resistance to anti-cancer therapy.
- 2012-2014 Evaluating ATAD2 as a therapeutic target in MYC-driven breast, endometrial and ovarian cancers
DF/HCC Men's Collaborative to Cure Women's Cancers
Co-PI

The main goal of this proposal is to develop ATAD2-specific chemical inhibitors for therapeutic application in defined populations of endometrial, breast and ovarian cancer patients.

- 2012-2014 Characterization of genetic changes associated with meningioma progression
Brain Science Foundation
PI
The goal of this proposal is to determine whether the mutations detected in grade I meningiomas are also early events in the formation of higher-grade meningiomas, and that the progression to higher grade is associated with additional genetic driver events that occur later in tumorigenesis.
- 2013-2014 Genomic approaches to target identification in metastases
DFCI-Novartis Drug Discovery Program
PI
The main goal of this project is the identification of somatic genetic events that drive breast adenocarcinoma metastasis to the brain.
- 2013-2014 Elucidating molecular evolution of pediatric low-grade gliomas through single-cell whole transcriptome profiling
DFCI/PS-OC
PI
The main goal of this project is to generate robust single-cell transcriptomic profiles from pediatric low-grade gliomas

Current

- 2012-2016 Identifying Vulnerabilities in Gliomas Due to Imbalances in Essential Genes
Sontag Foundation
PI
The main goal of this project is to understand the effects and specifically the vulnerabilities induced by hemizygous loss of essential genes (which turns out to be very frequent), informs our understanding of the effects of negative selection on the glioma genome.
- 2015-2016 Identifying therapeutic targets of MYB-QKI fusions in pediatric low-grade glioma
Ian's Friends Foundation
PI
The main goal of this project is to identify dependencies associated with MYB-QKI fusions in pediatric low-grade gliomas.
- 2015-2016 An Integrated Assembly Group to Define Genome Structure in Germline and Cancer
BROADnext10 Catalytic Steps
Co-PI
The main goal of this project is to integrate data from conventional and emerging technologies to generate complete genome structures, ultimately to assess associated variation that may influence human health and disease.
- 2015-2016 EvoSeq: a methodology to track and isolate individual cells throughout evolutionary selection
Broad SPARC (Scientific Projects to Accelerate Research and Collaboration)
Co-PI
The main goal of this project is to employ activating CRISPR/Cas9 technology to individually label cells with a diverse library of inert barcodes that permit the labeling and physical isolation of individual cells from within a population with DNA-sequence specificity.

- 2016-2016 Uncovering resistance mechanism of diffuse intrinsic pontine glioma to chemoradiation
Curing Kids' Cancer
PI
The main goal of this project is to identify genetic changes in diffuse intrinsic pontine gliomas associated with recurrence after chemoradiation, and to determine their association with treatment resistance.
- 2015-2017 Assessing driver rearrangements from whole-genome sequencing datasets
Dana-Farber/Novartis Drug Discovery Program 15001
PI
The main goal of this project is to develop computational approaches to sensitively detect structural alterations in cancer genomes, and to distinguish the driver from passenger events.
- 2015-2017 Integrated analysis of heterogeneity in and drivers of metastatic cancers
Dana-Farber/Novartis Drug Discovery Program 15101A
PI
The main goal of this project is to characterize genetic and transcriptomic heterogeneity across cancers.
- 2015-2017 Characterizing resistance mechanisms to BET-bromodomain inhibition in MYC-amplified medulloblastoma
Alex's Lemonade Stand Foundation
PI
The main goal of this project is to characterize resistance mechanisms to BET-bromodomain inhibition in MYC-amplified medulloblastomas.
- 2015-2020 Genetic evolution of glioblastoma during radiation and temozolomide therapy
NIH R01 CA188228
PI
The main goal of this project is to determine whether somatic genetic profiles of glioblastomas that recur after treatment with RT and TMZ differ substantially from pre-treatment GBMs, and whether the differences point to mechanisms by which GBMs resist those treatments.

Current Unfunded Projects

- 2014- Design and execution of all experiments/Analysis of copy-number alterations across multiple cancer types
The goal of this project is to analyze very large numbers of cancer specimen DNAs across multiple cancer types to resolve oncogene and tumor suppressor gene targets of copy-number change and to determine the universality or specificity of individual copy-number changes across different cancer types
- 2015- Design and oversight of all experiments/Evaluation of TERC as an amplified oncogene
The main goal of this project is to evaluate and potentially credential TERC as an amplified oncogene

Report of Local Teaching and Training

Teaching of Students In Courses

- 2011-13 CB 399: Cancer Genomics – Principles and Applications (Course Director) Harvard Medical School

