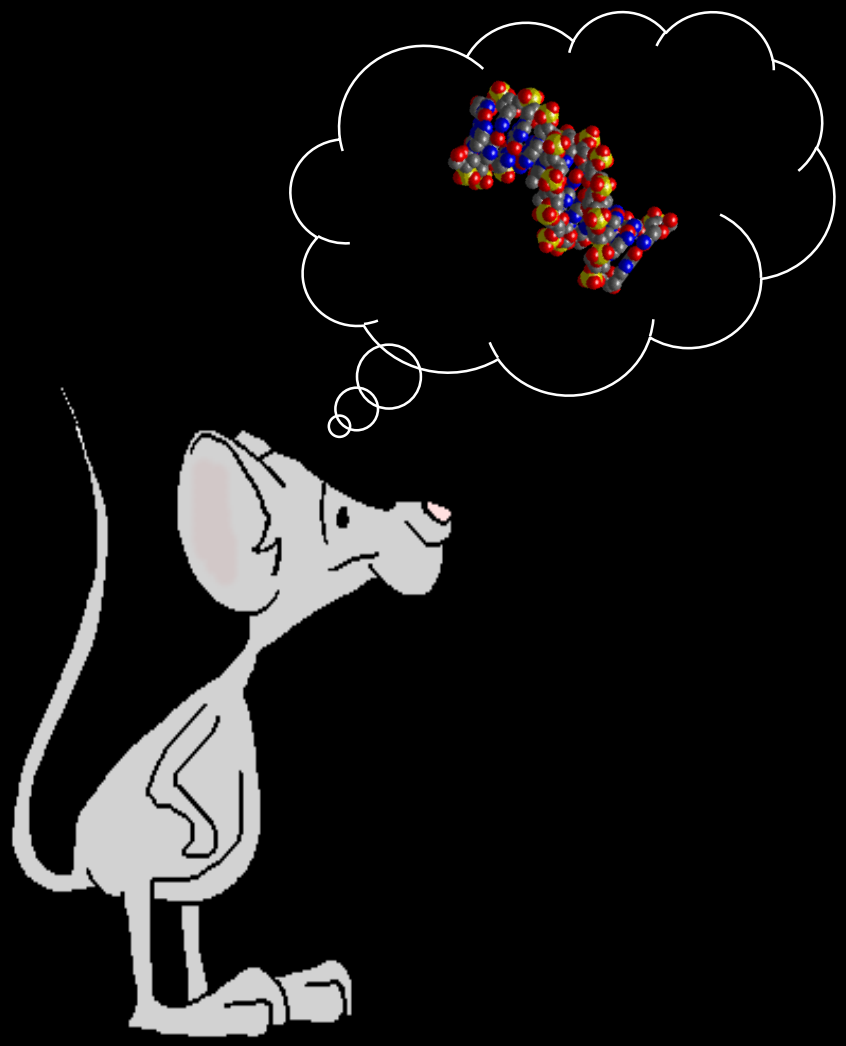
*McKnight Inter-Institutional Meeting*

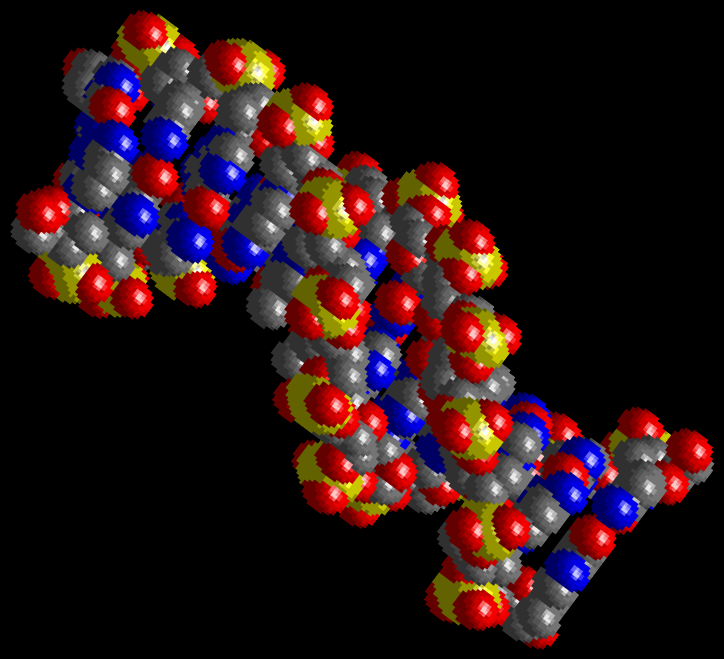
April 2015

# Epigenomics Core – Memory