The Faculty of Medicine of Harvard University Curriculum Vitae

Date Prepared: August 28, 2022

Name: Richard Allen Guyer

Office Address: General Surgery Residency Program

Massachusetts General Hospital

55 Fruit St, GRB-425 Boston, MA 02114

Home Address: 10 Allen St, Unit 1

Cambridge, MA 02140

Work Phone: (908) 447-3462

Work Email: rguyer@mgh.harvard.edu

BA

Education:

2002-2006

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|-----------|-----------|--|----------------------------|
| 2006-2008 | No degree | Special Sciences Program | University of Pennsylvania |
| 2008-2012 | No degree | Medicine and Microbiology (Laboratory of Ian Macara) | University of Virginia |
| 2012-2016 | MD, PhD | Medicine and Cell and | Vanderbilt University |

Economics and Mathematics

Developmental Biology (Laboratory of Ian Macara)

Postdoctoral Training:

06/16- Resident General Surgery Massachusetts General

physician Hospital

07/19- Research fellow Pediatric Surgical Research Massachusetts General

Laboratories Hospital

(Laboratory of Allan Goldstein)

Appointments at Hospitals/Affiliated Institutions:

2016 Resident Surgery Massachusetts General

Hospital

Davidson College

| 2016- | Clinical Fellow | Surgery | Harvard Medical School |
|-------|-----------------|---------|----------------------------|
| 2016- | Resident | Surgery | Newton-Wellesley Hospital |
| 2017- | Resident | Surgery | North Shore Medical Center |

Major Administrative Leadership Positions:

Local

2021-2022 Academic Development Administrative Massachusetts General Hospital

Resident (Surgery)

Professional Societies:

2015- American College of Surgeons

2016- Association for Academic Surgery

2016- Massachusetts Medical Society

2017- American Pediatric Surgical Association

2020-2022 Resident Member, Research Committee

Grant Review Activities:

2020- Research Committee American Pediatric Surgical Association

2020-2022 Permanent Member

Editorial Activities:

Ad hoc Reviewer

Stem Cells Translational Medicine

Biomolecules

International Journal of Molecular Sciences

Cells

Surgery

Computational and Structural Biotechnology Journal

Neural Regeneration Research

Other Editorial Roles

2022- Early Career Reviewer Board Journal of Biological Chemistry

| Honors and Prizes: | | | | | |
|--------------------|--|--|---|--|--|
| 2004 | Richard R. Bernard Society for Mathematics | Davidson College Department of Mathematics | Institutional undergraduate mathematics honor society | | |
| 2005 | Omicron Delta Epsilon Economics Honor Society | Davidson College Department of Economics | National undergraduate economics honor society | | |
| 2007 | Ruth and William Silen, MD Award | Harvard Medical School DICP | Best oral presentation at the 2007 New England Science Symposium | | |
| 2009 | Trevor Evans Award | Mathematical Association of America | For an exceptional article accessible to undergraduates published in Math Horizons | | |
| 2011 | NIH T32 Cancer Research Training Grant | University of Virginia | Research of breast cancer metastasis | | |
| 2016 | Medical Student Research Prize | Association for Academic Surgery/Association for Academic Surgery Foundation | Research of breast cancer metastasis conducted in Ian Macara's laboratory | | |
| 2019 | Marshall K. Barlett Research Fellowship | Massachusetts General Hospital Department of Surgery | Support for research in Allan Goldstein's laboratory | | |
| 2020 | National Research Service Award (F32) Postdoctoral Fellowship | National Institutes of Health | Support for research of the transcriptional control of postnatal enteric neurogenesis | | |

2022 Patricia K. Donahoe,

MD, Surgeon-

Scientist Research

Program

Resident Catalyst

Award

Massachusetts General Hospital Department of

Surgery

Support for laboratory research during senior residency training

Report of Funded and Unfunded Projects

Past

2020-2022 Transcription Factors Mediate Postnatal Neurogenesis from Enteric Glial

Cells

NIH/NIDDK; F32 DK121440

PI (\$141,936)

This project utilizes single-cell RNA sequencing and conditional gene

knockout models to identify transcriptional drivers of postnatal neurogenesis

in the enteric nervous system.