	Graduate students, postdoctoral fellows, and faculty	Two 4-hour sessions every two years
2012-16	CB211: Molecular and Systems Level Cancer Graduate Students	Harvard Medical School Two 1.5-hour sessions per week for 1.5 wks, every two years
2013	STAT 115/215: Introduction to Computational Biology and Bioinformatics Graduate Students	Harvard Medical School One 90-minute lecture
2014	DFCI/ Massachusetts General Hospital Hematology/Oncology Fellowship Lecture Series	Harvard Medical School
2014	14 Hematology/Oncology Fellows HBTM 235: Principles of Human Disease: Physiology and Pathology. Graduate and Undergraduate Students	One hour lecture Harvard College
2016	Broad Boot Camp Graduate students and postdoctoral fellows	One 90-minute lecture Broad Institute One two-hour lecture

Clinical Supervisory and Training Responsibilities

2009-	Supervision of Neurooncology and Medical Oncology Fellows in Neurooncology Clinic / Dana-Farber Cancer Institute	One 4-hour session per week
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Laboratory and Other Research Supervisory and Training Responsibilities

2009-present	Supervision of graduate students and post-doctoral fellows/Dana-Farber Cancer Institute, Boston, MA	Daily mentorship for 7 years
2015-present	Faculty mentor for graduate students/ Bioinformatics and Integrative Genomics Program, HMS, Boston, MA	5-10 hours per year

Formally Supervised Trainees and Faculty

2008-2010	Craig Mermel, MD-PhD student in laboratory of Matthew Meyerson – Published two manuscripts, including one in <i>Nature</i>
2010-2014	Travis Zack, Harvard graduate student in my laboratory/received PhD and admission as a medical student at HST - published first-author manuscripts in <i>Cell</i> and <i>Nature Genetics</i>
2010-2011	Maria Raeder, MD, PhD and visiting postdoctoral fellow/published a first-author paper in <i>PLoS One</i>
2011-2013	Peleg Horowitz, MD, PhD, BWH neurosurgical resident in my laboratory/Neurosurgical fellow, MD Anderson – published first-author papers in

- Nature Genetics* and *PNAS*, obtained DOD Postdoctoral Fellowship Award.
- 2011-present Ruben Ferrer-Luna, PhD, postdoctoral fellow/completing manuscript
- 2012-2014 Guillaume Berghold, MD, visiting graduate student in my laboratory/Attending physician at the University of Strasbourg - received PhD from Gustave Roussy in Paris, France and published co-first-author papers in Neurooncology, *Nature Genetics*, and *Clinical Cancer Research*, received awards from Sass and Nuovo-Soldati foundations
- 2012-2015 William Gibson, MD-PhD student/completing MD at HMS, awarded PhD by MIT, co-first author of three manuscripts, one accepted in principle at *Nature Genetics*, one in revision for *Cancer Cell*, one in review at *Cancer Discovery*, F30 award from NIH
- 2012-present Brenton Paoella, PhD, postdoctoral fellow/first author of manuscript in revision for *Cancer Cell*, F32 award from NIH
- 2012-present Pratiti Bandopadhyay, MD-PhD and postdoctoral fellow in my laboratory/Instructor in pediatric neurooncology at DFCI, published 7 first-author papers including one in *Nature Genetics*, received awards from multiple foundations and interviewing for faculty positions at UCSF and DFCI.
- 2012-present Jeremiah Wala, MD-PhD student in my laboratory/first author of a paper in *Bioinformatics*, and a *Perspective in Science*; coauthor of a paper in *Nature Genetics*; completing additional manuscripts
- 2013-2013 Jeff Meng, MD-PhD student rotating through my laboratory
- 2013-2015 Supervision of Linda Bi, MD-PhD, BWH neurosurgical resident/completing neurosurgical residency – first or co-first author of 6 papers
- 2013-2015 Pankaj Agarwalla, MGH neurosurgical resident/completing neurosurgical residency – coauthorship of 3 papers, completing first-author manuscript, F25 award from NIH
- 2014-2014 Perry Palmedo, PhD student rotating in my laboratory/coauthor of a paper in *Nature Genetics*
- 2014-present Caitlin Nichols, HMS BBS PhD student in my laboratory/
- 2014-present Jaeho Hwang, MD student affiliated with my laboratory/coauthor of a paper in *J Neurooncology*, awarded American Brain Tumor Association fellowship
- 2015-2015 Sebastian Koochaki, MD-PhD student rotating in my laboratory
- 2015-2016 Frederik Holst, PhD, visiting postdoctoral fellow/coauthor of papers in *PLoS One* and *Oncotarget* and of a paper accepted in principle to *Nature Genetics*, first author of a paper accepted in principle to *Scientific Reports*
- 2016-present Omar Yaghi, MD-PhD student rotating in my laboratory/

Formal Teaching of Peers (e.g., CME and other continuing education courses)

- 2007 Characterizing non-random chromosomal aberrations in cancer/ Grand Rounds Dana-Farber Cancer Institute Single presentation
- 2007 Assessing the Significance of Chromosomal Aberrations in Cancer/ Seminar Series Department of Oncology, Dana-Farber Cancer Institute Single presentation
- 2008 Assessing the Significance of Chromosomal Aberrations in Cancer/ Seminar Series Department of Neurooncology, Brigham and Women's Hospital Single presentation