Genes & Extra-Coding RNAs

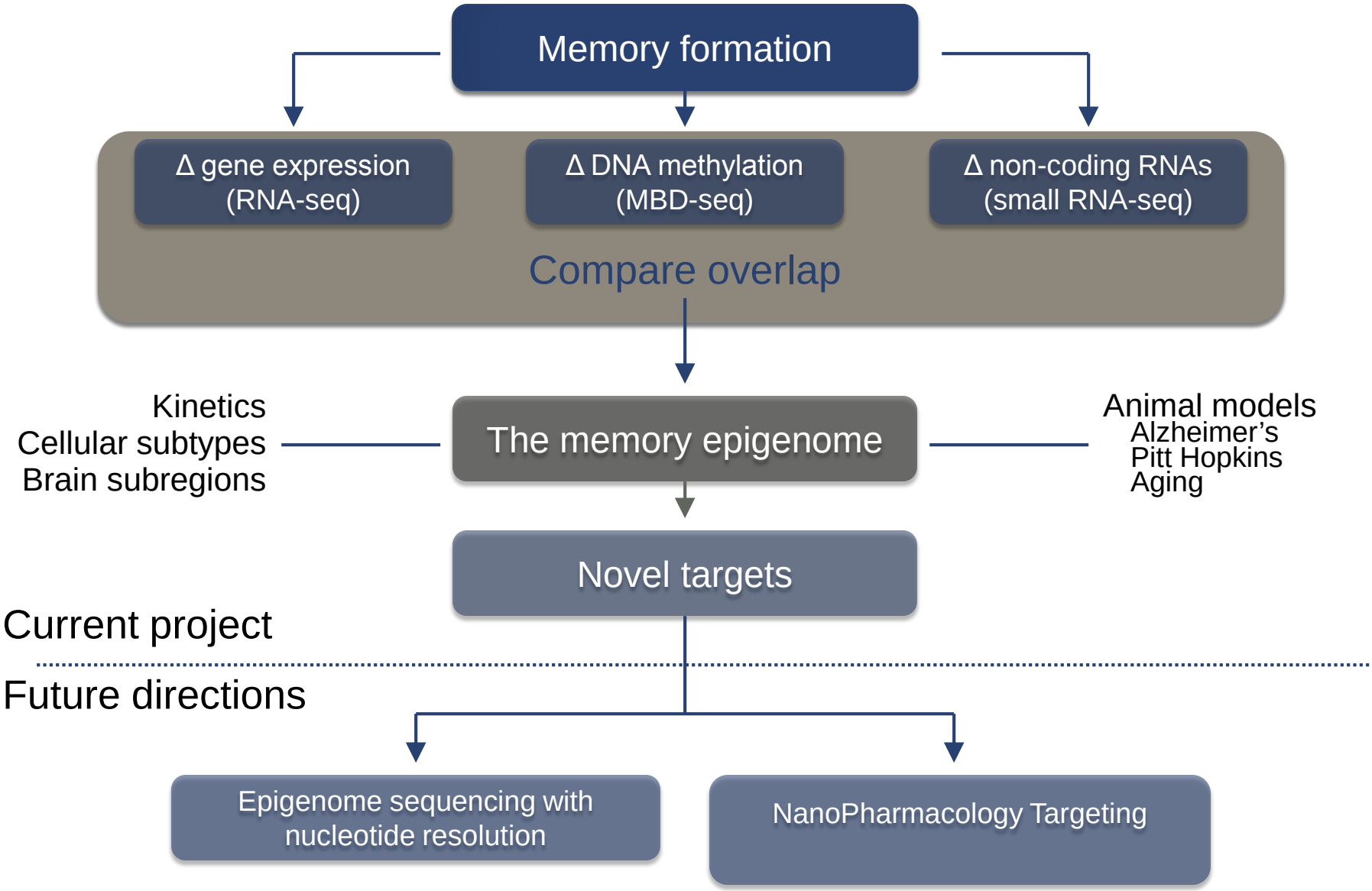
**J. David Sweatt**
Dept of Neurobiology
McKnight Brain Institute
UAB School of Medicine