Current

2022-2024 A Developmentally-Informed Approach to Neuroblastoma Biology

Massachusetts General Hospital Department of Surgery; Patricia K. Donahoe, MD, Surgeon-Scientist Research Program Resident Catalyst

Award

PI (\$100,000)

This project applies both cutting-edge sequencing tools and traditional

methods to uncover the developmental and epigenetic basis for

neuroblastoma tumorigenesis and response to therapy

Report of Local Teaching and Training

Clinical Supervisory and Training Responsibilities:

2016- Daily supervision of HMS students on

the Surgery rotation of the Principle Clinical Experience and on general

surgery sub-internships

Harvard Medical School Students

Massachusetts General Hospital

Daily supervision of third-year Tufts
medical students undertaking their
surgical clerkship at Newton-Wellesley
Hospital
Tufts University Medical Students

Newton-Wellesley Hospital

Local Invited Presentations:

| 🛚 No presentatio | ns below were sponsored by 3 rd parties/outside entities |
|------------------|--|
| 2018 | Blunt Abdominal Trauma / Lecture to Tufts University medical students |
| | Department of Surgery, Newton-Wellesley Hospital |
| 2018 | Compartment Syndromes / Lecture to Tufts University medical students |
| | Department of Surgery, Newton-Wellesley Hospital |
| 2019 | Reanalysis of published single cell RNA sequencing of enteric nervous system cells / monthly departmental research seminar Department of Surgery, Massachusetts General Hospital |
| 2020 | Single cell transcriptomics of postnatal enteric glial cells reveals similarity with embryonic enteric neuronal progenitors / Weekly research conference |
| | Pediatric Surgical Research Laboratories, Massachusetts General Hospital |
| 2020 | Using Single-Cell Transcriptomics to Understand and Treat Hirschsprung Disease / Pediatric Surgery/Pediatric Anesthesia Grand Rounds |
| | Departments of Pediatric Surgery and Anesthesia, MassGeneral Hospital for Children |
| 2021 | Single cell analysis of enteric glial cells identifies a molecular basis for postnatal enteric neurogenesis / Surgical Investigators' Club Department of Surgery, Massachusetts General Hospital |
| 2021 | A Developmentally-Informed Approach to Neuroblastoma Biology / Weekly research conference Pediatric Surgical Research Laboratories, Massachusetts General Hospital |
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| 2022 | Chromatin Remodeling and Cell Fate in the Neural Crest / Pediatric Surgery/Pediatric Anesthesia Grand Rounds Departments of Pediatric Surgery and Anesthesia, MassGeneral Hospital for Children |
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| 2022 | Chromatin Remodeling and Cell Fate in the Neural Crest / Surgical Investigators' Club Department of Surgery, Massachusetts General Hospital |
| 2022 | Heterogeneity and plasticity in neuroblastoma cell lines / Weekly research conference Pediatric Surgical Research Laboratories, Massachusetts General Hospital |
| 2022 | Overcoming the Review – Getting a F32 Funded / Academic Development Career Seminar Series Department of Surgery, Massachusetts General Hospital |
| 2022 | Postoperative management / Lecture to incoming house officers Newton-Wellesley Hospital |
| 2022 | Management of Blunt Abdominal Trauma / Lecture to Tufts University medical students Department of Surgery, Newton-Wellesley Hospital |
| 2022 | Presenting Patients on Surgical Rounds / Lecture to Tufts University medical students Department of Surgery, Newton-Wellesley Hospital |

Report of Scholarship

ORCID: 0000-0001-5075-1767

Peer-Reviewed Scholarship in print or other media:

Research Investigations

- 1. Yu J, Ishii M, Law M, Woodburn JM, Emami K, Kadlecek S, Vahdat V, **Guyer RA**, Rizi RR, Optimization of scan parameters in pulmonary partial pressure oxygen measurement by hyperpolarized 3He MRI. (2008) Magn Reson Med, 59(1):124-31.
- 2. Emami K, Cadman RV, Fischer MC, Zhu J, Woodburn JM, Kadlecek SJ, **Guyer RA**, Law M, Vahdat V, Friscia ME, Ishii M, Yu J, Shrager JB, Rizi RR, Early changes of

