SUNTRUST

Date: October 6, 2014

To: McKnight Brain Research Foundation Trustees
Henry H. Raattama, Jr. Legal Counsel

From: Melanie Cianciotto

Subject: MBRF Meeting: October 13 – 15, 2014 (Miami, FL)

Enclosed you will find the annual report for the Bioinformatics Core and the annual endowment report from the University of Miami. These reports were received after the meeting package was sent out last week. These materials can also be found as a supplemental package to the trustee meeting package on the secure website.

I look forward to seeing everyone in Miami!

MC/nd

cc: Mike Hill

Enclosures

Evelyn F. McKnight Brain Institute

October 3, 2014

Progress Report for the McKnight Inter-Institutional Bio-Informatics Core

Trustees , McKnight Brain Research Foundation

Dear Trustees:

First of all, on behalf of all the Evelyn F. McKnight Institute Chairs and Directors, thank you for your approval of financial support for establishing a new Evelyn F. McKnight Inter-Institutional Bioinformatics Core.

I am writing to provide the requested First Year Annual Report regarding implementing the new Evelyn F. McKnight Inter-Institutional Bioinformatics Core. The report comprises three sections. The first section describes the mission of the Core. The second section is a summary of scientific progress related to the activities of the Core. The final section is a summary of the expenditures thus far related to establishing and implementing the Core.

Evelyn F. McKnight Brain Institutes Inter-Institutional Bioinformatics Core:

Mission Statement:
The McKnight Brian Research Epigenetics Core will pioneer a comprehensive program to test an epigenetic hypothesis of cognitive aging, working collaboratively with all the Evelyn F. McKnight Brain Institutes. The goal is to establish a shared Inter-Institute resource to provide a catalyst for discoveries in the area of epigenetics of cognitive aging. This is envisioned to be a "core without walls" to provide support for bioinformatic analysis of high-throughput DNA/RNA sequencing and epigenomics, bio-informatics, and cross-correlation of human and animal studies.

Scientific Progress:
Fortunately, we were able to start the Bioinformatics Core project immediately following the approval of the proposed implementation plan by the McKnight Board last year. We have made very strong progress in undertaking the scientific goals of the Epigenetics Initiative, which I will describe in this section.

One long-term goal of the Epigenetics Initiative is to use Next-Generation Sequencing (NGS) and bio-informatics to test the idea that cognitive aging drives altered DNA methylation and altered transcription of known memory-associated genes in the hippocampus. We also will determine if CNS aging drives secondary alterations in two other major epigenetic pathways, i.e. non-coding RNAs (e.g. regulatory miRNAs) and extra-coding RNAs (which are non-polyA-tailed gene products that have recently been discovered to secondarily regulate targeted cytosine methylation at their gene of origin).

Thus the longer-term goal of the initiative is a comprehensive genomic/epigenomic/transcriptomic assessment of the consequences of cognitive aging in the CNS. In analyzing the effects of cognitive aging we will use innovative

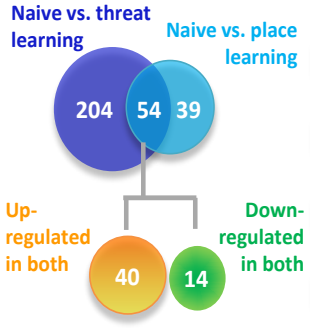
bioinformatics and high-throughput nucleotide sequencing approaches to comprehensively identify four categories of aging-associated modifications and molecules: **Category 1.** We will use Methyl Binding Domain-targeted DNA pull-down plus high-throughput sequencing (MBD-seq) to identify the complete set of hippocampal CA1 neuron genes that have their cytosine methylation altered in response to cognitive aging (i.e. how aging regulates the CA1 CpG methylome). **Category 2.** We will use whole-transcriptome mRNA-targeted high-throughput nucleotide sequencing (mRNA-Seq) to comprehensively identify and quantitate the genes whose transcription are altered (increased or decreased) in association with cognitive aging. **Category 3.** We will use whole-transcriptome small RNA-targeted high-throughput nucleotide sequencing (small RNA-seq) to comprehensively identify and quantitate the regulatory non-coding RNAs (siRNAs, micro-RNAs, snRNAs, piRNAs) whose levels are altered in response to cognitive aging. **Category 4.** We will purify non-polyA-tailed RNAs to selectively identify extra-coding RNAs, which have recently been discovered to auto-regulate targeted cytosine methylation at their gene of origin.

Our **predicted outcome** is that cognitive aging will lead to alterations in cytosine methylation at **memory-associated genes**. We also predict altered transcription of the associated gene product at those differentially methylated genomic loci, be that mRNA, extra-coding RNA, small non-coding RNA, miRNA, piRNA, or long non-coding RNA. We base this prediction on the documented capacity of these epigenetic mechanisms to regulate memory formation in vivo, and on prior results from the Sweatt, Barnes, and Foster labs that cognitive aging is associated with epigenetic and transcriptional alterations in the CNS.

Thus, a first step in this process is to define a set of "**memory-associated genes**" in the hippocampus. Along these lines, in a series of experiments executed in order to generate data supporting this central concept for the Core, the Sweatt lab in consultation with the other MBI groups utilized mRNA-Seq approaches coupled with NGS to demonstrate both our capacity to utilize these methods, and to demonstrate their application for pursuing the initiative. For these first experiments we used mRNA-Seq to identify the genes whose transcription is altered in area CA1 of the hippocampus of adult rats with either novel context exposure (the fear conditioning training box) or contextual fear conditioning itself (novel context plus paired foot-shocks, which we now refer to as *threat learning* using the new convention of LeDoux).

Using this approach we identified three hundred fifty-one (351) genes whose transcription is altered as a result of threat learning, novel place learning, or both – please see Figure 1. Thus we already have identified lists of genes whose transcription is altered in area CA1 by spatial learning and fear conditioning, which for the purposes of this progress report I refer to as "memory-associated genes". While space constraints obviously prohibit listing all these 351 genes and their fold-changes, p values, etc, Figure 1 lists a few representative examples of novel genes identified in this screen. These are in addition to previously identified genes such as *arc, bdnf, igf2, irs2, egr1, fos, CamKII, PDE4, PI3K, PKC epsilon, PKC delta, homer*, etc, that had already been implicated in memory. *(In a preliminary assessment at least nine genes on this list also have been implicated as being relevant to a human learning and memory disorder: Arhgef12, Arhgap15, Grin2A, Dgkb, Nrxn1, Nrg2, CNTNAP2, WFS1, and CaMKII*□).

Figure 1. NGS and Bio-Informatic Analysis Reveal Novel Memory-Associated Genes



Gene	Gene name	Gene function
Gng7	G-protein gamma subunit 7	K^+ channel regulator
Ptpru	Protein tyrosine phosphatase	Growth regulator
Rbm3	RNA-binding protein 3	Translational regulator
St5	Suppressor of tumorigenicity 5	Ras GEF, activator of ERK 1/2
Dusp1	Dual specificity phosphatase 1	ERK inactivator
Rgs14	Regulator of G-protein signaling 14	PKA/MAPK signaling
Wfs1	Wolframin	Human ID-Wolfram Syndrome

Figure 1: These data illustrate our having successfully established the relevant NGS, MBD-Seq, and bio-informatics platforms in the laboratories of the participating Epigenetics Initiative research groups.