# The Molecular Basis of Memory

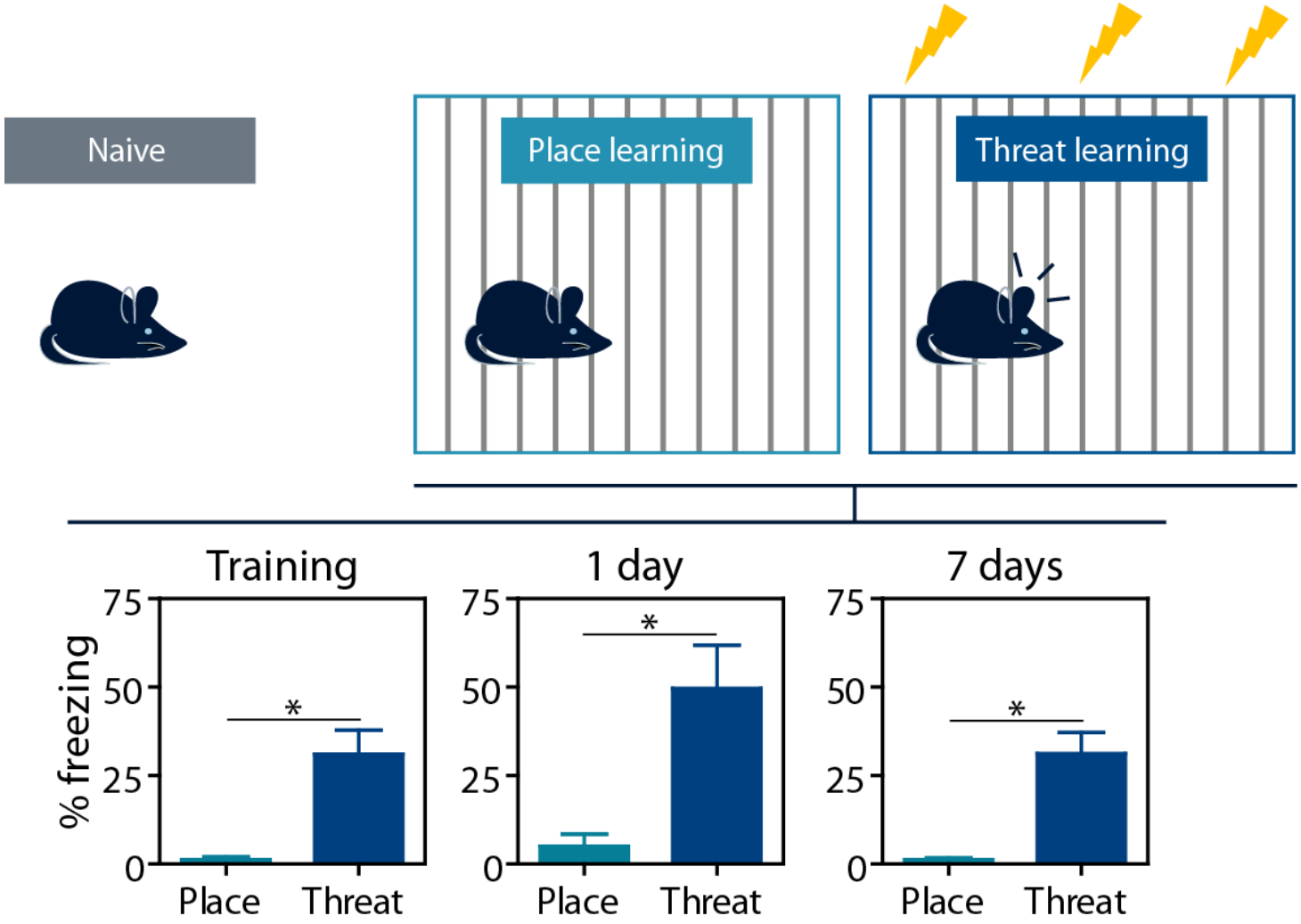




# » EPIGENOME-WIDE TARGET IDENTIFICATION