2010	The landscape of copy-number changes across multiple cancer types/ Seminar Series Department of Neurooncology, Brigham and Women's Hospital	Single presentation
2010	The landscape of copy-number changes across multiple cancer types/ Seminar Series Department of Neurooncology, Massachusetts General Hospital	Single presentation
2011	Targeting genomic losses in cancer cells/ Seminar Series Division of Neurooncology, Brigham and Women's Hospital	Single presentation
2013	Advances in Malignant Glioma Biology/ CME Course Dana-Farber/Harvard Cancer Center	Single presentation

Local Invited Presentations

Those presentations below sponsored by outside entities are so noted and the sponsors are identified.

2004	Towards a High-Resolution Map of Structural Mutations in Prostate Cancer/ Lecture Prostate SPORE Annual Meeting, Dana-Farber Harvard Cancer Center
2005	Towards a Genetic Understanding of Prostate Cancer/ Seminar Series Department of Genitourinary Oncology, Dana-Farber Cancer Institute
2006	Characterizing Targeted Chromosomal Aberrations in the Glioma Genome/ Lecture Annual Retreat, Broad Institute
2006	Prostate Cancer: Looking Under the Hood/ Lecture Visiting Committee, Dana-Farber Cancer Institute
2008	The Global Cancer Map: Copy-Number Changes in Cancer/ Lecture Dana-Farber/Novartis Scientific Retreat (Novartis)
2009	Evaluation of <i>MCL1</i> Amplification and Overexpression as Predictors of <i>MCL1</i> Dependency in Multiple Tumor Types/ Lecture Dana-Farber/Novartis Scientific Retreat (Novartis)
2010	The Landscape of Copy-number Changes Across Multiple Cancer Types/ Seminar Series Dana-Farber/Harvard Cancer Center Kidney SPORE Monthly Meeting
2010	Understanding the Implications of Copy-number Changes in Cancer/ Lecture Dana-Farber Cancer Institute Division of Cancer Biology Retreat
2010	Genomics in Neuro-oncology/ Lecture Dana-Farber/Brigham and Women's Center for Neuro-oncology Annual Retreat
2010	Making Sense of Copy-number Changes in Cancer/ Lecture Dana-Farber/Novartis Scientific Retreat (Novartis)
2011	Making Sense of Copy-number Changes in Cancer/ Lecture Boston Children's Hospital Seminar Series
2011	Mining Cancer Copy-number Profiles/ Seminar Series Broad Institute Cancer Program
2011	Genomics in Neuro-oncology/ Lecture Dana-Farber/Brigham and Women's Center for Neuro-oncology Annual Retreat
2011	Identifying Drivers of Metastasis Through Somatic Genetic Analysis/ Lecture DFCI-Novartis Genomics Cluster Meeting
2011	Finding Targets in Regions of Frequent Copy-number Change/ Lecture Dana-Farber/Novartis Scientific Retreat (Novartis)

- 2011 Identifying Drivers of Metastasis Through Somatic Genetic Analyses/ Lecture
Novartis-DFCI Signaling Cluster Meeting, Basel, Switzerland (Novartis)
- 2012 Genetic Profiling of Understudied Brain Tumors/ Lecture
Novartis-DFCI Signaling Cluster Meeting, Basel, Switzerland (Novartis)
- 2012 Targeting Genomic Losses in Cancer Cells/ Lecture
DFCI/BWH Neurooncology seminar series
- 2012 Effects of Selective Pressure in Brain and Other Cancer Genomes/ Lecture
DFCI Division of Molecular and Cellular Oncology Retreat
- 2012 Targeting Genomic Losses in Cancer Cells/ Lecture
The RNAi Consortium/Broad Institute
- 2012 Effects of Selective in Brain and Other Cancer Genomes/ Lecture
Cancer Biology Annual Retreat, Dana-Farber Cancer Institute
- 2012 Cancer Vulnerabilities Induced by Genomic Loss/ Lecture
Center for Cancer Systems Biology Annual Retreat
- 2012 Evaluating Genomic Losses in Cancer/ Lecture
NCI site visit, DFCI Physical Science Oncology Center
- 2012 Somatic Genetics of Meningiomas/ Lecture
Dana-Farber/Novartis Scientific Retreat (Novartis)
- 2012 Positive and Negative Selection in Cancer Genomes/ Lecture
Boston Children's Hospital Hematology/Oncology Seminar Series
- 2012 Selective Pressures on Cancer Genomes/ Lecture
DFCI Physical Sciences Oncology Consortium retreat
- 2012 Targeting Genes That Undergo Loss in Cancer/ Lecture
Broad Institute Annual Retreat
- 2013 Genomics in Neurooncology/ Lecture
DFCI/BWH Neurooncology Program Annual Retreat
- 2013 Pediatric Low-grade Astrocytomas: Tumors That Change with Age/ Lecture
DFCI Physical Sciences Oncology Consortium retreat
- 2013 Genetic Profiling of Brain Metastases/ Lecture
Novartis-DFCI Genomics Cluster Meeting, Boston, MA
- 2013 Positive and Negative Selection in Cancer Genomes/Seminar
Dana-Farber Cancer Institute Seminars in Oncology, Boston, MA
- 2013 Pan-cancer Patterns of Somatic Copy-number Alteration/ Lecture
Novartis-DFCI Genomics Cluster Meeting, Boston, MA
- 2014 Positive and Negative Selection in Cancer Genomes/ Seminar
Brigham and Women's Hospital Pathology Rounds, Boston, MA
- 2014 Genetic heterogeneity across primary and metastatic tumors/Lecture
Dana-Farber/Novartis Scientific Retreat (Novartis)
- 2014 Ambiguities in the interpretation of copy-number profiles/Lecture
Dana-Farber/Novartis Scientific Retreat (Novartis)
- 2015 Genomic studies of tumors of the brain and other tissues/Lecture
Dana-Farber Cancer Institute Division of Molecular and Cellular Oncology Annual Retreat
- 2016 SF3B1 as a CYCLOPS gene/Lecture
Dana-Farber/Novartis Drug Discovery Program meeting