We have these data in hand and indeed plan to submit these findings for publication soon, so we have already comprehensively identified, using genome-wide approaches, memory-associated transcriptionally regulated genes from hippocampal area CA1. Our predicted outcome is that some or all

of these 351 genes will be subject to transcriptional, cytosine-methylation-dependent, or non-coding RNA-dependent regulation in association with cognitive aging. Simply put, genome-wide NGS and bioinformatics approaches will allow us to comprehensively test 351 specific hypotheses in parallel, in this framework each hypothesis being that a given memory-associated gene is epigenetically targeted through cognitive aging-driven active DNA demethylation in hippocampal area CA1. While a positive result (i.e. cognitive aging-driven alteration of the memory gene methylation or transcription) will not prove that these mechanism are the only factor that drives cognitive aging *per se*, these experiments will allow defining the overlap of genes whose transcription change with context or threat memory formation with those that are subject to age-dependent regulation.

Overall a major goal of the Epigenetics Initiative is to comprehensively identify *both those genes that are subject to aging-driven transcriptional regulation* and the *subset of those genes that are regulated in various types of memory formation that decline with aging*. Furthermore, genes not in those overlapping sets will allow the characterization of memory genes that are not good candidates as targets for age-dependent regulation and aging-regulated genes that are not high priority targets as mediating aging-associated memory alterations. Toward this end, in the next phase of the project, which is currently underway as a collaboration among the Arizona, Florida, and UAB groups, we are executing experiments to define the complete set of genes whose transcription is altered in cognitively normal aged rats and rats exhibiting age-associated cognitive decline. Toward this end, the Florida and Arizona groups have already generated the tissue samples to allow us collaboratively to directly compare hippocampal samples from cognitively normal and cognitively impaired aged animals, by independently generating aged cohorts and using behavioral assessments to identify those with cognitive decline. In the next few weeks the Florida, UAB, and Arizona groups will all in parallel begin to undertake NGS to identify age-related transcriptional changes in these samples. This will then allow us as a group to define the transcriptomic changes, in a genome-wide fashion, that occur with cognitive aging.

Deliverables Related to Establishing the Core Infrastructure

The first deliverable proposed was the establishment of an inter-institutionally available core infrastructure through which all four McKnight Institutes (Miami, UF, UAB, and Arizona) will be able to obtain state-of-the-art bio-informatics analysis and next-generation sequencing capacity. This will allow the McKnight Institutes as a group to achieve and sustain a leading role in the emerging new discipline of neuroepigenetics, specifically as related to cognitive aging.

In Terms of Specific Deliverables, the Evelyn F. McKnight Inter-Institute Bio-informatics Core proposed to provide seven services (see Figure 2 for a broad overview):

1. High-throughput epigenomic and mRNA sequencing analysis and technical support. Currently, some sequencing capability is available at each of the institutes.
2. Top-flight bio-informatics, for both routine analysis and novel analytical techniques.
3. Shared data storage and rapid transfer of data and analyses between and among the four participating MBI's.
4. Supercomputer time for bio-informatic analysis.
5. Coordinated tissue sharing, both human and animal.
6. Facilitated collection of animal data regarding transcriptional dysregulation in aging, allowing focused hypotheses for human experiments to be developed.
7. Information on common standardized protocols in all these domains, for consistency across MBI groups.

I will provide a brief update on progress for each of these seven deliverables in the following section.

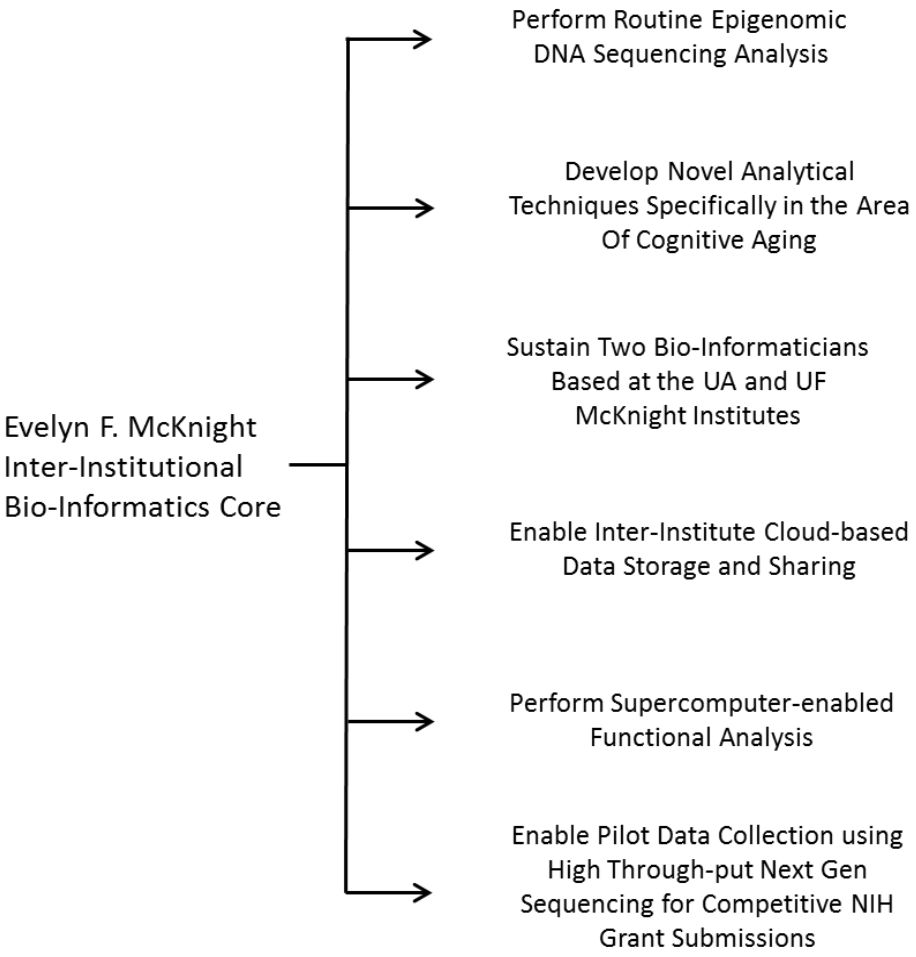


Figure 2

1. High-throughput epigenomic and mRNA sequencing analysis and technical support.

Sequencing capability is available at each of the institutes. UF and UA are developing advanced new methodologies to apply to next-generation sequencing as follows:

UF:

1) Equipment: We have the new Ion Chef up and running. The Ion Chef is used to make the RNA libraries.
2) Sequence Protocol Development:

2a) We have tested two protocols for RNA enrichment.