FOR COGNITIVE NANOPHARMACOLOGY



# » MAPPING THE MEMORY TRANSCIPTOME: THREAT LEARNING



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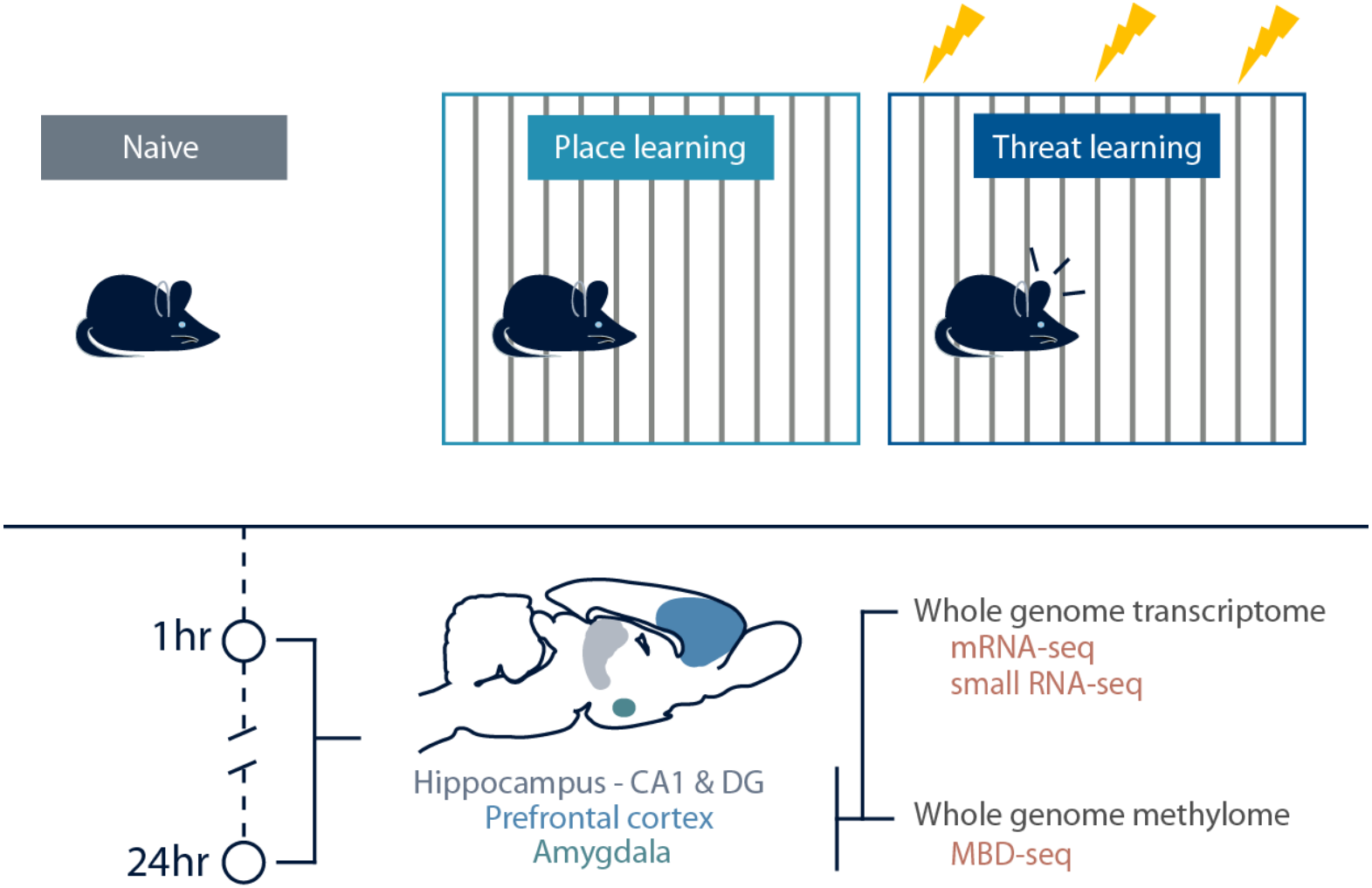
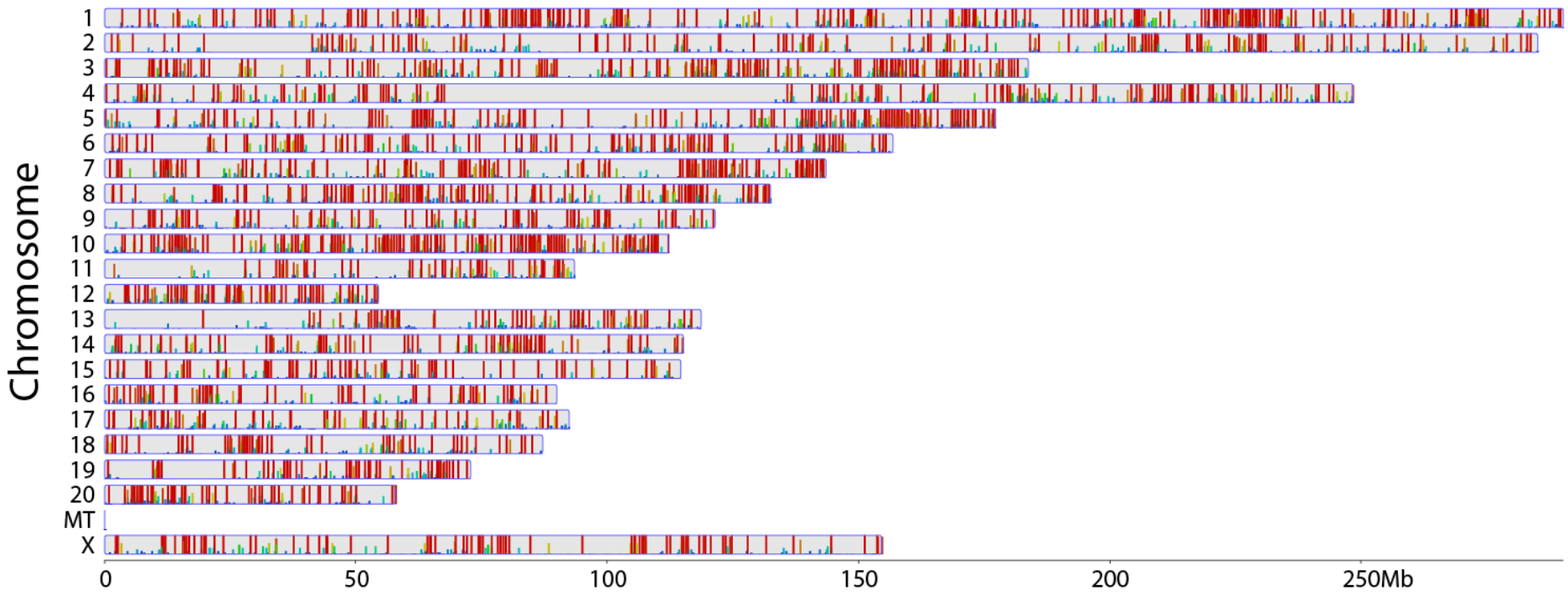