Report of Regional, National and International Invited Teaching and Presentations

Invited Presentations and Courses

Regional

- 2010 Reconstructing the Meningioma Genome/Lecture
Brain Science Foundation Board Meeting
- 2010 Making Sense of Copy-number Changes in Cancer/ Lecture
Sanofi-Aventis, Cambridge, MA (Sanofi-Aventis)
- 2011 Determining What Drives Meningioma/ Lecture
Brain Science Foundation Lunchtime Lecture Series
- 2012 Targeting MYC in Women's Cancers/ Lecture
Men's Collaborative for Women's Cancers, South Hamilton, MA
- 2012 Distinguishing effects of selection in cancer copy-number profiles/ Lecture
Dartmouth Medical School, Hanover, NH (Dartmouth Medical School)
- 2012 Characterization of Genetic Changes Associated with Meningioma Progression/ Seminar
Series
Brain Science Foundation
- 2013 Positive and negative selection in cancer genomes/ Lecture
University of Massachusetts Medical School, Worcester, MA
(University of Massachusetts)
- 2013 Interpreting Cancer Copy-number Alterations/ Lecture
Computational Aspects of Biological Information conference, Boston, MA (Microsoft)
- 2013 Pituitary Tumors/Lecture
Brain Science Foundation, Boston, MA
- 2014 The Genomic Landscape of Meningiomas/ Lecture
13th Annual International Neuro-Oncology Updates, Boston, MA
- 2014 Cancer copy-number changes: An overview/ Lecture
Radcliffe Seminar: Chromothripsis: Origins of Chromosome Shattering and Reassembly,
Cambridge, MA
- 2014 The International Cancer Genome Consortium Pan-Cancer Structural Variations
Analysis/Lecture
Chromothripsis, Clustered Mutation and Complex Chromosome Rearrangements
conference, Cambridge, MA (Abcam)
- 2014 Structural variations in cancer genomes/Lecture
Hallmarks of Cancer Symposium, Cambridge, MA
- 2014 PCAWG-6: Structural Variations/Lecture
International Cancer Genome Consortium PanCancer Analysis of Whole Genomes Face-
to-Face meeting, Cambridge, MA
- 2015 The genomic landscape of endometrial cancer progression (and some other
things)/Seminar
Brown University Computational Biology Seminar Series, Providence, RI

National

Those presentations below sponsored by outside entities are so noted and the sponsors are identified

2005 Developing High-Resolution Maps of Structural Mutations in Prostate Cancer/
Lecture American Physician Scientists Association of the American Society for Clinical
Investigation Inaugural Meeting, Chicago, IL

2005 High-Resolution Characterization of Structural Mutations in Prostate Cancer/ Lecture
American Urological Association Annual Meeting, San Antonio, TX

2007 Characterizing Non-random Chromosomal Aberrations in Cancer/ Lecture
American Association for Cancer Research Oncogenomics Meeting, Phoenix, AZ

2007 Genomic Identification of Significant Targets in Cancer: GISTIC/ Lecture
Starr Retreat, New York, NY (Starr Foundation)

2009 Statistical Analysis of Copy-number Profiles to Identify Driver Events/ Lecture
American Association for Cancer Research Annual Meeting, Denver, CO

2009 An Analysis of Copy-number Changes Across Multiple Cancer Types/ Talk
Genetics and Biology of Brain Cancers, Omni San Diego Hotel, San Diego, CA (AACR)

2009 Disease Experts Presentations/Co-Chair
The Cancer Genome Atlas Project Glioblastoma Multiform Data Analysis Workshop, San
Diego, CA

2010 The Landscape of Copy-number Changes Across Multiple Human Cancer Types/ Lecture
American Association for Cancer Research Annual Meeting, Washington DC

