From Conception to Issuance: Using Analytic Tools to Inform the Development of a Funding Opportunity in Social and Behavioral Epigenetics Research

Farah Bader (FIC), Tanya Agurs-Collins (NCI), Lena Diaw (NHLBI), Rao Divi (NCI), Jonathan King (NIH/NIA), Rosalind King (NICHD), Enid Light (NIMH/FIC), Somdat Mahabir (NCI),Valerie Maholmes (NICHD), Paige McDonald (NCI), Kathleen Michels (FIC), Matthew Reilly (NIAAA), Robert Riddle (NINDS), Erica Spotts (OBSSR), Lois Tully (NINR), Fred Tyson (NIEHS), Naimah Weinberg (NIDA), Linda Weglicki (NINR)

Abstract:

*The process for developing the OppNet-led initiative **Research on the Role of Epigenetics in Social, Behavioral, Environmental, and Biological Relationships throughout the Life-Span and Across Generations (R21) RFA-TW-13-002** has shown to be a useful case study for performing a gap analysis of the NIH portfolio in epigenetics and behavior. Using NIH-wide and Institute specific grants databases (eg. QVR, eSPA, PARIS) in combination with the commercial text mining/visualization tool, IN-SPIRE, a literature review, and input from NIH subject matter experts, an environmental scan of active epigenetics-relevant funded NIH projects led to the identification and verification of 147 projects relevant to epigenetics and behavior. Sub-analysis of this dataset involved a breakdown of the financial investment for each of the 13 ICs, the number of pertinent grants by IC, and the grant mechanisms utilized in each case. These grants were then fed into IN-SPIRE, a text mining tool that randomly generated de novo category clusters. Each cluster was visualized using correlation tools and other mapping outputs within IN-SPIRE. The correlation tools demonstrated that while there were numerous NIH projects related to drug abuse, memory and learning, neurodevelopment and maternal stress, there were few studies on the role of social and behavioral influences on the epigenome or vice versa and few grants on neurodegenerative disorders and diseases. Furthermore, there was a paucity of projects on the role of epigenetics trans-generationally or throughout the life course. Likewise, there was a dearth of studies on normal behavior and sensory processes, gender influences and differences, and on the basic mechanisms underlying personality and temperament. The following areas were also understudied: the intersection of sensation and perception with behavior; the role of epigenomics in feedback loops and interactions; the interplay between environmental, physiological, and immunological factors with social, economic and behavioral constructs and the role of microbiome interactions. Results from this analysis were presented to the OppNet Coordinating and Steering Committees and the concept for the development of a new funding opportunity to address these needs was approved. This funding opportunity has since been issued and has yielded 60 responsive applications, thereby enhancing the breadth and depth of NIH research in epigenetics and behavior. Employing a variety of databases, methodologies, and portfolio analysis tools in this process (rather than relying on a single tool or database with limited capabilities) has been valuable. Additionally, using a trans-collaborative NIH approach ensures that we are able to capture and adequately characterize all relevant on-going epigenetics projects and prevent duplicative efforts by other Institutes, so that we may confidently pave a path for defining future research directions.*

Objective:

We sought to characterize NIH-funded epigenetics research as it relates to behavioral research. The intent was to determine if there were areas of science in this burgeoning field that were emerging priorities but currently understudied and whether there was a need to develop a funding opportunity to address these gaps in research.

Methods

Text Search: We used QVR and eSPA to conduct a text search of "epigenetics and behavior" which generated a list of 39 projects. Ten additional projects were selected by member IC program officials, for a total of 49 projects that were used as a template by the Office of Portfolio Analysis staff to create fingerprint in RCDC. Following this, QVR Carts were constructed for each of the 49 individual projects and combined to form one cohesive project listing of 1,426 projects from 2007-2012. All unique, active grants as of September 9, 2012 were included as were fellowships and sub-projects. SBIR, training (T32), instrumentation and conference grants were excluded.

Screening Methods: Next, projects that overlapped with the RCDC categories on basic behavioral and social sciences were selected. This list was screened for terms such as "epigenetics", "methylation", "acetylation", "CpG islands", "histones" and "behaviors" to generate a list of 212 projects. NIMH used their own internal database (PARIS) to provide a listing of ten additional projects, yielding a total of 222 projects. Two team members then reviewed the abstracts and specific aims of the 222 projects to determine whether a specific project should be included or excluded. The final list was comprised of 147 validated projects relevant to epigenetics behavior funded by 13 ICs.

Content Analysis: The abstracts and specific aims from the 147 projects were then fed into the text mining, analysis, and visualization software, IN-SPIRE. The distribution of funding opportunities by the specific IC associated with each of the 147 projects was also analyzed. IN-SPIRE's scientific correlation tool was used to examine the relationship between various scientific topics and the number of grants funded by various ICs. The scientific focus of the NIH portfolio was compared to a bibliometrics study by Lester *et. al* (2011) of behavioral constructs and their relationships to epigenetic studies to determine gap areas.

