



INSIDE THIS ISSUE

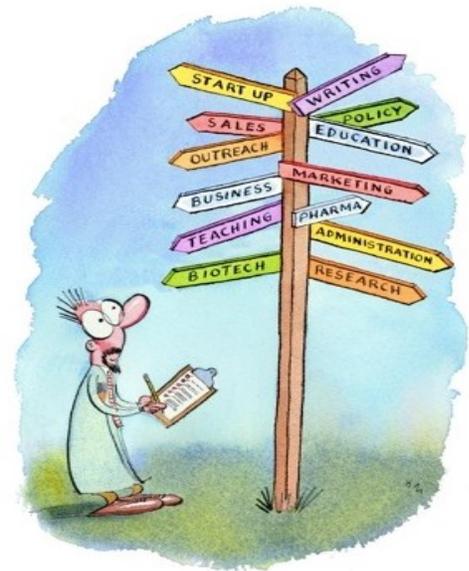
IDP	1
Div-Seq	2
Yoga	3
Featured Alumna	4
Student Publications	4
Faculty Additions	5
GradPlan	5

So you have to complete an Individual Development Plan...

By Megan Duffy

In recent years, completion of an Individual Development Plan (IDP) has become a requirement for all Neuroscience program (NSP) students. As students, we often dread spending time on requirements that seem to keep piling on. However, with the ever-changing funding climate and competitiveness of pursuing tenured academic positions, many students have voiced interest in pursuing non-academic careers, but few have ideas as to what those non-academic career paths are, or what additional training opportunities will help make them more marketable outside of a university setting.

I came into grad school much like many of my peers, with the long-term goal of becoming a PI and running my own lab. I was required to complete an IDP my first semester as a student in the NSP and to my surprise, the Career Fit listed Principal Investigator at the bottom of the list after taking into account my skills, values, and interests. This experience provided a reality check moment with both myself and my mentor to figure out what was best for me long term. As of my last IDP, career areas that fit me best are research administration (non-profit), science policy, and science writing: three options I would have never considered when I started graduate school. I have since taken steps to “get my feet wet” in each of these



areas by interviewing programs managers at foundations, writing a monthly blog for the NIH Ph.D. Student/ Postdoc Blog, attending science policy workshops at conferences, and improving other skills specific to those areas.

Throughout your academic career at MSU, your skills, values and interests will change. While it may seem like a pointless exercise, reconsidering your IDP once a year may help you reach the right career path sooner and point you in a direction that will allow you to be the most prepared for it in the future. Take 15 minutes once a year to do it—your future self will thank you.

Neuroscience Program
 Giltner Hall
 293 Farm Lane, Room 108
 East Lansing, MI 48824

Phone (517) 353-8947
 Webpage:
 neuroscience.msu.edu

Editor: Katie Miller



Div-Seq: Explaining the Importance and Methodology of a Recent Genomic Breakthrough

By Erin McKay

Comparative genetic expression studies are an established and powerful means to identify molecular and cellular processes promoting the physiological and behavioral emergence of many disorders¹. Attention has also been paid to the differences in transcriptomes not only broadly between glial and neuronal cells, but as a means of separating cellular subtypes within these categories^{2,3}. RNA-seq has emerged as the preferred method in this field due to its ability to quantify and measure splice variants of the same gene transcript and high resolution detection of small mRNAs⁴. This experimental approach involves the isolation of messenger RNA from the origin of choice, conversion to a complementary DNA sequence, next-gen sequencing, and comparison of the target sequences to a reference genome which represents the most complete transcriptome profile of the source organism as possible⁵. An interest has developed in using RNA-seq to document the genetic expression changes that underlie the differentiation of neural progenitor cells into specific neuronal and glial subtypes. However, this is difficult to accomplish due to bias encountered during cell sorting procedures that can compromise RNA quality in cell types more resistant to dissociation and weaknesses in strategies to tag newborn neurons^{3,6}. It is precisely these two limitations that Dr. Aviv Regev, Dr. Feng Zhang, and their colleagues cited as motivation for developing Div-seq as a method to track the transcriptional changes of cells responsible for adult neurogenesis⁷.