- lung function and structure in an elastase model of emphysema--a hyperpolarized 3He MRI study. (2008). J of Appl Physiol, 104(3):773-86.
- 3. **Guyer RA**, Hellman M, Emami K, Kadlecek SJ, Cadman RV, Law M, Ishii M, Vadhat V, Yu J, Rizi RR, A robust method for measuring regional pulmonary parameters in the presence of noise. (2007) Acad Radiol, 15(6):740-52.
- 4. LaPar DJ, Stukenborg GJ, **Guyer RA**, Stone ML, Bhamidipati CM, Lau CL, Kron IL, Ailawadi GA. Primary Payer Status is Associated with Mortality and Resource Utilization for Coronary Artery Bypass Grafting Operations. (2012). Circulation, 126(11 Suppl 1):S132-9.
- 5. **Guyer RA**, Macara IG, Loss of the Polarity Protein PAR3 Activates STAT3 Signaling via an Atypical Protein Kinase C (aPKC)/NF-kB/Interleukin-6 (IL-6) Axis in Mouse Mammary Cells. (2015) The Journal of Biological Chemistry, 290(13):8457-68.
- 6. Dennis BM, Gondek SP, **Guyer RA**, Hamblin SE, Gunter OL, Guillamondegui OD, Use of an evidence-based algorithm for patients with traumatic hemothorax reduces need for additional interventions. (2017) J Trauma Acute Care Surg, 82(4):728-732.
- 7. Wandell G, Miller C, Rathor A, Thee Wei T, **Guyer RA**, Turner J, Hwang P, Davis G, Humphreys I, A Multi-Institutional Review of Outcomes in Biopsy-Proven Acute Invasive Fungal Sinusitis. (2018) Int Forum of Allergy Rhinol, 8(12):1459-1468.
- 8. Nagy N, **Guyer RA**, Hotta R, Zhang D, Newgreen DF, Halasy V, Kovacs T, Goldstein AM, RET overactivation leads to concurrent Hirschsprung disease and intestinal ganglioneuromas. (2020) Development, 147(21):dev190900.
- 9. Bhave S, Arciero E, Baker C, Ho WL, **Guyer RA**, Goldstein AM, Pan-enteric neuropathy and dysmotility are present in a mouse model of short-segment Hirschsprung disease and may contribute to post-pullthrough morbidity. (2021) J Pediatr Surg, 56(2):250-256.
- 10. Stavely R, Bhave S, Ho WLN, Ahmed M, Pan W, Rahman AA, Ulloa J, Bousquet N, Omer M, **Guyer RA**, Nagy N, Goldstein AM, Hotta R, Enteric mesenchymal cells support the growth of postnatal enteric neural stem cells. (2021) Stem Cells, 39(9):1236-1252.
- 11. Westfal ML, Okiemy O, Chung PHY, Feng J, Lu C, Miyano G, Tam PKH, Tang W, Wong KKY, Yamataka A, **Guyer RA**, Doody DP, Goldstein AM, Optimal timing for soave primary pull-through in short-segment Hirschsprung disease: A meta-analysis. (2021) J Pediatr Surg, 57(4):719-725.