Figure 1. Epigenetics-Behavior Grants by IC (Total Dollar Investments from 2007-2012)

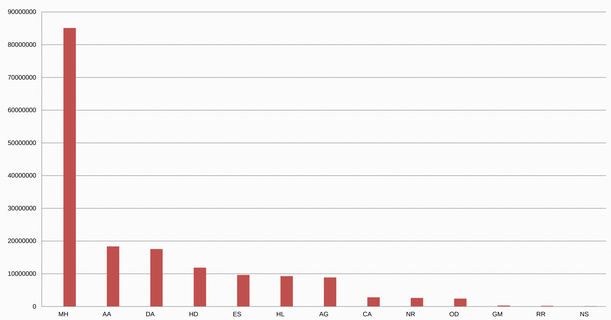

Figure 2. Epigenetics and Behavior Projects by Number of Grants Per IC (2007-2012)

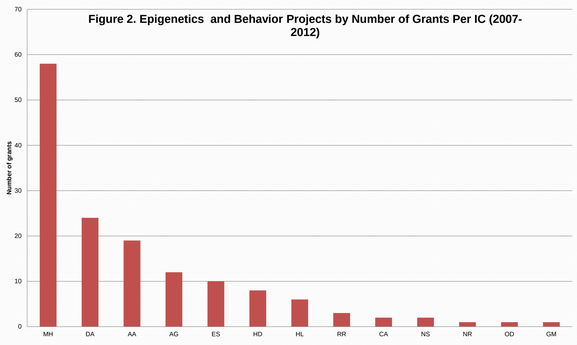

Figure 3. Distribution of Scientific Topics by IC with Epigenetics-Behavior Portfolio (Correlation matrix in IN-SPIRE)

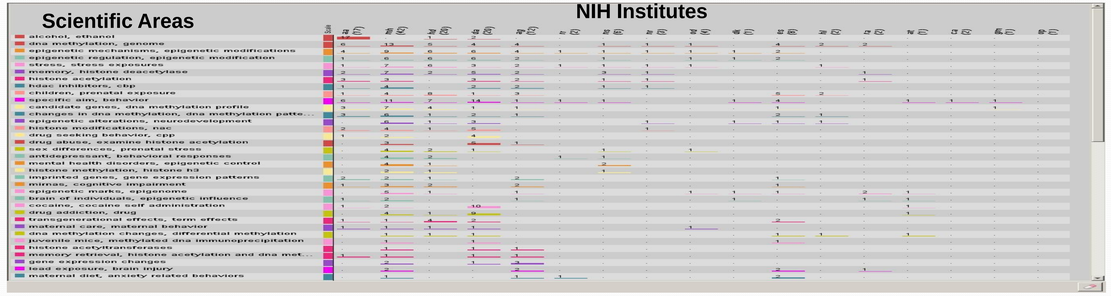

Figure 4. Theme view clustering of grants from the epigenetic-behavior portfolio

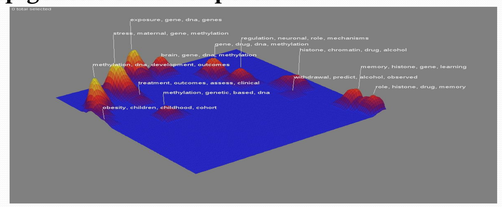

Table 1. Epigenetics Gap Area Identified

Normal behavior and sensory processes
Gender influences and differences
Basic Mechanisms underlying personality and temperament
Socio-behavioral interactions and processes
Role of epigenomics in feedback loops and interactions
Environmental, physiological, and immunological interplay with Social, economic, and behavior constructs
Microbiome interactions
Trans-generational effects and interactions

Results:

- NIMH had the largest investment and the highest quantity of grants, followed by NIDA and NIAAA, and other neuroscience institutes.
- 33% of the portfolio utilized human subjects research while 67% used animal subjects.
- Cohort studies with children were sparse.
- Most of the awards were research mechanisms, but a few fellowships, cooperative agreements, career development and subprojects awards were also identified. The rest of the mechanisms are scattered.
- As of September 2012, only 4 NIH funding opportunities specifically targeted epigenetics research (data not shown).
- In Figure 3 for neuroscience related categories, there were 35 grants on substance abuse, 14 neurodevelopment grants, 29 grants on memory, 9 grants on cognitive impairment, 33 grants on various stress and parenting topics, and 10 maternal care grants.
- There were relatively few projects examining the role of epigenetics trans-generationally and throughout the life course, or examining the role of epigenetics in neurodegenerative disorders and diseases.
- After reviewing the literature related to epigenetics and behavior, and consulting with subject matter experts in our concept development team, we formulated the priority areas mentioned in Table 1 above using the framework constructed by the 2011 Lester *et. al* study to originate these areas.

Conclusions:

This exercise demonstrates the utility of a unique methodology for exploring a specific scientific landscape and determining the need for new funding opportunities. By using the knowledge gleaned from subject matter experts, the Office of Portfolio Analysis, and various NIH-wide and IC-specific databases, we were able to develop a list of grants that accurately reflect the NIH's investments in epigenetics and behavioral research despite the challenge of ensuring that the various data sources maintained a consistent definition of the topic. The use of the text mining tool, "IN-SPIRE," facilitated a 'deeper dive' into the scientific content of the awards, which enabled us to select themes for our FOA and to ascertain the type of studies we would later request from our applicants. The resulting trans-collaborative effort across 13 Institutes and Centers has produced 60 responsive applications, many of which are addressing the understudied gap areas that we identified, including trans-generational impacts, socio-behavioral constructs, temperament, and immunological interactions. However, more work remains to be done in terms of stimulating research on the topic of socio-behavioral epigenetics, as the number of funding opportunities in this area has not increased following the publication of the FOA: Research on the Role of Epigenetics in Social, Behavioral, and Biological Relationships throughout the Lifespan and Across Generations (R21).

References:

Lester, BM, Tronick E, Nestler, E, Abel T, Kosofsky B, Kuzawa CW, Marsit CJ, Maze I, Meaney MJ, Monteggia LM, Reul JM, Skuse DH, Sweatt JD, Wood MA. Behavioral epigenetics. Ann NY Acad Sci. 2011 May; 1226: 14-3

Acknowledgements:

OppNet Concept Team