2011 An Analysis of Copy-number Changes Across Multiple Cancer Types/ Lecture
Department of Defense 2011 IMPACT Conference, Orlando, FL

2011 Making Sense of Copy-number Changes in Cancer/ Lecture
NCI Center for Cancer Research Eminent Lecture Series, Bethesda, MD

2011 Copy Number Analysis of TCGA cancers and Display via the TCGA Tumorscape web
portal/ Lecture
The Cancer Genome Atlas Project Steering Committee Meeting, Bethesda, MD

2011 Mining Cancer Copy-number Profiles/ Lecture
Novartis, Emeryville, CA (Novartis)

2011 Making Sense of Copy-number Changes in Cancer/ Lecture
Memorial Sloan-Kettering Cancer Center (MSKCC) for Cancer Systems Biology Retreat,
New York, NY

2011 TCGA KIRC Copy-number Findings/ Lecture
The Cancer Genome Atlas Project
Kidney Renal Clear-Cell Data Analysis Workshop, Houston, TX

2012 Treating Brain Cancers: Where Are We Headed?/ Lecture
Gray Matters Foundation, Newark, NJ (Gray Matters Foundation)

2012 Pan-cancer Analysis of Copy-number Changes in TCGA cancers/ Lecture
The Cancer Genome Atlas Project Pan-Cancer Symposium, Santa Cruz, CA

2013 Positive and Negative Selection in Cancer Genomes/ Lecture (AACR)
American Association for Cancer Research Annual Meeting, Washington DC

2013 New Therapeutic Targets of Meningiomas/ Lecture (AANS)
American Association of Neurologic Surgery Annual Meeting, New Orleans, LA

2013 Pan-cancer Analysis of Copy-number Changes in TCGA cancers/ Lecture
The Cancer Genome Atlas Project
Steering Committee Meeting, Seattle, WA

2013 Novel Oncogenes in Meningiomas and Pediatric Low-grade Gliomas/ Lecture
Radiation Therapy Oncology Group, Philadelphia, PA (RTOG)

2013 Pan-cancer Patterns of Somatic Copy-number Alteration/Seminar
MSKCC, New York, NY (MSKCC)

- 2014 Understanding Cancers Through Their Genomes /Lecture
American Academy for the Advancement of Science Annual Meeting, Chicago, IL
- 2014 SF3B1 as a CYCLOPS Gene/ Lecture
Sontag Foundation Annual Meeting, Palm Springs, CA (Sontag Foundation)
- 2014 Positive and Negative Selection in Cancer Genomes/Neurooncology Seminar
MSKCC, New York, NY (MSKCC)
- 2014 Genetic analyses of brain metastases/Lecture
Society for Neurooncology Annual Meeting, Miami, FL
- 2014 DNA copy-number analysis/Seminar
Society for Neurooncology Annual Meeting, Miami, FL
- 2015 SF3B1 as a CYCLOPS gene/Lecture
Sontag Foundation Annual Meeting, Jacksonville, FL
- 2015 Genomic analyses of brain metastases/Lecture
American Association for Cancer Research Advances in Brain Cancer meeting,
Washington, DC
- 2015 PCAWG-6: Structural Variations/Lecture
International Cancer Genome Consortium Pan-Cancer Analysis of Whole Genomes Face-
to-Face Meeting, Santa Cruz, CA
- 2015 Positive and negative selection in cancer genomes/Seminar
MD Anderson Cancer Center Science to Medicine Seminar Series, Houston, TX
- 2016 MYB-QKI rearrangements in pediatric low-grade gliomas/Lecture
NRG Oncology Semiannual Meeting, Atlanta, GA
- 2016 Pan-Cancer Telomeres/Lecture
The Cancer Genome Atlas PanCanAtlas Face-to-Face Meeting, Santa Cruz, CA
- 2016 SF3B1 as a CYCLOPS Gene/ Lecture
Sontag Foundation Annual Meeting, Palm Springs, CA (Sontag Foundation)
- 2016 SF3B1 as a CYCLOPS Gene/ Lecture
The Cancer Genome Atlas PanCanAtlas Essential Genes Working Group Teleconference

International

Those presentations below sponsored by outside entities are so noted and the sponsors are identified

- 2005 Characterizing Targeted Chromosomal Aberrations/ Lecture
Harvard-Karolinska Institut Prostate Cancer Symposium, Orebro, Sweden
- 2009 Understanding the Complexity of the Cancer Genome/ Lecture
University of Nottingham Seminar on Low Grade Glioma of Childhood, Nottingham, UK
- 2010 Making Sense of Copy-number Changes in Cancer/ Keynote Lecture
Novartis Workshop on Cancer Genomics, Basel, Switzerland (Novartis)
- 2013 Positive and Negative Selection in Cancer Genomes/ Lecture
Princess Margaret Cancer Center Grand Rounds, Toronto, ON, Canada
(Princess Margaret Cancer Center)
- 2014 Somatic Copy-number Changes in Cancer/ Lecture (European Cooperation in Science and
Technology)
Translational Genomics in Biomedicine conference, Barcelona, Spain
- 2014 Interpreting Cancer Copy-number Changes/ Lecture
CCBIO 2nd Annual Symposium, Bergen, Norway (CCBIO)
- 2015 PCAWG-6: Structural Variations/Lecture