- 12. Bhave S, Ho WLN, Cheng K, Omer M, Bousquet N, **Guyer RA**, Hotta R, Goldstein AM, Tamoxifen administration alters gastrointestinal motility in mice. (2022) Neurogastroenterol Motil 34(5):e14357.
- 13. Stavely RS, Hotta R, Picard N, Rahman AA, Pan W, Bhave S, Omer M, Ho WL, **Guyer RA**, Goldstein AM. Schwann cells in the subcutaneous adipose tissue have neurogenic potential and can be used for regenerative therapies. (2022) Sci Transl Med 14:eabl8753.
- 14. Cramm SL, Lipskar AM, Graham DA, Kunisaki SM, Griggs CL, Allukian M, Russell RT, Chandler NM, Santore MT, Aronowitz DI, Blakely ML, Campbell B, Collins DT, Commander SJ, Cowles RA, DeFazio JR, Echols JC, Esparaz JR, Feng C, Guyer RA, Hanna DN, He K, Kahan AM, Keane OA, Lamoshi A, Lopez CM, McLean SE, Pace E, Regan MD, Scholz S, Tracy ET, Williams SA, Zhang L, Rangel SJ, for the Eastern Pediatric Surgery Network. Association of Gangrenous, Suppurative, and Exudative Findings With Outcomes and Resource Utilization in Children With Nonperforated Appendicitis. (2022) JAMA Surgery doi:10.1001/jamasurg.2022.1928.
- 15. *Bhave SB, *Guyer RA, Picard N, Omer M, Hotta R, Goldstein AM. Ednrb-/- mice with Hirschsprung disease are missing Gad2-expressing enteric neurons in the ganglionated small intestine. (2022) Front Cell Dev Biol doi:10.3389/fcell.2022.917243
- 16. Sborov KD, Dennis BM, de Oliveira Filho GR, Bellister SA, Statzer N, Stonko DP, Guyer RA, Wanderer JP, Beyene RT, McEvoy MD, Allen BFS. Acute pain consult and management is associated with improved mortality in rib fracture patients. (2022) Reg Anesth Pain Med doi: 10.1136/rapm-2022-103527

Non-peer reviewed scholarship in print or other media:

Reviews, chapters, and editorials

- 1. Macara IG, **Guyer RA**, Richardson G, Huo Y, Ahmed M, Epithelial Homeostasis. (2014) Current Biology, 24:R815-25.
- 2. **Guyer RA**, Mueller JL, Goldstein AM, Applications of Single-Cell Sequencing Technology to the Enteric Nervous System. (2022) Biomolecules 12(3):452.

Case reports

1. **Guyer RA**, Turner JH, Delayed Presentation of Traumatic Cerebrospinal Fluid Rhinorrhea: Case Report and Literature Review. (2015). Allergy and Rhinology, 6:188-190.

2. Mueller JL, **Guyer RA**, Adler JT, Mullen JT, Metastatic renal cell carcinoma to the small bowel: three cases of GI bleeding and a literature review. (2018) CEN Case Reports, 7:39-43.

Other non-peer reviewed scholarship

- 1. **Guyer RA**, Radiology Paging a Good Mathematician: Why Math Can Contribute More to Medicine Than You Might Think. (2008) Math Horizons.
- 2. **Guyer RA**, Schwarze ML, Gosain A, Maggard-Gibbons M, Keswani SG, Goldstein AM, Top ten strategies to enhance grant-writing success. (2021) Surgery S0039-6060(21)00656-5.
- 3. **Guyer RA**, Stavely RS, Robetson K, Bhave S, Hotta R, Kaltschmidt JA, Goldstein AM, Single-Cell Multiome Sequencing Clarifies Enteric Glial Cell Diversity and Identifies an Intraganglionic Population Poised for Neurogenesis. (2022) BioRxiv 10.1101/2021.08.24.457368.
- 4. *Guyer RA, *Picard N, Mueller JL, Murphy AJ, Cornejo KM, Hotta R, Goldstein AM. Differentiated neuroblastoma cells remain epigenetically poised for de-differentiation to an immature state. (2022) BioRxiv 10.1101/2022.07.10.499470.

