BIOGRAPHICAL SKETCH

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NAME: Loyal A. Goff

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

POSITION TITLE: Assistant Professor of Neuroscience & Genetic Medicine

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
The College of New Jersey, Ewing, NJ	B.S.	05/2001	Biology
Rutgers University, Piscataway, NJ	Ph.D.	04/2008	Cell & Developmental Biology
Massachusetts Institute of Technology, Cambridge, MA	Postdoctoral	01/2014	Computational Biology
Harvard University, Cambridge, MA	Postdoctoral	08/2014	ncRNA Biology / Neurodevelopment

NOTE: The Biographical Sketch may not exceed five pages. Follow the formats and instructions below.

A. Personal Statement

My research is focused on the identification and characterization of neural cell types, key cell fate decisions during development, and the effects of disease-associated mutations on these choices. My lab uses bulk and single-cell RNA-Seq, as well as functional genomics tools, to characterize enriched populations of neuronal subtypes during development and identify functional relationships between transcriptional differences and physiological properties of distinct neuronal subtypes. Of particular interest is the expanding role for the tissue and cell-type-specific long non-protein coding RNA molecules (lncRNAs). I am interested in the mechanisms by which non-coding RNAs regulate target gene expression in the context of neuronal differentiation, their coordinate interactions with regulatory protein complexes, and functional roles in establishment and maintenance of specific neuronal identities. Recently, my focus has been on the identification and characterization of novel lncRNAs involved in key developmental processes within the brain, including lncRNAs induced in neuronal development, lncRNA-mediated specification of neuronal subtypes, and the roles for lncRNAs in neurodegenerative and developmental disorders. By leveraging the power of high-throughput RNA-Sequencing, functional genomics, and single-cell transcriptional analysis, we can dissect, with high resolution, the key cellular decisions that direct neural development and organization, and identify where and how these events are misregulated during disease.

B. Positions and Honors

Positions and Employment

04/2008-10/2008 *Research Assistant* Rutgers University – Cell Biology and Neuroscience
10/2008-01/2014 *Postdoctoral Fellow* MIT – Computer Science and Artificial Intelligence Lab
04/2009-08/2014 *Postdoctoral Fellow* Harvard University – Stem Cells and Regenerative Biology
09/2014-Current *Assistant Professor* Johns Hopkins School of Medicine – Institute of Genetic Medicine

Professional Memberships

- Society for Neuroscience (2007-Present)

- American Society for Human Genetics (2015-Present)

Honors

- NSF Postdoctoral Research Fellowship in Biology: Biological Informatics program (2009)
- NIH Ruth L. Kirschstein NRSA for Individual Postdoctoral Fellows (2009) (awarded but declined)

C. Contribution to Science

1. Throughout my career, I have been interested in the various mechanisms of RNA-mediated biological activity and regulation, and the potential roles for this class of macromolecule in the acquisition and maintenance of specific cellular identities. My early publications centered on both technology development and applications to address the question of how miRNAs direct the differentiation of multipotent stem cells towards a particular lineage. I was responsible for the design and development of one of the first multi-species microRNA microarray platforms, and utilized this technological advance to interrogate the differential regulation and functional contributions of microRNAs across a wide variety of stem cell differentiation contexts. By integrating microRNA and mRNA expression patterns, I was able to characterize the identity and differentiation potential of several neural stem cell clones with the ultimate goal of using microRNAs to direct differentiation towards cell fates with therapeutic transplantation potential in traumatic spinal cord injury.
    a. **Goff, L.A.,** Yang, M., Bowers, J., Getts, R.C., Padgett, R.W., and Hart, R.P. (2005). Rational probe optimization and enhanced detection strategy for microRNAs using microarrays. RNA Biol 2, 93–100.
    b. **Goff, L.A.,** Boucher, S., Ricupero, C.L., Fenstermacher, S., Swerdel, M., Chase, L.G., Adams, C.C., Chesnut, J., Lakshmipathy, U., and Hart, R.P. (2008). Differentiating human multipotent mesenchymal stromal cells regulate microRNAs: prediction of microRNA regulation by PDGF during osteogenesis. Exp. Hematol. 36, 1354–1369. PMCID: PMC2782644
    c. **Goff, L.A.*,** Davila, J.*, Swerdel, M.R., Moore, J.C., Cohen, R.I., Wu, H., Sun, Y.E., and Hart, R.P. (2009). Ago2 immunoprecipitation identifies predicted microRNAs in human embryonic stem cells and neural precursors. PLoS ONE 4, e7192. **Authors contributed equally.* PMCID: PMC2745660
    d. Davila, J.L.*, **Goff, L.A.***, Ricupero, C.L.*, Camarillo, C., Oni, E.N., Swerdel, M.R., Toro-Ramos, A.J., Li, J., and Hart, R.P. (2014). A Positive Feedback Mechanism That Regulates Expression of miR-9 during Neurogenesis. PLoS ONE 9, e94348. **Authors contributed equally.* PMCID: PMC3979806

