The Fellows Newsletter is published monthly by the Office of Education, Division of Intramural Research, National Heart, Lung, and Blood Institute and distributed to NHLBI DIR members to promote the interest of DIR Fellows.

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**From the Director of the Office of Education**
The NHLBI DIR is fully committed to the success of our fellows. This commitment takes many different forms, but includes promoting an environment where fellows can prepare themselves for their chosen careers. Preparation includes scientific training as well as the “soft skills” necessary for success. In my article below, I point out that each fellow must be in charge of their own career development – seeking out the help they need, both scientific and in mentorship. While labs and our outstanding cores can provide the scientific training and resources, there are many other courses and opportunities on campus to learn the other skills necessary for survival. Fellows must also seek out mentorship that suits their needs, whether it comes from within their laboratory or elsewhere. The Office of Education is open to suggestions about how we might increase our activities to better serve your needs. Please contact us directly, or speak to one or more members of (or join) the Fellows Advisory Committee. This is the way in which we can make sure we are serving your needs.

**Who is Responsible for my Career?**
By Herbert M. Geller

The phrase "Every nation has the government it deserves" dates from 19th century France, and has become a current political rallying point. Is the same true at the laboratory level? Does every Fellow get the level of mentoring they deserve? Who decides how much and what kind of mentoring is appropriate and adequate? These are questions that arise very frequently in our laboratory culture.

A mentor’s responsibility is to guide. But in order to have a guide, the fellow needs to determine where they are going! While many NHLBI fellows enter with a clear idea of...
Transcription factors (TFs) often take the role of master regulators of developmental programs that allow for changes in cell fate. They activate or repress gene transcription by direct binding to DNA motifs typically in association with co-factors and chromatin remodelers that facilitate or repress binding of polymerase II. Developmental TFs may become expressed in cell type- or tissue-specific manner and transiently control gene transcription before becoming replaced with another key TF that controls a distinct set of genes. Such TF turnover will facilitate the progression to distinct cell fates that is necessary for differentiation. Yet, other TFs may remain continuously expressed during various stages of differentiation and still must be able to activate a distinct transcription program to allow for distinct cell fate determination. One such TF, GATA3, is a key regulator of T cell development and is expressed across distinct T cell lineages including naïve CD4-positive cells and differentiated T helper cells. Despite the critical function of GATA3 during multiple stages of T cell development, the global scope of GATA3-mediated gene expression and GATA3 binding has remained largely unexplored. In order to understand the cell type-specific functions of GATA3, Wei et al. undertook a genome-wide analysis of GATA3 binding in as many as 10 well-defined lymphocyte lineages by ChIP-seq. In addition, GATA3-dependent changes in gene expression, that resulted from deletion of GATA3 in various GATA3-deficient T cells, were examined.

Genome-wide mapping of GATA3 binding revealed both conserved, as well as cell type-specific binding sites. The number of binding sites was positively correlated with expression levels of GATA3, but even cells with similar number of binding sites exhibited distinct binding patterns, although substantial overlap of binding sites still existed. This indicated that an additional cell type-specific set of factors is involved in recruitment of GATA3. This idea was supported by further motif enrichment analysis of GATA3 binding sites that were identified. The most prevalent binding motif in all cell lines was the zinc-finger motif WGA-TAA followed by additional secondary motifs that included motifs of various other TFs that are associated with T cell development such as Ets, Runx, AP1 and Tcf11. Importantly, the frequency of secondary motif occurrence varied with cell type and suggests that the presence of additional TFs regulate GATA3 recruitment in a cell type-specific manner.

RNA-seq comparison between WT and GATA3 deficient T cells revealed that the greatest number of differentially expressed genes (623) was found in T helper type 2 (Th2) cells and included a number of Th2 specific genes. Among all 90 Th2 specific genes 49% are positively regulated by GATA3 in line with its essential role for Th2 cell differentiation. Interestingly, several Th1 and Th17 specific genes became upregulated as a consequence of GATA3 deletion, indicating that GATA3 not only acts as an activator but also as a repressor, and specifically a repressor of non-Th2 specific genes. Somewhat surprisingly, 133 genes bound by Gata3 were shared between all T cell types examined whereas no differentially expressed genes were shared, clearly illustrating that distinct transcriptomes are present in each cell type, but also that GATA3 binding was not always directly correlated with gene expression. An explanation may be that binding of GATA3 poises some genes for activation or repression at a later stage of differentiation. For example, GATA3 is bound to the locus of Th-POK, a key regulator of CD4+ differentiation, at an early stage, but does not become expressed before later stages of T cell development. Lastly, the authors examined the epigenetic signature around GATA3 binding sites in Th2 cells and found that ablation of GATA3 results in decrease of histone 3 lysine 4-dimethylation at genes associated with positive regulation by GATA3 and decrease of histone 3 lysine 27-trimethylation at genes associated with negative regulation. Even though an overall small number of genes was differentially expressed, histone modification changes took place at a much larger number of GATA3-bound sites, suggesting that changes in histone modifications are a direct result of GATA3 loss and not a consequence of transcriptional changes.

Altogether, the study by Wei et al. has provided important insights into how GATA3-mediated gene regulation and target gene binding at a genome-wide level is able to control T cell development across different T cell lineages.


what they want next, many alter their
goals sometime during their fellowship.
As Yogi Berra once said "If you don't
know where you are going, you will
wind up somewhere else." And as
goals change, an ideal mentor can as-
sist you in both redefining your goals
and identifying the steps you need to
get there. So the first step in a men-
toring relationship is to be able to ar-
ticulate your career goals. Once that's
done, creating an Individual Develop-
ment Plan will allow you to formalize
not only your goals, but also identify
your strengths and weaknesses that
relate to your goals. These can then
be subjects of conversations with your
mentor.