The Div-seq method combines a dissociation protocol for obtaining solely nucleic mRNA (single-nucleus RNA-seq) and an intraperitoneal injection of EdU (5-ethynyl-2'-deoxyuridine) to label proliferating cells. First, the use of the snRNA-seq method is touted for its ability to produce results that greatly overlap with whole cell transcript levels while avoiding cellular induced stress alternations⁸. Simply, while whole tissue is homogenized and the cell membrane lysed with a detergent the nuclear RNA is protected by the nuclear envelope until the cells are sorted with an appropriate fluorescent label⁸. EdU is used to label adult neural stem cells at the time of its injection into adult mice through its ability as a thymidine analog to be incorporated into DNA during the S-phase of the cell cycle, critically without the need to denature the DNA⁹. The combination of these two methods gave Dr. Regev and her colleagues the ability to trace the transcriptional trajectory of adult neuronal stem cells and their progeny in the hippocampus when sacrificing mice at varying days post injection.

For the analysis of their data they used a complex biclustering on stochastic neighbor embedding (tSNE) of the locally expressed genes they detected. In the simplest sense, after identifying distinct neuronal subregions differentiated by their transcript sequencing

results, they used a principal component analysis to linearize this variability using the genes for which the greatest variance is observed and therefore contributed most to the inter-group distance. This then had to be compressed into a 2 dimensional space from the resulting matrix of plotted cells. They then used an algorithm to scale the pairwise distances between each cell and its closest neighbor in the high dimensional matrix to a 2 dimensional distance with a weighted cosine distance. The cosine distance for each cell to its neighbor on this linear dimension was then used to separate each point. The final biclustering also accounted for subsets of genes in each regional cluster to add a second separation of neuronal and glial subtypes based on differences in genes with highly localized expression patterns revealed by the tSNE mapping.

Why is this so exciting? The researchers were able to document the dynamic transcriptional shifts in adult neural stem cells as they reached their regional and subtype specification over fourteen days. This gives insight into the temporal trajectory and cellular processes each cell type engages in as it matures. They found differences in immature neuron diversity when extending this method to another neurogenic region. This further underscores the need to recognize the regional differences in neuronal maturation and final cellular type between neurogenic regions.

References

- Twine, N. A., Janitz, K., Wilkins, M. R. & Janitz, M. Whole transcriptome sequencing reveals gene expression and splicing differences in brain regions affected by Alzheimer's disease. *PLoS One* **6**, (2011).
- Cahoy, J. D. *et al.* A Transcriptome Database for Astrocytes, Neurons, and Oligodendrocytes: A New Resource for Understanding Brain Development and Function. *J. Neurosci.* **28**, 264–278 (2008).
- Zeisel, A. *et al.* Cell types in the mouse cortex and hippocampus revealed by single-cell RNA-seq. *Science (80-.)*. **347**, 1138–1142 (2015).
- Marguerat, S. & Bähler, J. RNA-seq: From technology to biology. *Cell. Mol. Life Sci.* **67**, 569–579 (2010).
- Wang, Z., Gerstein, M. & Snyder, M. RNA-Seq: a revolutionary tool for transcriptomics. *Nat. Rev. Genet.* **10**, 57–63 (2009).
- Shin, J. *et al.* Single-Cell RNA-Seq with Waterfall Reveals Molecular Cascades underlying Adult Neurogenesis. *Cell Stem Cell* **17**, 360–372 (2015).
- Habib, N. *et al.* Div-Seq: Single-nucleus RNA-Seq reveals dynamics of rare adult newborn neurons. *Science (80-.)*. **353**, 925–928 (2016).
- Krishnaswami, S. R. *et al.* Using single nuclei for RNA-seq to capture the transcriptome of postmortem neurons. *Nat. Protoc.* **11**, 499–524 (2016).
- Buck, S. *et al.* Detection of S-phase cell cycle progression using 5-ethynyl-2'-deoxyuridine incorporation with click chemistry, an alternative to using 5-bromo-2'-deoxyuridine antibodies. *Biotechniques* **44**, 927–929 (2008).