2. Long non-coding RNAs (lncRNAs) are a recently described class of regulatory RNA genes with a high degree of cell-type specificity that are likely to contribute to specific cellular identities and functions. LncRNAs have demonstrated roles in differentiation, cell fate specification, apoptosis, body axis patterning, and a growing list of disorders including cancer. As part of my postdoctoral work I was responsible for the identification of thousands of human and mouse lncRNAs that are induced during various cellular differentiation programs or restricted to subpopulations of cells. As part of these studies I was able to demonstrate the physiological relevance of these genes as a class, and identify at least one novel mechanism by which lncRNAs contribute to nuclear organization. By establishing a cohort of neuronal lncRNA gene knockout mice, my research has determined that indeed several lncRNA loci are required for life, and many others have expression and developmental phenotypes within the brain.
    a. Cabili, M.N., Trapnell, C., **Goff, L.,** Koziol, M., Tazon-Vega, B., Regev, A., and Rinn, J.L. (2011). Integrative annotation of human large intergenic noncoding RNAs reveals global properties and specific subclasses. Genes & Development. PMCID: PMC3185964
    b. Sun, L.*, **Goff, L.A.*,** Trapnell, C.*, Alexander, R., Lo, K.A., Hacisuleyman, E., Sauvageau, M., Tazon-Vega, B., Kelley, D.R., Hendrickson, D.G., et al. (2013). Long noncoding RNAs regulate adipogenesis. Proceedings of the National Academy of Sciences 110, 3387–3392. **Authors contributed equally*. PMCID: PMC3587215
    c. Sauvageau, M.*, **Goff, L.A.*,** Lodato, S.*, Bonev, B., Groff, A.F., Gerhardinger, C., Sanchez-Gomez, D.B., Hacisuleyman, E., Li, E., Spence, M., et al. (2013). Multiple knockout mouse models reveal lincRNAs are required for life and brain development. Elife 2, e01749. **Authors contributed equally.* PMCID: PMC3874104

d. **Goff, L.A.*,** Groff, A.F.*, Sauvageau, M.*, Trayes-Gibson, Z., Sanchez-Gomez, D.b., Morse, M., Martin, R.D., Elcavage, L.E., Liapis, S.C., Gonzalez-Celeiro, M., Plana, Ol., Li, E., Gerhardinger, C., Tomassay, G.S., Arlotta, P., Rinn, J.L., (2015) Spatiotemporal expression and transcriptional perturbations by long noncoding RNAs in the mouse brain. PNAS 112(22): 6855-6862. * *Authors Contributed Equally.* PMCID: PMC4460505