RiboMinus technology is designed to enrich the whole spectrum of RNA transcripts by selectively depleting ribosomal RNA molecules (rRNA), regardless of their polyadenylation status or the presence of of a 5'-cap structure. This technique has the advantage of preserving long noncoding RNA, but gives a low yield of total RNA. Traditionally, enrichment poly(A)+ RNAs has been used, which provides a more abundant yield of RNA, but does not preserve noncoding RNAs that are likely important for epigenetic regulation of transcription. Both techniques tend to correlate for relative expression of RNA.

2b) Ultra-small sample/Single-cell sequencing.

We have developed and successfully validated the protocol for RNA-seq sequencing from single hippocampal CA1 neurons, interneurons from mice and rat as well as single IPSP cells from human. Currently, any

cell (>4 mkm cell body diameter, 2-5 pg of starting total RNA) can be used for RNA-seq tests. As a part of the optimization of the protocol we have experimentally determined the cost-efficient sequence coverage sufficient for unbiased genome-scale profiling of individual neurons as function of aging and neuroplasticity tests. All protocols are reliable and can be scaled up to process 96 cells per run. Current implementation of these protocols reduced cost for single-cell/ultra-small sample profiling down to $60/sample. There are pilot development of protocols which can further reduce the cost.

2c) Ultra-small sample/Single-cell Methylome profiling.

We have developed and successfully validated bisulfite sequencing protocol to perform unbiased methylome profiling from ultra-small amount of starting material with single base resolution. The current validated limits are about a hundred pg and can be applied to samples of a couple of dozen mammalian neurons. In model organisms with larger neurons we successfully tested the same protocol on single cells probing both interneurons and motor neurons. This protocols are essential for the overall success of the project since they allows to probe specific populations of cells within morphologically and functionally defined cell populations in the brain.

ARIZONA:

1) Equipment: The laboratories at TGen have 6 Illumina HiSeq2500 sequencers available for use for the projects associated with the Epigenetics Core. TGen also has one sample prep robot for the hands-off creation of DNA and RNA sequencing libraries.
2) Sequence Protocol Development: TGen has optimized all necessary RNA sequencing library prep approaches

2a) rRNA depletion: The RiboMinus rRNA depletion approach is optimized. Importantly we have optimized this for single cell and ultra-low input samples.

2b) Ultra-small sample/Single-cell sequencing. TGen has developed and optimized RNA-Sequencing library preparation approaches for ultra-low input samples as well as single cell samples. The ultra-low input samples (down to 10pg of total RNA input) were optimized on laser capture microdissected material as well as FACS collected cells. This creates the possibility for whole transcriptome sequencing of several manners of collected material – lysate collected in an electrophysiology pipet, cells sorted by FACS, and/or cells collected from fresh frozen animal brain tissue.

2. Top-flight bio-informatics, for both routine analysis and novel analytical techniques.
3. Shared data storage and rapid transfer of data and analyses between and among the four participating MBI's.
4. Supercomputer time for bio-informatic analysis.

Because these three categories are completely inter-related, I have described progress in these areas in a single section.

UF:

Bioinformatic Core:

We have developed a scalable parallel pipeline, the autonomics pipeline, to assemble and annotate (blast nr/swissprot, quantification, pfam, GO & KEGG) and map the output from our sequencing machines. The pipeline now runs on the University of Florida's HiPerGator supercomputer (cluster).

Currently tested the pipeline output is limited by the number of processing units used for development (128 PEs). Staying within these computational limits, we can run 12 assemblies concurrently.

We have also tested the pipeline with 1280 PEs and found that it does in fact scale up to run over 100 assemblies concurrently which can be used for virtually all practical means within the ongoing epigenomic initiative. The pipeline software runs as daemon which looks in the database every 10 minutes to see what needs to be submitted

for running on the cluster. The daemon also monitors the status of all submitted jobs, updates the database with any status changes, and submits jobs as needed to the cluster.

However, we would like to increase our computational investment even more than this (see below). As a result it would provide virtually overnight feedback to individual investigators from even large-scale sequencing project. With sufficient resources, the autonomics pipeline will scale up to complete the assembly and annotation/mapping of ~ 100 subprojects in ~2 weeks (with the possible exception of blast nr in non-traditional model organisms would be used).

Next steps. Protocols are under development to provide automatic uploading the sequencing data to the community databases and visualized both annotation and mapping data. Specifically, we focus on analysis of DNA methylation data following bisulfite sequencing. The majority of the software that runs the autonomics pipeline is written in object oriented Python. The code interacts with the MySQL database via SQLAlchemy.

UF Hipergator2 hardware is expected to be upgraded with 24,000 PEs with the opportunity for our core to use up 10,000 PEs (or more if needed). Such opportunities would allow to perform nearly real-time annotation and mapping which can be integrated with functional/plasticity and aging tests using the same group of animals. There are opportunities at the core to reserve and use required storage needs for the high-throughput analyses of multiple projects (budget for the appropriate amount storage is $125/TB/year).

ARIZONA:

Bioinformatic Capabilities and Advances: Dr. Huentelman's lab at TGen includes a team of entirely informatics-focused scientists who work alongside biologists on a daily basis. The TGen team leverages optimized scalable analysis pipelines and powerful supercomputing resources to generate the analysis of deep transcriptome (>50 million unique counts) data in less than one day. Quality control and assurance metrics as well as annotation of the transcripts is automated as well. TGen's compute capacity is approximately 1 million compute hours each month.

Shared data storage and rapid data transfer is established and achieved using novel data "torrenting" approaches (using BitTorrent Sync). This results in near real-time secure sharing of data as it is generated. It is user friendly and simple to utilize.

In short, the analytical pipelines, compute needs, and data storage approaches are optimized and in place.

5. Coordinated tissue sharing, both human and animal.

6. Facilitated collection of animal data regarding transcriptional dysregulation in aging, allowing focused hypotheses for human experiments to be developed.

These two areas are integrated, so as with 2, 3 and 4, I have grouped them together.

UF:

We have run 10 aged and 5 young through the behavioral battery. The probe trial for acquisition looks good with considerable variability in cognitive function for aged animals (see Fig 3). In addition, our data matches that of the AZ group. Finally, we performed methylation analysis on sub-regions of hippocampus to develop and test methylation protocols. We have sent samples to AL and are awaiting results.