- 2015 International Cancer Genome Consortium Pan-Cancer Analysis of Whole Genomes Face-to-Face meeting, Verona, Italy
- 2015 Genetic forces in pediatric gliomagenesis and endometrial cancer progression/Seminar
Gustave Roussy Hospital Special Seminar, Paris, France
- 2015 Three stories about the cancer genome/Seminar
Tata Memorial Centre Advanced Centre for Treatment, Research and Education in Cancer (ACTREC) Special seminar, Mumbai, India
- 2015 Three stories about the cancer genome/Seminar
Molecular Genetics Colloquium, University of Toronto, Toronto, Canada
- 2016 PCAWG-6: Structural Variations/Lecture
International Cancer Genome Consortium Pan-Cancer Analysis of Whole Genomes Face-to-Face meeting, Barcelona, Spain

Report of Clinical Activities and Innovations

Current Licensure and Certification

- 2002 Massachusetts Medical License
- 2004 American Board of Internal Medicine Diplomat
- 2005 American Board of Internal Medicine, Medical Oncology Diplomat

Practice Activities

- | | | | |
|-----------|---|--|---------------------|
| 2006-2009 | Attending Physician,
Outpatient Care | Genitourinary clinic, Dana-
Farber Cancer Institute | One half day per wk |
| 2009- | Attending Physician,
Outpatient Care | Neurooncology clinic, Dana-
Farber Cancer Institute | One half day per wk |

Report of Technological and Other Scientific Innovations

- Prognostic Marker for Endometrial Carcinoma US Patent Application, 12/962,946, filed December 8, 2010

We identified a set of prognostic markers in endometrial carcinoma, including immunohistochemical staining of stathmin, which requires little further development for adoption in the clinic and reflects potentially reversible PI3 kinase activation.

Report of Education of Patients and Service to the Community

Activities

- | | |
|------|---|
| 2010 | Gliomas: The Basic Science/ Lecture
Neuro-oncology clinic annual patient retreat, Dana-Farber Cancer Institute |
| 2010 | Reconstructing the Meningioma Genome/Lecture
Brain Science Foundation Meningioma Awareness Day 2010 |
| 2011 | Gliomas: the Basic Science/ Lecture |

2012	Neuro-oncology clinic annual patient retreat, Dana-Farber Cancer Institute Targeting cancer in the genome age/ Lecture DFCI Blum Family Resource Center
2012	Gliomas: The basic science/ Lecture Neuro-oncology clinic annual patient retreat, Dana-Farber Cancer Institute
2014	Gliomas: The basic science/ Lecture Neuro-oncology clinic annual patient retreat, Dana-Farber Cancer Institute

Report of Scholarship

Publications

Peer reviewed publications in print or other media

Research investigations:

1. Boess FG, **Beroukhim R**, Martin IL. Ultrastructure of the 5-hydroxytryptamine₃ receptor. *J Neurochem.* 1995;64(3):1401-5.
2. **Beroukhim R**, Unwin N. Three-dimensional location of the main immunogenic region of the acetylcholine receptor. *Neuron.* 1995;15(2):323-31.
3. **Beroukhim R**, Unwin N. Distortion correction of tubular crystals: improvements in the acetylcholine receptor structure. *Ultramicroscopy.* 1997;70(1-2):57-81.
4. Paez JG, Lin M, **Beroukhim R**, Lee JC, Zhao X, Richter DJ, Gabriel S, Herman P, Sasaki H, Altshuler D, Li C, Meyerson M, Sellers WR. Genome coverage and sequence fidelity of phi29 polymerase-based multiple strand displacement whole genome amplification. *Nucleic Acids Res.* 2004;32(9):e71. PMID: PMC419624
5. Rubin MA, Varambally S, **Beroukhim R**, Tomlins SA, Rhodes DR, Paris PL, Hofer MD, Storz-Schweizer M, Kuefer R, Fletcher JA, Hsi BL, Byrne JA, Pienta KJ, Collins C, Sellers WR, Chinnaiyan AM. Overexpression, amplification, and androgen regulation of TPD52 in prostate cancer. *Cancer Res.* 2004;64(11):3814-22.
6. Allinen M, **Beroukhim R**, Cai L1, Brennan C1, Lahti-Domenici J, Huang H, Porter D, Hu M, Chin L, Richardson A, Schnitt S, Sellers WR, Polyak K. Molecular characterization of the tumor microenvironment in breast cancer. *Cancer Cell.* 2004;6(1):17-32.
7. Zhao X, Weir BA, LaFramboise T, Lin M, **Beroukhim R**, Garraway L, Beheshti J, Lee JC, Naoki K, Richards WG, Sugarbaker D, Chen F, Rubin MA, Jänne PA, Girard L, Minna J, Christiani D, Li C, Sellers WR, Meyerson M. Homozygous deletions and chromosome amplifications in human lung carcinomas revealed by single nucleotide polymorphism array analysis. *Cancer Res.* 2005;65(13):5561-70.
8. Garraway LA, Widlund HR, Rubin MA, Getz G, Berger AJ, Ramaswamy S, **Beroukhim R**, Milner DA, Granter SR, Du J, Lee C, Wagner SN, Li C, Golub TR, Rimm DL, Meyerson ML, Fisher DE, Sellers WR. Integrative genomic analyses identify MITF as a lineage survival oncogene amplified in malignant melanoma. *Nature.* 2005;436(7047):117-22.
9. LaFramboise T, Weir BA, Zhao X, **Beroukhim R**, Li C, Harrington D, Sellers WR, Meyerson M. Allele-specific amplification in cancer revealed by SNP array analysis. *PLoS Comput Biol.* 2005;1(6):e65. PMID: PMC1289392
10. Mellinghoff IK, Wang MY, Vivanco I, Haas-Kogan DA, Zhu S, Dia EQ, Lu KV, Yoshimoto K, Huang JH, Chute DJ, Riggs BL, Horvath S, Liau LM, Cavenee WK, Rao PN, **Beroukhim R**, Peck TC, Lee JC, Sellers WR, Stokoe D, Prados M, Cloughesy TF, Sawyers CL, Mischel PS. Molecular determinants of the response of glioblastomas to EGFR kinase inhibitors. *N Engl J Med.*

