Ancestral influences on descendant generations: a case study using the olfactory system in rodents

Brian Dias, PhD.

Assistant Professor, Emory University School of Medicine
Department of Psychiatry and Behavioral Sciences
Yerkes National Primate Research Center

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Standing on the shoulders of helpful giants...

THANK YOU

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- Debiec, Sullivan, Francis Lee
- Milad (K & M), Graham
- Rick Richardson
- Russo, Dietz, Nestler
- Roth, Sweatt
- Tottenham
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Social Media Statement
Epigenetics

Reality and Promises of Epigenetics

Reality

Unknowns

G x E

Stressful experiences interact with the genome

Promises

Do positive environments interact with the genome

Manipulating gene expression in sperm and egg
G x E
BRIEF REPORT

Transgenerational Effects of Posttraumatic Stress Disorder in Babies of Mothers Exposed to the World Trade Center Attacks during Pregnancy

Rachel Yehuda, Stephanie Mulherin Engel, Sarah R. Brand, Jonathan Seckl, Sue M. Marcus, and Gertrud S. Berkowitz
Physiological markers of anxiety are increased in children of abused mothers

Tanja Jovanovic, ¹ Ami Smith, ¹ Asante Kamkwalala, ¹ James Poole, ¹
Tara Samples, ¹, ⁵ Seth D. Norrholm, ¹, ² Kerry J. Ressler, ¹, ³, ⁴ and Bekh Bradley ¹, ²
Ancestral environments affect biology of descendants

Cardiovascular and diabetes mortality determined by nutrition during parents’ and grandparents’ slow growth period

G Kaati¹, LO Bygren*,¹ and S Edvinsson²
How do descendants inherit information from ancestors?
Information about ancestral nutritional environment can be inherited by descendants

**LETTER**

Chronic high-fat diet in fathers programs β-cell dysfunction in female rat offspring

Sheau-Fang Ng¹, Ruby C. Y. Lin², D. Ross Laybutt³, Romain Barres⁴, Julie A. Owens⁵ & Margaret J. Morris¹

Nature, 2010

**Paternally Induced Transgenerational Environmental Reprogramming of Metabolic Gene Expression in Mammals**

Benjamin R. Carone,¹,¹⁰ Lucas Fauquier,¹,¹⁰ Naomi Habib,⁴,⁵,¹⁰ Jeremy M. Shea,¹,¹⁰ Caroline E. Hart,¹ Ruowang Li,² Christoph Bock,⁶,⁷ Chengjian Li,¹ Hongcang Gu,⁶ Phillip D. Zamore,¹,³ Alexander Meissner,⁶,⁷ Zhiping Weng,² Hans A. Hofmann,⁶ Nir Friedman,⁴,⁹ and Oliver J. Rando¹,*

Cell, 2010
Ancestral environment prior to conception affects behavior of descendant generations

F0 female rats exposed to fungicide – Mate preference affected in F3 generation

Transgenerational epigenetic imprints on mate preference

David Crews*, Andrea C. Gore‡‡, Timothy S. Hsu§, Nygerma L. Dangleben‡, Michael Spinetta§, Timothy Schallert§, Matthew D. Anway¶, and Michael K. Skinner¶

PNAS, 2007

Social defeat of F0 male mice – F1 generation showed depression-like behavior

Paternal Transmission of Stress-Induced Pathologies

David M. Dietz, Quincey LaPlant, Emily L. Watts, Georgia E. Hodes, Scott J. Russo, Jian Feng, Ronald S. Oosting, Vincent Vialou, and Eric J. Nestler

Biol Psychiatry, 2011

Also: Franklin (Mansuy), Roth (Sweatt), Rodgers (Bale) and others
All olfactory sensory neurons (OSNs) in the nose expressing a single odorant receptor, project to a discrete region called a glomerulus in the olfactory bulb.
M71-LacZ transgenic mice
M71 receptor (*Olfr151*) expressing neurons stained blue

Acetophenone activates M71 OSNs (Bozza et al., 2002). Propanol does not.
Condition F0 generation with Odor (Odor+Shock)

Mate

Test descendant generations
How do descendants inherit information from ancestors?

Condition F0 generation with Odor (Odor+Shock)

Test descendant generations
F0 olfactory fear conditioning results in F1 generation being sensitive to F0 conditioned odor

n = 9-13

Dias & Ressler, Nat Neurosci (2014)
F0 olfactory fear conditioning results in enhanced neuroanatomical representation in F1 generation

Dias & Ressler, Nat Neurosci (2014)
Like Father – Like Son: How?

Transmitted vs Inherited
Inheritance of structure and function

1. IVF
2. F2 generation
1. Cross-fostering
M71 glomeruli in the olfactory bulbs of $F_1$ males are larger when F0 conditioning occurs with Acetophenone (Offspring derived from F0-sperm via IVF)


n = 16-19

Thank you: Emory Transgenic Mouse Core
Like Father – Like Son: Inherited BUT How?

olympicjokes.com
Epigenetic mechanisms may explain enhanced transcription of the M71 odorant receptor
*Olfr151 (M71) is hypo-methylated in sperm of F0-Ace males*

Inheritance of olfactory sensitivity & neuroanatomy from ancestral generation

Modified version from commentary by Moshe Syzef
Nat Neurosci (2014)
Reality and Promises of Epigenetics for Animal Science

Reality

G x E

Stressful experiences interact with the genome
What can we do with this information?

How is there cross-talk between environment and germ cells?

How do genetic loci marked by salient environmental cues escape epigenetic reprogramming?


Reik, Milekic (Gingrich), Smith (Mill), Radford (Ferguson-Smith)
Sources of information transfer in sperm

1. **Nose to gametes**: Exosomes containing ncRNA (miRNA, piRNA, tRFs)
   
   Active project: Profiling circulating exosomes and sperm RNA (*Commercial*)

2. **What is going on in the sperm**: Focus on methylation

   Active project: Genome-wide 5hmC and 5mC analysis (*Collab: Peng Jin*)
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Promises

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