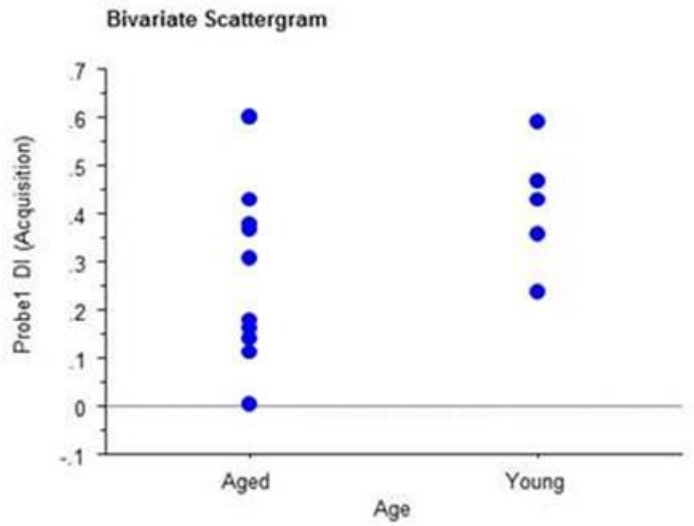


Figure 3

ARIZONA

We tested 22 rats (15 old [21mo], 7 young [6mo])on the "Foster version" (Guidi et al., 2014)of the Morris swim task that tests spatial memory and hippocampal function. The distribution of behavioral performance in our rats is shown in Figure 4.

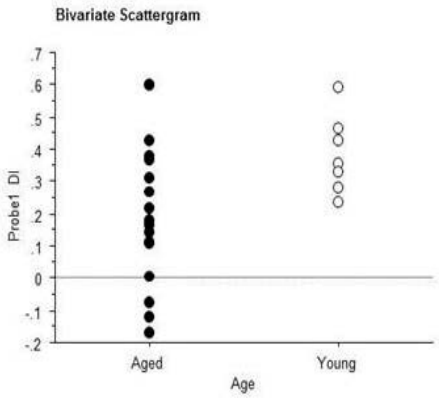


Figure 4

Young Rat 9780 (DI = 0.33)
Old Rat 9782 (DI = 0.27) – good old rat
Old Rat 9781 (DI = - 0.166) – bad old rat

We chose 1 young rat from these animals with 'intermediate behavior', 1 old rat with behavior comparable to the young rat, and 1 old rat whose behavior was 2 standard deviations below these other animals. In addition, the 3 rats chosen were also tested on a spontaneous object recognition task, and a temporal recognition task prior to sacrifice. To extract the tissue from these animals, rats were anesthetized with isoflurane prior to decapitation, brains were quickly extracted, briefly rinsed in cold saline, placed on a microdissection metal plate on ice and hemisected. The right hemisphere was dissected first for "RNA" analyses, in this order: hippocampus was extracted first and placed ventral side up using a microspatula the dentate gyrus was teased free of the CA subregion along the hippocampal fissure. Further transection into CA1 and CA3 subregions was performed. Each subregion was placed in a 1.5 □l microfuge tube and quick frozen in liquid nitrogen. The amygdala was extracted next and placed in a separate microfuge tube and placed in liquid nitrogen. The left hemisphere was dissected after the right was finished, exactly as for the right hemisphere and this tissue will be used for "DNA" analyses. The approximate regions dissected are as illustrated in Figure 5. All samples have been sent to Alabama.

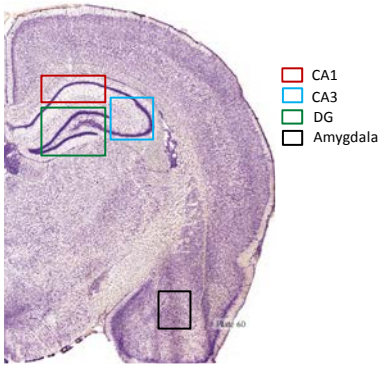


Figure 5

7. Information on common standardized protocols in all these domains, for consistency across MBI groups.

UF:

It does not appear the Ion Proton can be used for examining DNA methylation but it is cost efficient for complementary RNA-seq tests from the same samples. Therefore, we have secured the use of the Illumina NextSeq 500/ Illumina2500 equipment from a core facility at the University of Florida. Currently, we are testing the Model based Analysis of Bisulfite Sequencing (MOABS) for analysis of DNA methylation.

ARIZONA:

Currently both sequencing and analysis sites are working within their preferred domains and using their preferred analytical approaches. However, the common thread is the use of the exact same experimental samples for analysis. That means that at the conclusion of this first pilot experiment both sites can be compared and contrasted easily. This is important because it will provide clarity to all other MBI investigators as to the strengths and weaknesses of each sequencing + analytical approach. At that point we can begin to select standardized protocols for consistency with the full knowledge of what those protocols can and cannot detect, sequence, and measure. Wet laboratory and analytical standardization is a goal that will commence after the completion of the initial pilot study.

Financial Update:

The trustees of the MBRF have approved a block grant of $300,000 annually for two years. The business plan approved by the McKnight Board split out the budget so that the UF and UA components were separate, in case there was a need for their phased implementation at the two sites.

The funds were and will be deposited in the Inter-Institutional Bioinformatics Account , and the Heads of the McKnight Brian Institute at the University of Florida (Dr. Ashizawa), the University of Arizona (Dr. Barnes) have the authority to receive funds to be disbursed from the Inter-Institutional Bioinformatics Account. As overall organizer of the project, Dr. Sweatt at UAB also has authority to approve disbursement of funds if necessary.

It is important to emphasize that while the equipment infrastructure and services will be based at the University of Florida and the University of Arizona, and thus the accounting and costs disbursement will be administered through those two entities, all four MBI's can utilize the Core and all have equal access to its services.

Evelyn F. McKnight Inter-Institute Bio-informatics Core

University of Arizona Expenses as of September 2014

Personnel:
Full-time Bio-informatician:
Role: data analysis and computational methods development

$52,000

Animal Costs:
Rats - Purchase and Per Diems

$1,000

University of AZ total expenditures to date: $53,000

University of Florida Expenses as of September 2014

Supplies:
Sequencing reagents, prep kits, etc.

$18,700

Animal Costs:
Rats - Purchase and Per Diems

$2,300

University of Florida total expenditures to date: $21,000

Notes on Financials:

1) Bioinformatician: The bioinformatician in Arizona is responsible for the processing of the projects allotted to Arizona's infrastructure. This will include data sharing. Additionally, the bioinformatician in Arizona will provide expert analytical approaches to the data including the creation of publication quality figures to illustrate the key findings of the work.

2) Animals: Includes young and old animals to be given a behavioral test battery before sacrifice for the cognitive aging experiments,

3) Supplies: Includes animal costs, the reagents used for preparing the brain tissue, and sequencing costs. The reagents used for preparing the brain tissue, laser capture supplies, sequencing costs and the costs of scaling up data sharing platforms are included in this category. The infrastructure costs for cloud-hosting the data files and the data sharing, to insure the rapid transfer of very large quantities of data between the Core and the participating investigators physically located at the various MBI's also fall in this category.

Summary and closing comments:

Once again, we thank the Board members for your support of this Initiative. In implementing the Epigenetics Initiative I feel we have been productive, focused, collaborative, and exceptionally innovative. I believe the Initiative has identified a novel area that will both propel new discoveries in cognitive aging and produce a high-profile scientific focal point with which the McKnight "brand" will be identified nationally and internationally. The discovery of innovative therapeutic approaches to cognitive enhancement in aging is a strong, viable target outcome for the initiative.