Thesis:

1. Tumor Suppressor Mechanisms of the Polarity Protein Par-3, Doctoral thesis submitted to the faculty of Vanderbilt University

Abstracts, Poster Presentations, and Exhibits Presented at Professional Meetings:

- 1. Bousquet N, **Guyer RA**, Hotta R, Goldstein AM, CD49b Expression In Neuroblastoma Distinguishes Chemosensitive, Proliferative Cells From Chemoresistant, Quiescent Cells. Virtual podium presentation at American College of Surgeons Clinical Congress, virtual conference, 10/2021.
- 2. **Guyer RA**, Bhave S, Stavely S, Hotta R, Goldstein AM, Single cell RNA sequencing reveals enteric glial subpopulations with therapeutic potential in Hirschsprung disease. Virtual podium presentation at American College of Surgeons Clinical Congress, virtual conference, 10/2020.
- 3. **Guyer RA**, Bhave S, Stavely R, Hotta R, Li Z, Ngan E, Goldstein AM, Single-cell Analysis Shows Postnatal Enteric Glial Cells Closely Resemble Embryonic Neural Stem

Cells. Virtual oral quickshot presentation at Academic Surgical Congress, virtual conference, 2/2021.

- 4. **Guyer RA**, Mueller J, Bhave S, Stavely R, Hotta R, Goldstein AM, Reduced Expansion In Culture of Enteric Glial Cells From Hirschsprung Disease Mice. Oral podium presentation at Academic Surgical Congress, Orlando, FL. 2/2022.
- 5. **Guyer RA**, Bhave S, Stavely RS, Hotta R, Goldstein AM, Joint Single-Nucleus ATAC and RNA Sequencing Reveal Chromatin Closing at Distal Regulatory Elements During Glial-to-Neuron Differentiation. Oral podium presentation at the 6th International Symposium on Development of the Enteric Nervous System, Ferrara, Italy, 4/2022.
- 6. **Guyer RA**, Picard N, Mueller JS, Hotta R, Goldstein AM, Neuroblastoma Cells Include Heterogeneous Populations of Highly Plastic Quiescent and Proliferative Cells Marked by CD49b Expression. Oral podium presentation at the American Pediatric Surgical Association Annual Meeting, San Diego, CA, 5/2022.

Narrative Report

I am a general surgery resident with formal training as a cell and developmental biologist, and with aspirations to become an academic pediatric surgeon. I was a dual-degree MD/PhD student at the University of Virginia and Vanderbilt University, and I earned a PhD in Ian Macara's laboratory. Following medical school, I came to Harvard Medical School and Massachusetts General Hospital for clinical training in surgery and a postdoctoral fellowship in the MGH Pediatric Surgical Research Laboratories. I am scheduled to graduate from residency in June 2024, after which I hope to undertake a clinical fellowship in pediatric surgery.

My research expertise is focused on understanding how cells achieve and maintain a differentiated phenotype, with particular emphasis on the epigenetic mechanisms that control gene expression. I seek to understand how chemical changes to DNA and DNA-associated proteins direct neural crest to commit to differentiated fates, and how perturbations to this process contribute to neoplasia. My work has been supported by numerous grant awards, both during graduate school and during my postdoctoral training. These grants include appointment to the University of Virginia Cancer Research T32 training grant, the Marshall K. Barlett Research Fellowship from the MGH Department of Surgery, an NIH F32 postdoctoral fellowship, and, most recently, the Patricia K. Donahoe Resident Research Catalyst Award from the MGH Department of Surgery. I have published 16 peer-reviewed research papers, and I have several more currently in preparation. I have also presented at numerous national and international meetings, including the American Society for Cell Biology, International Symposium on the Development of the Enteric Nervous System, American College of Surgeons, Academic Surgical Congress, and American Pediatric Surgical Association. I am currently working to understand how chromatin structure directs specification of enteric neurons, and how disruption of epigenetic

^{*} Co-first author

mechanisms lends inappropriate plasticity to neuroblastoma cells. These projects leverage traditional methods in cell and developmental biology as well as utilizing cutting-edge tools for single-cell transcriptomic and epigenetic analysis.

In my role as a clinical general surgery resident, I care for patients with surgical disease at Massachusetts General Hospital, Newton-Wellesley Hospital, and North Shore Medical Center. Since coming to Harvard Medical School as a trainee, I have endeavored to provide outstanding surgical care to patients, contribute to the education of medical students and junior residents through teaching, and to advance medical science through basic discovery. Through teaching, lectures, written work, basic biological research, and involvement with professional societies, I am seeking to improve the care of babies and children suffering from congenital malformations and cancer.