2005;353(19):2012-24.

11. Koochekpour S, Zhuang YJ, **Beroukhim R**, Hsieh CL, Hofer MD, Zhou HE, Hiraiwa M, Pattan DY, Ware JL, Luftig RB, Sandhoff K, Sawyers CL, Pienta KJ, Rubin MA, Vessella RL, Sellers WR, Sartor O. Amplification and overexpression of prosaposin in prostate cancer. *Genes Chromosomes Cancer*. 2005;44(4):351-64.
12. **Beroukhim R**¹, Lin M¹, Park Y, Hao K, Zhao X, Garraway LA, Fox EA, Hochberg EP, Mellinghoff IK, Hofer MD, Descoteaux A, Rubin MA, Meyerson M, Wong WH, Sellers WR, Li C. Inferring loss-of-heterozygosity from unpaired tumors using high-density oligonucleotide SNP arrays. *PLoS Comput Biol*. 2006;2(5):e41. PMID: PMC1458964
13. Perner S¹, Demichelis F¹, **Beroukhim R**¹, Schmidt FH, Mosquera JM, Setlur S, Tchinda J, Tomlins SA, Hofer MD, Pienta KG, Kuefer R, Vessella R, Sun XW, Meyerson M, Lee C, Sellers WR, Chinnaiyan AM, Rubin MA. TMPRSS2:ERG fusion-associated deletions provide insight into the heterogeneity of prostate cancer. *Cancer Res*. 2006;66(17):8337-41.
14. Lee JC, Vivanco I, **Beroukhim R**, Huang JH, Feng WL, DeBiasi RM, Yoshimoto K, King JC, Nghiemphu P, Yuza Y, Xu Q, Greulich H, Thomas RK, Paez JG, Peck TC, Linhart DJ, Glatt KA, Getz G, Onofrio R, Ziaugra L, Levine RL, Gabriel S, Kawaguchi T, O'Neill K, Khan H, Liao LM, Nelson SF, Rao PN, Mischel P, Pieper RO, Cloughesy T, Leahy DJ, Sellers WR, Sawyers CL, Meyerson M, Mellinghoff IK. Epidermal growth factor receptor activation in glioblastoma through novel missense mutations in the extracellular domain. *PLoS Med*. 2006;3(12):e485. PMID: PMC1702556
15. Mertz KD, Setlur SR, Dhanasekaran SM, Demichelis F, Perner S, Tomlins S, Tchinda J, Laxman B, Vessella RL, **Beroukhim R**, Lee C, Chinnaiyan AM, Rubin MA. Molecular characterization of TMPRSS2-ERG gene fusion in the NCI-H660 prostate cancer cell line: a new perspective for an old model. *Neoplasia*. 2007;9(3):200-6. PMID: PMC1838578
16. Thomas RK, Baker AC, DeBiasi RM, Winckler W, Laframboise T, Lin WM, Wang M, Feng W, Zander T, MacConaill L, Lee JC, Nicoletti R, Hatton C, Goyette M, Girard L, Majumdar K, Ziaugra L, Wong KK, Gabriel S, **Beroukhim R**, Peyton M, Barretina J, Dutt A, Emery C, Greulich H, Shah K, Sasaki H, Gazdar A, Minna J, Armstrong SA, Mellinghoff IK, Hodi FS, Dranoff G, Mischel PS, Cloughesy TF, Nelson SF, Liao LM, Mertz K, Rubin MA, Moch H, Loda M, Catalona W, Fletcher J, Signoretti S, Kaye F, Anderson KC, Demetri GD, Dummer R, Wagner S, Herlyn M, Sellers WR, Meyerson M, Garraway LA. High-throughput oncogene mutation profiling in human cancer. *Nat Genet*. 2007;39(4):347-51.
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 21. Engelsen IB, Stefansson IM, **Beroukhim R**, Sellers WR, Meyerson M, Akslen LA, Salvesen HB. HER-2/neu expression is associated with high tumor cell proliferation and aggressive phenotype in a population based patient series of endometrial carcinomas. *Int J Oncol*. 2008;32(2):307-16.
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 24. Li C, **Beroukhim R**, Weir BA, Winckler W, Garraway LA, Sellers WR, Meyerson M. Major copy proportion analysis of tumor samples using SNP arrays. *BMC Bioinformatics*. 2008;9:204. PMID: PMC2375907
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¹These authors contributed equally to this work.