Sincerely,

David Sweatt,
On behalf of all the participating Investigators

UHealth
UNIVERSITY OF MIAMI HEALTH SYSTEM
Neurology

UNIVERSITY OF MIAMI
MILLER SCHOOL
of MEDICINE

September 30, 2014

J. Lee Dockery, M.D.
Michael L. Dockery, M.D.
Nina Ellenbogen Raim, M.D., J.D.
Gene G. Ryerson, M.D.
Robert M. Wah, M.D.
The Evelyn F. McKnight Brain Research Foundation
SunTrust Bank
Mail Code FL-ORL-2100
200 S. Orange Ave., 10th Floor SOAB
Orlando, FL 32801

Dear Trustees:

On behalf of the University of Miami Leonard M. Miller School of Medicine, please find enclosed the growth pool annual investment report for the fiscal year ending May 31, 2014 prepared by Colonial Consulting. Per the terms of our endowment agreement (section 5.3) the University of Miami forwards this report to you annually. I have also included the market value analysis for the endowment for the same fiscal period.

Should you have any questions, please feel free to contact Susan Fox-Rosellini at (305) 243-5198.

Thank you for your continued support and collaboration in our efforts.

Warmest regards, Thanks so much.

Ralph Sacco, M.D., M.S.

Enclosures

cc: Clinton Wright, M.D.
Ms. Rebecca Lee, MATFL
Ms. Marsha Kegley
Ms. Ileana Nunez
Ms. Melanie A. Cianciotto
Henry H. Raattama, Jr., Esq.

Department of Neurology
P.O. Box 016960 | Miami, FL 33101
Ph: 305-243-6732

McKnight053114
Summary

Evelyn F. McKnight Brain Institute
at the Miller School of Medicine
Market Value Analysis
5/31/2014

McKnight Contribution	$5,000,000
UM Match	5,050,913
Transfers from Other University Funds	1,362,153
Investment Return	4,100,534
Distributions for Spending	(3,414,257)
5/31/14 Endowment Balance	$12,099,343
Unmatched Balance	$0

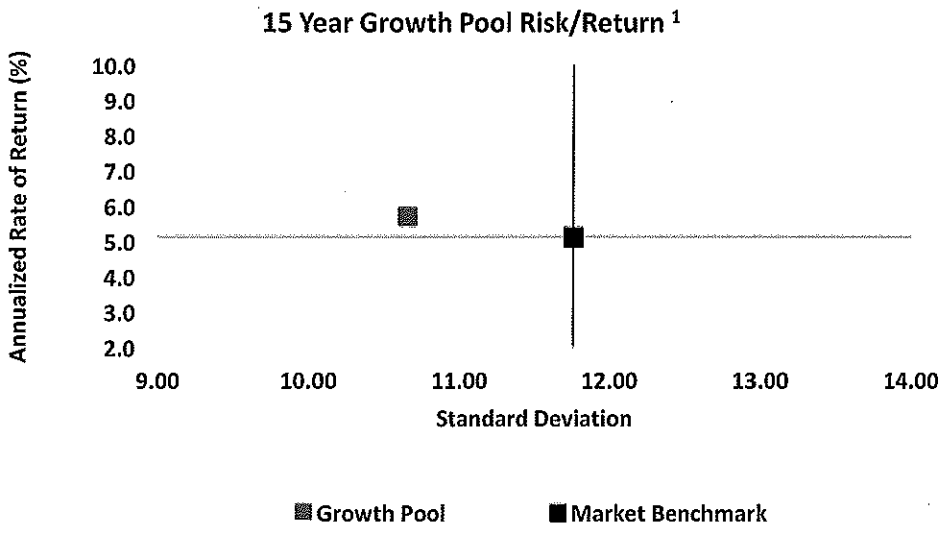
McKnight053114
Annual

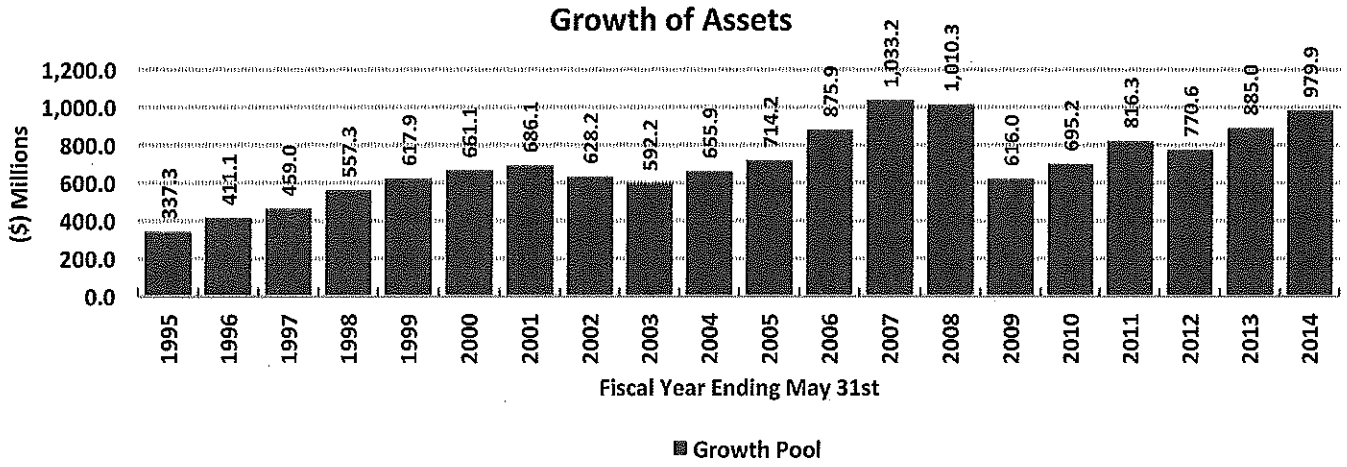
University of Miami
Evelyn F. McKnight Brain Institute
Summary Analysis at Market Value
June 1, 2013 - May 31, 2014

	Evelyn F. McKnight 262080	F.Peterson/ McKnight 262293	Schoninger Professorship in Neurology 262453	Schoninger Neuropsychology Clinic 262454	Other sources	Total
Beginning Balance at Market, 6/1/13	$7,596,171	$1,054,690	$0	$0		$8,650,861
Investment Return	922,302	129,307	32,367	80,916		1,164,891
Distributions for Spending	(331,200)	(47,023)	0	0	($110,085)	(488,308)
Transfers from other University funds	141,766				110,085	251,851
Matching gifts	(979,951)	0	1,000,000	2,500,000		2,520,049
Ending Balance at Market, 5/31/14	$7,349,087	$1,136,974	$1,032,367	$2,580,916	$0	$12,099,343

University of Miami - All Managed Assets
Performance Periods Ending: May 31, 2014

Total Returns (Periods Greater Than 1 Year are Annualized)						
Growth Pool	Inception	1 yr	3 yr	5 yr	7 yr	10 yr
Growth Pool Total Composite	12/31/1990	12.9	8.0	12.1	3.9	6.6
Growth Pool Market Benchmark[1]	12/31/1990	14.1	8.7	12.4	3.9	6.4
Value (+/-)		-1.2	-0.7	-0.4	0.0	0.2





1. The Market Benchmark is a weighted average of market indices reflecting the Growth Pool's strategic allocation through time.