What Yoga Does to Your Brain

By Natosha Mercado

Yoga is well-known as an ancient practice that originated in India over 5,000 years ago. Traditionally, yoga practice emphasizes meditation, physical movements and postures, and controlled breathing techniques. In addition, a major yogic concept is unity between the mind and body; in fact, the term “yoga” primarily means “union” or “integration”. While the physical benefits of regular yoga practice are easily identified (e.g., weight loss, increased flexibility and strength, reduced blood pressure, etc.), its effects on the brain are not often so apparent. The beneficial changes induced in the brain as a result of regular yoga practice are not yet thoroughly understood, however they are certainly intriguing. Below are six examples of the beneficial effects of yoga practice on the brain and behavior, as evidenced by recent scientific investigation.

1. Relieves stress and improves mood

Many are aware that yoga may help relieve stress. Not surprisingly, this finding is increasingly backed by science. For example, in a 2013 study by senior author Dr. Helen Lavretsky and colleagues, caregivers of people with dementia showed reversal of stress-induced genetic changes after practicing yogic meditation for just 12 minutes per day for eight weeks (Black et al., *Psychoneuroendocrinology*, 2013).

2. Improves focus and memory

A study published in 2013 (Gothe et al., *J Phy Act Health*, 2013) found that just one 20-minute session of Hatha yoga significantly improved performance (compared to baseline) on tests of working memory and inhibitory control administered immediately after the yoga session. Interestingly, the participants performed better on these cognitive tasks after yoga than after a bout of aerobic exercise for the same amount of time.

3. Boosts happiness via living in the moment

In an interesting study involving samples from 2,250 adult participants, Harvard psychologists Matthew Killingsworth and Daniel Gilbert revealed that participants reported feeling less happy when they let their minds wander instead of being present in the moment (Killingsworth & Gilbert, *Science*, 2010). Fortunately, yoga and meditation are simple solutions to mind wandering, as they encourage living in the moment by teaching followers to quiet the wandering mind. While a study that directly examines the effects of yoga practice on happiness has yet to be conducted, it can be reasonably inferred that the act of living in the moment, rather through yoga or other means, may increase overall feelings of well-being and happiness.

4. Slows age-related decline

Another study from the lab of Dr. Helen Lavretsky assessed the effects of yoga and meditation on cognition in older adults with mild cognitive impairment (Eyre et al., *J Alzheimers Dis.*, 2016). Participants who participated in a yoga intervention for 12 weeks showed improvement in depression, visuospatial memory, and verbal memory. Indeed, improvement in depression and visuospatial memory scores was greater than that experienced by a control group that underwent memory enhancement training. Another study found that long-term yoga practice appears to slow the typically observed age-related decline in gray matter, specifically in areas of the brain devoted to self-awareness (Villemure et al., *Front Hum Neurosci*, 2015).

5. Improves psychiatric disorders

Yoga has been shown to produce beneficial effects on mental health, particularly in psychiatric disorders such as depression, anxiety, ADHD, schizophrenia, and PTSD (Balasubramaniam et al., *Front. Psychiatry*, 2013; Jindani et al., *Evid Based Complement Alternat Med*, 2015; Stoller et al., *Am J Occup Ther*, 2012). However, little research has been conducted on the mechanisms through which yoga acts to improve mental health; this is a known weakness in the existing literature.

6. Increases levels of GABA and BDNF

Perhaps not surprisingly, yoga practice is associated with increased GABA levels in the brain, a neurotransmitter whose increased activity is known to improve mood and decrease anxiety. In fact, a recent study found that a 12-week yoga intervention was associated with greater mood improvement than a metabolically matched walking exercise, and that yoga was associated with increased thalamic GABA levels (Streeter et al., *J Altern Complement Med*, 2010). Another recent study found that patients with major depression who participated in a yoga intervention showed an increase in serum BDNF (a marker of neuroplasticity) and a concomitant decrease in serum cortisol; they also displayed improvement in depression scores following the intervention (Naveen et al., *Int Rev Psychiatry*, 2016).

The benefits of yoga for brain health and well-being are certain. It's no wonder yoga has been around for thousands of years, transcending time and cultural barriers. In the daily lives of busy Westerners, the mind-body connection is often ignored; too often we allow stress to dominate our lives, impeding our ability to think calmly and clearly, feel at peace, and live happily in the moment. Luckily, yoga is here to save the day. With yoga, one can easily improve the mind-body connection, and consequently one's own physical and psychological well-being. If this evidence is not convincing, I encourage you to begin your own practice – experience the results for yourself!



