Daniel Baker, Fall 2015
Professional Development Assignment Final Report

The main Goals of my Professional Development Assignment were to reintegrate myself back into the day-to-day operations of experimental work in my lab in an effort to increase output and funding of my research program. This was to be accomplished by my participation in the design, execution, and evaluation of experiments to support either ongoing projects, i.e. 1) analysis of the structure, function, and inhibition of sphingosine kinase-1, 2) design, synthesis, and characterization of novel autotaxin inhibitors, 3) evaluation of autotaxin inhibition as an effective co-therapy against neuroblastoma, and 4) analysis of the structure and function of diacylglycerol kinase-beta.

The bulk of my personal time and effort during this PDA was spent on the University of Tennessee Health Science Center in the lab of my postdoctoral research mentor, Gabor Tigyi, Harriet Van Vleet Professor and Chair of the Department of Physiology. The main goals of this interaction were to 1) develop methodology to determine the stability and ultimately the pharmacokinetics and pharmacodynamics of autotaxin inhibitors identified at UM or in collaboration with UTHSC, 2) attempt to identify and characterize a putative endogenous autotaxin inhibitor initially identified during my postdoctoral time at UTHSC, and 3) to collect preliminary data on the utility of autotaxin inhibition toward combination therapy to treat neuroblastoma.

Progress has been made on all of these fronts with additional work and collaborations growing out of my close interactions with UTHSC and St. Jude researchers. In addition, I have developed a consulting relationship with RxBio Inc. that has lead to funding for my graduate student Babatunde Raji. Additional details of each project will be provided if desired, but have been omitted herein for the sake of brevity. I have included sections detailing presentations given during the funding time, grants submitted, manuscripts submitted, as well as manuscripts and grant applications in preparation from data collected.

Presentations given:
2. Pham, T.C. and Baker, D.L., "Analysis of Site Directed Mutants of Diacylglycerol Kinase-Beta by LC-MS/MS and Bisubstrate Kinetics", Joint Meeting of the 71st Southwest and 67th Southeast Regional American Chemical Societies, 2015.
3. Pham, T.C. and Baker, D.L., "Analysis of Site-Directed Mutants of Sphingosine Kinase-1 by LC-MS/MS and Bisubstrate Kinetics", Joint Meeting of the 71st Southwest and 67th Southeast Regional American Chemical Societies, 2015.
Proposals submitted:
1. October, 2015. **Not Funded.** Role: Mentor
   Academic years 2017-2020
   NSF Predoctoral Fellowship: “Application of Mass Spectrometry to the Characterization of Sphingosine Kinase-1 Activity” The goal of this proposal is to secure funding to support graduate student Keri Hannie’s work on the functional analysis of sphingoine kinase-1.
2. October, 2015 (**5th percentile, awaiting Council Meeting for Funding**). Role: Co-PI
   NIH R15 application (Parrill PI)
   4/1/2106-3/31/2019 ($408,733) “GPR88 Ligand Discovery”
3. December 2015. **Funded.** Role: PI
   Contract with RxBio Inc. “Synthetic Optimization of RX-100, RXBio”
   1/1/2016-5/31/2016, $9,045 total costs for 0.5 RA support of Babatunde Raji (including tuition & fees and indirect costs)
   9/1/2016-8/31/2021 ($1,707,118)
   NIH, RO1: “Native and Water-Soluble GPCR in GPR88 Deorphanization”

Manuscripts submitted:

Manuscripts in preparation:
1. “Analysis of the bi-substrate kinetics of sphingosine kinase-1 inhibitors”, Truc Chi T. Pham, Samantha B. Gacasan and Daniel L. Baker (To be submitted to Bioorganic & Medicinal Chemistry, May 2016)
2. “Analysis of site directed mutants of sphingosine kinase-1 by LC-MS/MS and bisubstrate kinetics”, Truc Chi T. Pham, Melanie Sparks and Daniel L. Baker (To be submitted to BMC Biochemistry, May 2016)
3. “New assay development for determining bi-substrate kinetics of diacylglycerol kinase β isoform and effect of selective mutation on its activity”, Truc Chi T. Pham and Daniel L. Baker (To be submitted to BMC Biochemistry, May 2016)

Proposals in preparation:
1. Due June 1, 2016, Elsa U. Pardee Cancer Research Foundation, Research Grant,
   “Neuroblastoma cell line knockouts as tools to study Autotaxin inhibition as a combination therapy approach”
(target budget $100,000 direct costs, 1/1/2017-12/31/2017) Role: PI

2. Due June 25, 2016, NIH R15 (AREA) “Structure function and inhibition of sphingosine kinase-1” (target budget $300,000 direct costs, 4/1/2017-3/31/2020) Role: PI