University of Miami
Manager Structure - Market Values and Allocations
As of May 31, 2014

		Growth Pool	
Manager	Asset Class	$Mil	%
GAMCO Investors	US Midcap Value Equity	34.8	3.6%
Tukman Capital	US Large Cap Core Equity	43.1	4.4%
Adage Capital	US Large Cap Core Equity	88.3	9.0%
Brown Brothers Harriman	US Large Cap Core Equity	17.0	1.7%
McClain Value Management	US All Cap Value Equity	25.2	2.6%
Artisan Small Cap	US Small Cap Growth Equity	24.7	2.5%
DFA Small Cap Value [1]	US Small Cap Value Equity	30.0	3.1%
Silchester International	Non-US DM/EM Value Equity	70.5	7.2%
Marathon Asset Management	Non-US DM Core Equity	52.8	5.4%
Gryphon International	Non-US DM/EM Growth Equity	58.5	6.0%
DFA Emerging Value [1]	Non-US EM Equity	24.9	2.5%
Westwood Global	Non-US EM Equity	37.3	3.8%
Vanguard Emerging Markets[1]	Non-US EM Equity	6.9	0.7%
Davidson Kempner	Event Arbitrage	44.5	4.5%
Watershed Capital	Event Arbitrage	36.9	3.8%
Oaktree Capital	High Yield Bonds	20.4	2.1%
Regiment Capital	High Yield Bonds	29.7	3.0%
Wellington Diversified Hedge	Real Assets	23.9	2.4%
Cambrian CamCap Resources	Real Assets	22.6	2.3%
WCP Real Estate Strategies	Real Estate	0.2	0.0%
Viking Global Equities III	Long/Short	32.0	3.3%
Wellington Archipelago	Long/Short	28.5	2.9%
Tiger Consumer	Long/Short	31.6	3.2%
Glenview Capital	Long/Short	0.1	0.0%
Addison Clark	Long/Short	28.4	2.9%
Lansdowne Global Financials	Long/Short	8.6	0.9%
Brenner West	Long/Short	5.3	0.5%
TIFF Partners IV	Private Equity	8.6	0.9%
TIFF Partners V	Private Equity	1.0	0.1%
TIFF PEP 2006	Private Equity	2.7	0.3%
TIFF PEP 2007	Private Equity	3.5	0.4%
TIFF PEP 2008	Private Equity	7.8	0.8%
OCM Principal Opportunities	Private Equity	3.0	0.3%
Denham Commodity Fund V	Private Equity	3.4	0.3%
Clayton, Dubilier & Rice Fund IX	Private Equity	1.4	0.1%

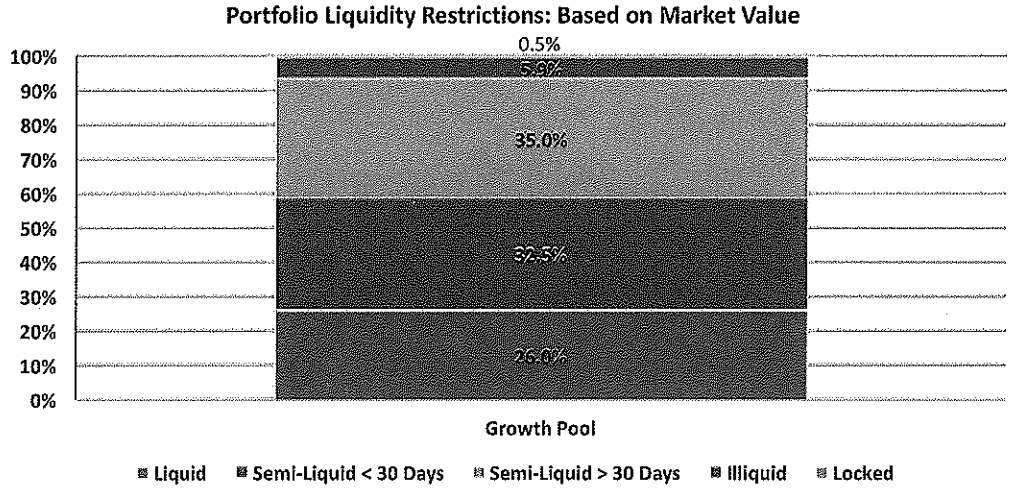
1. Index or enhanced index strategies

Continued on Next Page

University of Miami
Manager Structure - Market Values and Allocations
As of May 31, 2014

		Growth Pool	
Manager	Asset Class	$Mil	%
Parmenter Realty III	Real Estate	2.5	0.3%
WCP Real Estate Fund I	Real Estate	1.7	0.2%
WCP Real Estate Fund II	Real Estate	5.4	0.6%
SRI Nine REIT	Real Estate	8.4	0.9%
Metropolitan Real Estate	Real Estate	1.7	0.2%
LBA Realty	Real Estate	6.3	0.6%
Warburg Energy	Energy	NA	NA
PIMCO Total Return	Aggregate Bonds	31.5	3.2%
Western Asset Management	Aggregate Bonds	NA	NA
Colchester Global Bonds	Global Bonds	46.9	4.8%
Vanguard Inflation Protected[1]	US TIPS	14.3	1.5%
Cash Clearing Account		2.9	0.3%
Total Managed Assets		979.9	100.0%

Allocation to Index or Enhanced Index Strategies	
	Growth Pool
% of Total:	7.8%
% of Domestic Equity:	11.4%



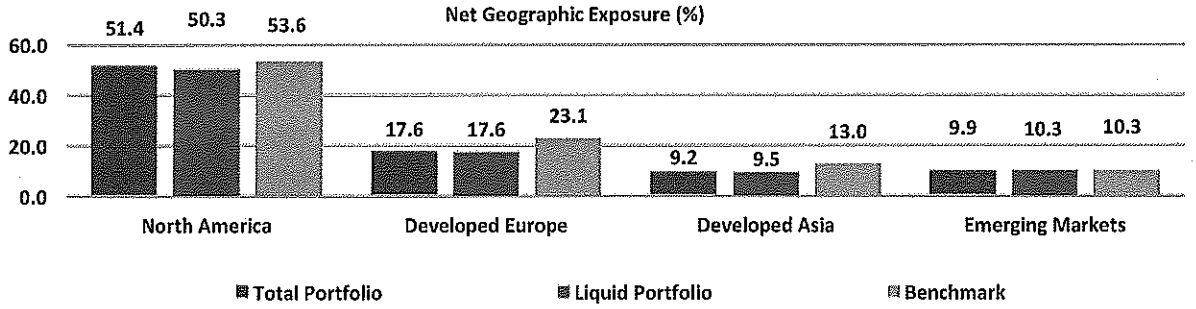
University of Miami Growth Pool

Portfolio Exposures [1]