Nicole Polinski, PhD '16



Nicole K Polinski, PhD

Nicole graduated from the MSU Neuroscience program in May, 2016 and transitioned straight into a position within the scientific team of The Michael J. Fox Foundation (MJFF) in New York City. As a Research Programs Officer at MJFF, her primary responsibilities are related to the MJFF preclinical tools portfolio. MJFF takes an active role in designing and creating important tools for Parkinson's disease research that will expedite novel discoveries and speed a cure for Parkinson's disease. Nicole's role, related to preclinical tools, involves managing projects with contract research organizations to develop and distribute MJFF-sponsored research tools, announcing new tools to the research community, analyzing distribution data for MJFF-supported tools, and updating the MJFF tools catalog webpage. Responsibilities outside of the preclinical tools portfolio include administrative support for the granting database and scientific evaluation of grant pre-proposals submitted to the MJFF funding programs.

Recent Publications

Counts SE, Ikonovic MD, **Mercado N**, Vega IE, Mufson EJ (2016). Biomarkers for the early detection and progression of Alzheimer's disease. *Neurotherapeutics*.

Halievski K, Kemp MQ, Breedlove SM, Miller KE, Jordan CL (2016). Non-cell autonomous regulation of retrograde axonal transport in a SBMA mouse model. *eNeuro*.

Kneysberg A, Collier TJ, Manfredsson FP, Kanaan NM (2016). Quantitative and semi-quantitative measurements of axonal degeneration in tissue and primary neuron cultures. *J Neurosci Methods*.

Lowrance SA, Lonadi A, **McKay E**, Douglas X, Johnson JD (2016). Sympathetic nervous system contributes to enhanced corticosterone levels following chronic stress. *Psychoneuroendocrinology*.

Pfau DR, Hobbs NJ, Breedlove SM, Jordan CL (2016). Sex and laterality differences in medial amygdala neurons and astrocytes of adult mice. *Journal of Comparative Neurology*.

Sinclair EB, Culbert KM, Gradl DR, Richardson KA, Klump KL, Sisk CL. Differential mesocorticolimbic responses to palatable food in binge eating prone and binge eating resistant female rats. *Physiology and Behavior*.

Xu Y, **Halievski K**, Henley CL, Atchison WD, Katsuno M, Adachi H, Sobue G, Breedlove SM, Jordan CL (2016). SBMA motor dysfunction may be due to failed neuromuscular transmission. *Journal of Neuroscience*.



Faculty Additions

MSU's Neuroscience program welcomes the following faculty members:

Amy Arguello, Ph.D. Psychology

Alison Bernstein, Ph.D. Translational Science Molecular Medicine

Jan Brascamp, Ph.D. Psychology

Stacie Demel, D.O./Ph.D. Pharmacology and Toxicology

Julia Ganz, Ph.D. Integrative Biology

Casey Henley, Ph.D. Zoology

Adam Moeser, D.V.M., Ph.D. Large Animal Clinical Science

Jason Moser, Ph.D. Psychology

Fathi Salem, Ph.D. Electrical Engineering and Computer Science

Katy Thakkar, Ph.D. Psychology

Alexa Veenema, Ph.D. Psychology

GradPlan

Earlier this year, an email was sent out to all students and PI's regarding GradPlan. Effective Spring Semester 2017, the University has eliminated all paper forms. All information for Final Degree and Certifications, Record of Guidance Committee and Record of Comprehensive exams will be drawn from the students Grad Plan (<https://gradplan.msu.edu>).

Grad Plan will ask for each student to submit his/her guidance committee and chair and courses they have taken or will take to be counted towards their degree. Without this information, your degree will not be approved by the department or graduate school. It is imperative that each student go into their grad plan and input his/her information.

If you have any questions regarding the process, please do not hesitate to reach out to Julie Delgado, delgadof@msu.edu, to ask questions.

Check Us Out on the Web!

Facebook, Twitter and Blogs:

NSP Website

<https://neuroscience.natsci.msu.edu/>

NSP Facebook

<https://www.facebook.com/msu.neuroscience>

Twitter for NSP

<https://twitter.com/msuneuroscience>

Twitter for NatSci Students

http://twitter.com/msu_preprof

Twitter for SpartaNature

<http://twitter.com/SpartaNature>