*Co-first authors; when these included my trainees their names have been bolded

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1. **Beroukhim, R**. Single nucleotide polymorphism microarrays in the analysis of cancer. In Tomlinson, C. (ed.), *Microarrays: Their design and use*, The Biomedical & Life Sciences Collection, Henry Stewart Talks Ltd, London; 2009.

Thesis

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High-resolution characterization of chromosomal aberrations in the prostate cancer genome using single nucleotide polymorphism arrays. 2006 Inter-Prostate SPORE Meeting; 2006 Feb 4-6, Houston, Texas.

Narrative Report

My principal effort at DFCI and HMS is in translational research, with a focus on understanding the somatic genetics of cancer and particularly brain cancers. I also have a clinical practice in neurooncology at DFCI with occasional inpatients at BWB, and devote my remaining time to teaching, administrative tasks, and peer review.

In graduate school under Dr Nigel Unwin, I developed algorithms to improve the resolution of electron crystallographic protein structures. I determined the three-dimensional location of the main immunogenic region of the nicotinic acetylcholine receptor (which plays a central role in myasthenia gravis) and set the stage for later research that resolved the nicotinic acetylcholine receptor to atomic resolution.

As a postdoctoral fellow under Drs William Sellers and Matthew Meyerson, I developed computational methods for the study of cancer somatic genetics, including GISTIC, which distinguishes copy-number alterations that are likely to drive oncogenesis from other random alterations and is central to the analysis of the copy-number profiles across many projects worldwide. I characterized thousands of cancer specimens across histologic types and identified dozens of recurrently altered genomic regions, pointing to several new oncogenes and tumor suppressor genes that have been validated on the basis of my work; mechanistic and negative selective forces shaping copy-number profiles; and commonalities among driver events across cancers.

Since gaining independence I have continued to develop computational methods to evaluate cancer genomes, including detecting rearrangements and significantly recurrent rearrangements and functionally relevant associations between genetic events. I identified oncogenic *SMO* and *AKT1* mutations in meningiomas (the basis for international clinical trials targeting these mutations), oncogenic *MYB* and *MYBL1* rearrangements in pediatric gliomas (the basis for new WHO diagnostic criteria), functional consequences of *PARK2* deletions, and the genetic features of endometrial cancer metastases. I co-chair the International Cancer Genome Consortium effort to characterize structural alterations across 2800 cancer whole genomes.

I have also determined associations between genomic alterations and cancer phenotype, including the identification of novel dependencies resulting from partial loss of non-driver genes; responsiveness of medulloblastomas to BET-bromodomain inhibition (the basis of a pending clinical trial) and mechanisms by which they acquire resistance; and independent prognostic indicators in endometrial cancer.

I am lead PI of a multi-PI R01 and of solo and multi-PI foundation- and industry-funded grants. I have published 15 last- or co-last author papers including four in *Nature Genetics* and *Cell*.

I maintain 10% clinical effort and spend ~10% of my time in administrative roles, including admissions committees for the HMS Bioinformatics and Integrative Genomics (BIG) and MD-PhD programs and the MGH/DFCI neurooncology fellowship program, the ethics advisory committee at DFCI, and the Broad Institute Cancer Program Steering Committee.

I give ~10 hours of lectures across various courses each year. I also mentor graduate and postdoctoral

trainees within my laboratory, clinical neurooncology and medical oncology fellows, and other graduate and postdoctoral trainees through membership of advisory and examination committees and as a BIG faculty mentor.

In sum, I am a physician-scientist active in laboratory investigation, translational research, patient care, institutional service, and training of students, fellows, and physicians. These activities occur at DFCI, the Broad Institute, and BWH, and flow mainly through my focus on the genomic features of oncogenesis and cancer progression in brain and other cancers, and the implications of these in identifying novel cancer dependencies, therapeutic strategies, and biomarkers.