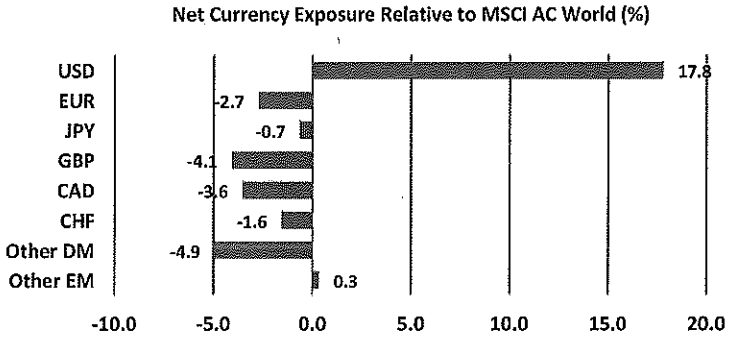
Data as of June 30, 2014

Investment Type Exposure	Total Portfolio				Liquid Portfolio			
	Long (%)	Short (%)	Gross (%)	Net (%)	Long (%)	Short (%)	Gross (%)	Net (%)
Public Equity	76.0	-11.9	87.9	64.1	80.6	-12.7	93.3	68.0
Equity Derivatives/ETFs	0.2	-1.0	1.2	-0.8	0.2	-1.0	1.3	-0.8
Credit	13.0	-1.0	14.0	12.0	13.8	-1.1	14.9	12.7
Credit Derivatives/ETFs	1.0	-4.1	5.1	-3.1	1.0	-4.4	5.4	-3.3
Interest Rates	6.0	0.0	6.0	6.0	6.4	0.0	6.4	6.4
Commodities	0.8	-0.1	0.9	0.7	0.9	-0.1	1.0	0.7
Real Estate	2.6	0.0	2.6	2.6	0.0	0.0	0.0	0.0
Private Equity	3.1	0.0	3.1	3.1	0.0	0.0	0.0	0.0
Currencies	0.0	-0.2	0.2	-0.2	0.0	-0.3	0.3	-0.3
Cash & Equivalents/Other [3]	1.5	0.0	1.5	1.5	1.6	0.0	1.6	1.6
Total Portfolio	104.3	-18.4	122.7	85.9	104.6	-19.6	124.1	85.0

Geographic Exposure	Total Portfolio				Liquid Portfolio			
	Long (%)	Short (%)	Gross (%)	Net (%)	Long (%)	Short (%)	Gross (%)	Net (%)
North America	62.1	-10.6	72.7	51.4	61.4	-11.1	72.5	50.3
Developed Europe	19.5	-1.9	21.3	17.6	19.5	-1.9	21.4	17.6
Developed Asia	9.7	-0.5	10.3	9.2	10.0	-0.6	10.6	9.5
Emerging Markets	10.4	-0.5	10.9	9.9	10.8	-0.5	11.3	10.3



Net Currency Exposure	Liquid (%)
US Dollar (USD)	70.0
Euro (EUR)	6.5
Japanese Yen (JPY)	7.0
British Pound (GBP)	3.2
Canadian Dollar (CAD)	0.4
Swiss Franc (CHF)	1.8
Developed Markets	2.7
Emerging Markets	8.1



1. Nominal and delta-adjusted exposures are used where possible to reflect non-linearity in portfolio positioning.
2. Exposure data includes that most recently available for each investment.
   "As of" dates may vary based on the timing of each manager's reporting.
3. The Other category includes: Preferreds, Convertibles, and Trade Claims.

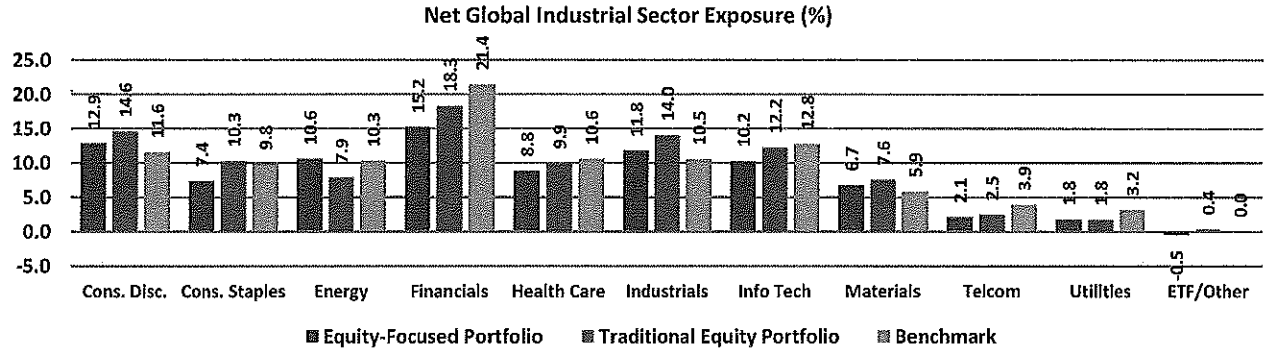
University of Miami Growth Pool

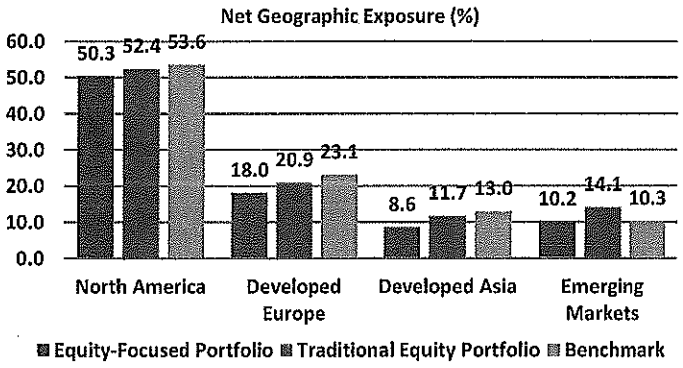
Equity Portfolio Exposures [1,2]