3. As high-throughput sequencing technologies have evolved, so has the need for robust software and computational tools to enable exploration and analysis of these large datasets. As a result, I have been involved in the development of several key computational/informatic tools to facilitate increased adoption of, and access to RNA-Seq data. As part of this process, I am responsible for the development of several training programs aimed at encouraging molecular biologist to learn to analyze these complex data themselves. I am the principal author of the popular cummeRbund utility; an R/bioconductor package that facilitates exploration and visualization of differential RNA-Seq data. In addition, I have contributed to the development of several additional tools as part of the widely-used Tuxedo suite of utilities for bulk and single-cell RNA sequencing analysis.
    a. Trapnell, C., Roberts, A., **Goff, L.,** Pertea, G., Kim, D., Kelley, D.R., Pimentel, H., Salzberg, S.L., Rinn, J.L., and Pachter, L. (2012). Differential gene and transcript expression analysis of RNA-seq experiments with TopHat and Cufflinks. Nat Protoc 7, 562–578. PMCID: PMC3334321
    b. Washietl, S., Will, S., Hendrix, D.A., **Goff, L.A.,** Rinn, J.L., Berger, B., and Kellis, M. (2012). Computational analysis of noncoding RNAs. Wiley Interdiscip Rev RNA 3, 759–778. PMCID: PMC3472101
    c. Trapnell, C., Hendrickson, D.G., Sauvageau, M., **Goff, L.,** Rinn, J.L., and Pachter, L. (2013). Differential analysis of gene regulation at transcript resolution with RNA-seq. Nat. Biotechnol. 31, 46–53. PMCID: PMC3869392
    d. **Goff, L.,** Trapnell, C., (2012). Analysis, exploration, manipulation, and visualization of Cufflinks high-throughput sequencing data. R package version 2.1. website.

4. Through various collaborative and independent projects, I have contributed to the identification of novel mechanisms for RNA-mediated regulation and to the development of transcriptome-wide technologies to elucidate functional RNA elements. In each case, my contributions included data acquisition and analysis, as well as experimental design, wet-bench experiments, and technology development.
    a. Di Ruscio, A., Ebralidze, A.K., Benoukraf, T., Amabile, G., **Goff, L.A.,** Terragni, J., Figueroa, M.E., De Figueiredo Pontes, L.L., Alberich-Jorda, M., Zhang, P., et al. (2013). DNMT1-interacting RNAs block gene-specific DNA methylation. Nature 503, 371–376. PMCID: PMC3870304
    b. Gregory, B.D., Rinn, J., Li, F., Trapnell, C., and **Goff, L.A.** (2013). High-throughput methodology for identifying RNA-protein interactions transcriptome-wide. US Patent Office. US 2013/0338009 A1.
    c. Silverman, I.M., Li, F., Alexander, A., **Goff, L.,** Trapnell, C., Rinn, J.L., and Gregory, B.D. (2014). RNase-mediated protein footprint sequencing reveals protein-binding sites throughout the human transcriptome. Genome Biol 15, R3. PMCID: PMC4053792
    d. Hacisuleyman, E.*, **Goff, L.A.*,** Trapnell, C., Williams, A., Henao-Mejia, J., Sun, L., McClanahan, P., Hendrickson, D.G., Sauvageau, M., Kelley, D.R., et al. (2014). Topological organization of multichromosomal regions by the long intergenic noncoding RNA Firre. Nat. Struct. Mol. Biol. 21, 198–206. **Authors contributed equally*. PMCID: PMC3950333

5. My recent work has focused on transcriptional characterization of enriched subpopulations of neuronal cell types during development. A major obstacle to our understanding of the organization and development of the mammalian brain has been the inherent complexity and cellular heterogeneity of this important tissue. To address this, I contributed to the development of a technique for enrichment of specific neuronal subtypes that enabled, for the first time, comprehensive transcriptional profiling of relatively homogenous populations of neurons. This achievement permits the focused characterization of specific classes of neurons and the identification of both coding and non-coding genes that contribute to the establishment of distinct neuronal identities.
    a. Lodato, S., Molyneaux, B.J., Zuccaro, E., **Goff, L.A.,** Chen, H.-H., Yuan, W., Meleski, A., Takahashi, E., Mahony, S., Rinn, J.L., et al. (2014). Gene co-regulation by Fezf2 selects