In the ideal situation, your research
supervisor is also your mentor. How-
ever, each lab chief has their own style
and personality, and each Fellow has a
different set of needs such that the lab
chief might not be the best mentor for
a fellow whose needs are outside of
their skill set. In addition, the lab chief
might have a research agenda that
does not coincide with a fellow's career
agenda. The simplest solution is to
find someone who to trust and estab-
lish a relationship with them such that
they can serve as your mentor. This
solution takes away some of the ten-
sion that boils up if a fellow chooses a
career path that is foreign to their su-
pervisor. Another advantage is that
communication about a lab situation
and how it affects the future is less
contentious. In fact, even if you have a
good relationship with your advisor,
having a mentor who is not your su-
pervisor can bring these same benefits.
Through the magic of the internet or
the telephone, this mentor doesn't
even need to be at NIH (but should
have some experience or insight into
how your can achieve your future ca-
reer goals, such as a tie to your home
country).

So what's the best advice? Find a
mentor who is open to helping you,
but keep in mind that you will get the
best mentoring by being pro-active:
know where you want to go, identify
what you need to get there, and find
one (or more) mentors who can assist
in the process. As always, the Office
of Education is available to serve your
needs in this area, so take advantage of
us.

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Science Rotations for NHLBI Fellows

Have you thought about leaving the bench? Are you interested in a career which takes advantage of your scien-
tific and analytical skills? If so, you may be interested in participating in NHLBI DIR Rotations with any of the
organizations listed below. Rotations typically last 3 – 6 months, most often full-time, and are scheduled at the
end of your NHLBI fellowship. Rotations or details can also be arranged for displaced Staff Scientists.

Contact the Office of Education if you are interested.

Fellows Rotation in Extramural Research —
• With the NHLBI Extramural Program to focus on Research Administration or Review

• With any of several National Labs administered by Battelle

• With the NHLBI Office of Technology Transfer

The FASEB Public Policy Research Fellows Program —www.faseb.org
• With the FASEB in Bethesda to focus on Science Policy

Center for Innovative Technology — www.cit.org
• To focus on Business Development with Virginia’s Center for Innovation Technology in Herndon, Virginia

Adjuvant Global Partners — www.adjuvant.com
• To focus on Venture Capital and Business Development in their Bethesda, MD office.

Research!America —www.researchamerica.org
• To focus on Science Policy Research in Alexandria, Virginia
New NHLBI Fellows

Jue Chen, Ph.D., is an IRTA Fellow in the Laboratory of Biochemistry under Dr. Rodney Levine. Dr. Chen earned her Ph.D. in Molecular and Systems Pharmacology from Emory University. She was a lab instructor at Emory University for the Neuroscience Graduate Program in which she taught first year neuroscience graduate students. Dr. Chen is still deciding what her NIH research project will be.

Tiffany Nguyen, Ph.D., is an IRTA Fellow in the Laboratory of Cardiac Physiology under Dr. Tish Murphy. Dr. Nguyen earned her Ph.D. in Pharmacology from the Medical College of Georgia, Augusta, GA. She was previously a Graduate Research Assistant in the Department of Pharmacology and Toxicology at the Medical College of Georgia, and is also a member of the American Society for Pharmacology and Experimental Therapeutics. Dr. Nguyen initial research project is to study the role of S-nitrosylation of cyclophilin D on the regulation of mitochondrial permeability transition pore.

Alicia Evangelista, Ph.D., is an IRTA Fellow in the Laboratory of Cardiac Physiology under Dr. Tish Murphy. Dr. Evangelista earned her Ph.D. in Molecular Medicine from the Boston University School of Medicine. She was the recipient of the Young Investigator Award at the Mechanism of Vasodilatation Meeting in Matsushima, Japan. Dr. Evangelista’s initial research project will be studying the oxidative protein markers of cardioprotection, with a specific focus on differences male and female risk of cardiovascular disease.

Justin Wilson, Ph.D., is an IRTA Fellow in the Laboratory of Kidney and Electrolyte Metabolism under Dr. Mark Knepper. Dr. Wilson earned his Ph.D. in Physiology and Biophysics from Howard University. He has been the recipient of many honors and awards among them being the Jack Cook Scholarship and the FASEB Award to Experimental Biology, Washington DC. Dr. Wilson’s initial project is to develop an antibody for LAT52.

Kenrick Semple, Ph.D., is an IRTA Fellow in the Laboratory of Molecular Immunology under Dr. Lance Pohl. Dr. Semple earned his Ph.D. from Medical Sciences from the University of South Florida, Tampa, Florida. He was previously a Graduate Research Assistant at the University of Maryland, Baltimore, and the H. Lee Moffitt Cancer Center and Research Institute at the University of South Florida, College of Medicine. Dr. Semple is currently focusing on the role of Myeloid-Derived suppressor cells and Regulatory T cells in drug induced allergic reactions.

Juliane Caviston, Ph.D., is an IRTA Fellow in the Laboratory of Cell Biology under Dr. Julie Donaldson. Dr. Caviston earned her Ph.D. in Cell and Molecular Biology from the University of Pennsylvania, School of Medicine, Philadelphia, PA. She was previously a Post Doctoral Trainee at the Fox Chase Cancer Center in Philadelphia. Dr. Caviston’s initial research project will be examining the role of Arf1 in actin remodeling.