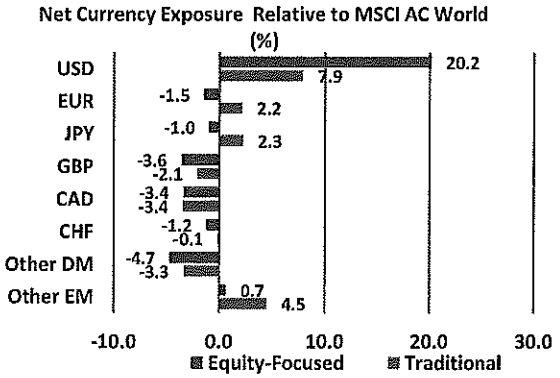
Data as of June 30, 2014

Global Industrial Sector Exposure	Equity-Focused Portfolio				Traditional Equity Portfolio			
	Long (%)	Short (%)	Gross (%)	Net (%)	Long (%)	Short (%)	Gross (%)	Net (%)
Consumer Discretionary	16.3	-3.4	19.7	12.9	15.7	-1.1	16.8	14.6
Consumer Staples	8.8	-1.5	10.3	7.4	11.2	-0.9	12.1	10.3
Energy	11.8	-1.2	12.9	10.6	8.7	-0.8	9.6	7.9
Financials	17.5	-2.3	19.8	15.2	18.5	-0.2	18.6	18.3
Health Care	10.7	-1.8	12.5	8.8	11.1	-1.1	12.2	9.9
Industrials	13.4	-1.6	15.1	11.8	15.2	-1.2	16.4	14.0
Information Technology	12.4	-2.2	14.6	10.2	12.6	-0.4	13.0	12.2
Materials	7.5	-0.8	8.4	6.7	8.3	-0.7	8.9	7.6
Telecom Services	2.2	-0.1	2.4	2.1	2.5	0.0	2.5	2.5
Utilities	2.7	-0.9	3.7	1.8	3.0	-1.3	4.3	1.8
ETF/Other	1.0	-1.5	2.5	-0.5	1.0	-0.7	1.7	0.4
Total Portfolio	104.4	-17.4	121.8	87.0	107.8	-8.3	116.1	99.5

Geographic Exposure	Equity-Focused Portfolio				Traditional Equity Portfolio			
	Long (%)	Short (%)	Gross (%)	Net (%)	Long (%)	Short (%)	Gross (%)	Net (%)
North America	62.2	-11.9	74.1	50.3	58.4	-6.0	64.4	52.4
Developed Europe	19.9	-1.9	21.8	18.0	21.8	-0.9	22.8	20.9
Developed Asia	9.2	-0.6	9.9	8.6	11.7	0.0	11.7	11.7
Emerging Markets	10.7	-0.6	11.3	10.2	14.3	-0.2	14.5	14.1







1. Nominal and delta-adjusted exposures are used where possible to reflect non-linearity in portfolio positioning.
2. Equity-Focused includes long-only, beta-one, and long/short equity portfolios where applicable. Traditional includes long-only and beta-one equity portfolios where applicable.
3. Exposure data includes that most recently available for each investment. "As of" dates may vary based on the timing of each manager's reporting.

University of Miami - Growth Pool

Inception to Date Performance vs. Relevant Benchmark(s)

Periods Ending - May 31, 2014

Net of Fees

Total Returns (%) - Annualized if Greater Than 1 Year		Value Added (+/-)		
US Large/Mid Cap Equity	ROR	Primary	Secondary [1]	Years
GAMCO Investors (01/01/91)	13.5	0.1	3.1	23.4
Russell Mid Cap Value	13.4			23.4
Custom Style Benchmark	10.4			23.4
Tukman Capital (06/30/98)	5.7	0.4	3.0	15.9
S&P 500	5.3			15.9
Custom Style Benchmark	2.7			15.9
Adage Capital (06/30/04)	11.6	4.0	NA	9.9
S&P 500	7.6			9.9
Brown Brothers Harriman (4/30/13)	17.3	-4.0	NA	1.1
S&P 500	21.3			1.1
McClain Value (07/31/10)	13.6	-4.2	NA	3.8
Russell 3000 Value	17.8			3.8
US Small Cap Equity				
Artisan Small Cap Growth (5/31/13)	13.1	-3.6	NA	1.0
Russell 2000 Growth	16.7			1.0
DFA Small Cap Value (09/30/98)	12.5	2.6	4.9	15.7
Russell 2000 Value	10.0			15.7
Custom Style Benchmark	7.6			15.7
Non-US Developed Equity				
Silchester International (06/30/05)	10.4	4.8	NA	8.9
MSCI EAFE Value	5.6			8.9
Gryphon International (03/31/05)	6.2	-0.1	NA	9.2
MSCI EAFE Growth	6.3			9.2
Marathon Asset Management (08/31/09)	11.3	2.3	NA	4.8
MSCI EAFE Index	8.9			4.8
Non-US Emerging Equity				
DFA Emerging Value (11/30/07)	-0.6	-0.1	NA	6.5
MSCI Emerging Free	-0.5			6.5
Westwood Global Investors (10/31/08)	17.8	4.0	NA	5.6
MSCI Emerging Free	13.8			5.6
Vanguard Emerging Markets (4/30/12)	2.3	-0.4	NA	2.1
MSCI Emerging Free	2.7			2.1
Event Arbitrage				
Davidson Kempner (10/01/93)	9.9	-0.6	NA	20.7
HFRI Event Driven	10.4			20.7
Watershed Capital (12/31/07)	3.7	-0.9	NA	6.4
HFRI Event Driven	4.6			6.4

1. NA: Not Applicable

University of Miami - Growth Pool

Inception to Date Performance vs. Relevant Benchmark(s)

Periods Ending - May 31, 2014

Net of Fees

Total Returns (%) - Annualized if Greater Than 1 Year		Value Added (+/-)		
Real Assets	ROR	Primary	Secondary [1]	Years
Wellington Diversified Inflation Hedges (08/31/06)	2.9	5.0	NA	7.8
DJ UBS Commodity	-2.1			7.8
Cambrian CamCap Resources (9/30/11)	3.5	5.2	NA	2.7
DJ UBS Commodity	-1.7			2.7
High Yield Bonds				
Oak Tree (12/31/98)	7.2	-0.3	NA	15.4
Merrill Lynch High Yield	7.5			15.4
Regiment Capital (06/30/07)	5.9	-2.9	NA	6.9
Merrill Lynch High Yield	8.8			6.9
Long/Short Equity				
Viking Global Equities III (11/30/10)	14.4	-3.0	9.5	3.5
S&P 500	17.5			3.5
HFRI Equity Hedged	4.9			3.5
Wellington Archipelago (11/30/04)	8.4	0.8	3.3	9.5
S&P 500	7.6			9.5
HFRI Equity Hedged	5.1			9.5
Tiger Consumer (02/28/06)	5.6	-1.7	1.7	8.3
S&P 500	7.3			8.3
HFRI Equity Hedged	3.9			8.3
Addison Clark (03/31/08)	5.9	-2.8	2.5	6.2
S&P 500	8.6			6.2
HFRI Equity Hedged	3.4			6.2
Lansdowne Global Financials (3/31/12)	6.6	-11.4	-0.7	2.2
S&P 500	18.0			2.2
HFRI Equity Hedged	7.4			2.2
Brenner West (11/30/13)	6.3	-1.4	3.2	0.5
S&P 500	7.6			0.5
HFRI Equity Hedged	3.0			0.5
Fixed Income				
Pimco Total Return (11/30/13)	2.3	-1.0	NA	0.5
Barclays Capital Aggregate	3.3			0.5
Colchester Global Bond (12/31/09)	5.3	2.4	NA	4.4
Citigroup World Government Bond	2.9			4.4
Vanguard Inflation Protected Securities (03/31/10)	5.1	-0.1	NA	4.2
Barclays Capital US TIPS	5.2			4.2

1. NA: Not Applicable