neurotransmitter identity and connectivity of corticospinal neurons. Nature Neuroscience 17, 1046–1054. PMCID: PMC4188416

b. Molyneaux, B.J.*, **Goff, L.A.*,** Brettler, A.C., Chen, H.-H., Brown, J.R., Hrvatin, S., Rinn, J.L., and Arlotta, P. (2015). DeCoN: genome-wide analysis of in vivo transcriptional dynamics during pyramidal neuron fate selection in neocortex. Neuron 85, 275–288. **Authors Contributed Equally* PMCID: PMC4430475

c. **Goff, L.A.**, Rinn, J.L. (2015) Linking RNA Biology to lncRNAs. Genome Research 25:1442-1455. PMCID: PMC4579330

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1FeogldaNj7/bibliography/40255272/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

2016-MSCRFI-2805 (Goff - PI) 6/01/2016 – 05/31/2019
Maryland Stem Cell Research Commission
Single cell analysis of hippocampal neurogenesis defects in Kabuki Syndrome 1
The major goals of this project are to characterize the molecular mechanisms responsible for learning and memory dysfunction as a result of defective neurogenesis associated with Kabuki Syndrome 1 patient mutations.

SLI (Goff – Co-PI) 06/01/2016 – 05/30/2018
Johns Hopkins Science of Learning Institute
Cell-type specific heterogeneity in experience-induced gene expression
The major goals of this project are to generate preliminary data on common and variable transcriptional signatures of plasticity across distinct populations of neuronal cell types and sensory inputs.

IOS-1665692 (Brown/Goff) 03/01/2017 – 02/28/2021
National Science Foundation
Cell type specific gene expression differences induced by experience-dependent plasticity

TBD (Goff – Co-PI) 05/01/2017 – 04/30/2018
TargetALS Foundation
Cellular Mechanisms of Cortical Hyperexcitability
This project will explore the cell-type-specific effects of familial ALS mutations on hyperexcitability of cortical neurons, and the common and distinct gene expression changes that evoke this phenotype in ALS mouse models.

JHU Discovery Fund (Goff – PI) 07/01/2017 – 06/30/2018
Johns Hopkins Discovery Fund Synergy Award
Systematic characterization of transcriptional variation in retinal development at single cell resolution
This project aims to comprehensively describe the transcriptional variation and state transitions across the span of mammalian retinal development using single cell RNA-Seq.

Completed Research Support

R01 NS078164 Arlotta(PI) 07/01/2014-06/30/2015
Projection neuron control over interneuron positioning into neocortical circuitry
I developed informatic approach to identify putative cell surface determinants, from differential RNA sequencing data, that facilitate the recruitment and integration of migrating interneurons into specific layers of the developing neocortex.
Role: Postdoctoral Fellow

R01 MH102416 Rinn(PI) 01/01/2014-12/31/2016

Functional Roles of Long Noncoding RNAs During Neuronal Development

I am the co-author of the grant proposal and responsible for experimental design, candidate lincRNA selection, and preliminary characterization of neuronal lincRNAs. However, my involvement with this particular award ended once my postdoctoral fellowship concluded.

Role: Postdoctoral Fellow

0905973 Goff(Fellow) 08/01/2009-7/31/2011

NSF Postdoctoral Research Fellowship in Biology for FY2009 – 0905973

RC1 CA147187 Hart(PI) 03/24/2010-02/28/2012

Genome-wide chromatin modification targeting by endogenous small RNAs

I was the principle author of the grant proposal and responsible for experimental design and integrative analysis of small RNA RIP-Seq data from human embryonic and neural stem cells with thermodynamically favorable target site predictions in the promoters of differentially regulated genes.

Role: Postdoctoral Fellow