# » GENOME-WIDE RNA PROFILING

Rattus norvegicus genome (24,792 genes)




Identification of the *Rattus* Hippocampal CA1Transcriptome

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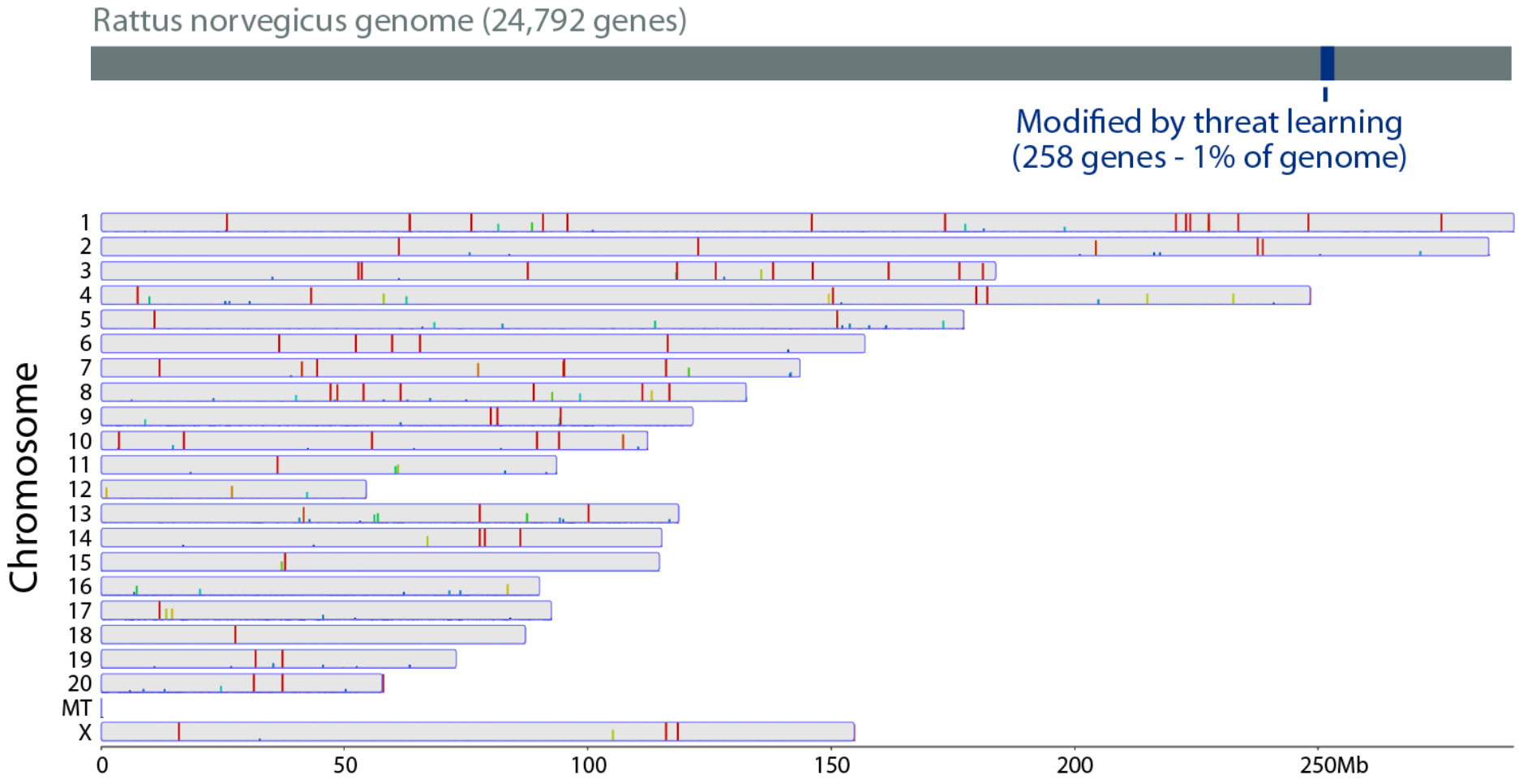
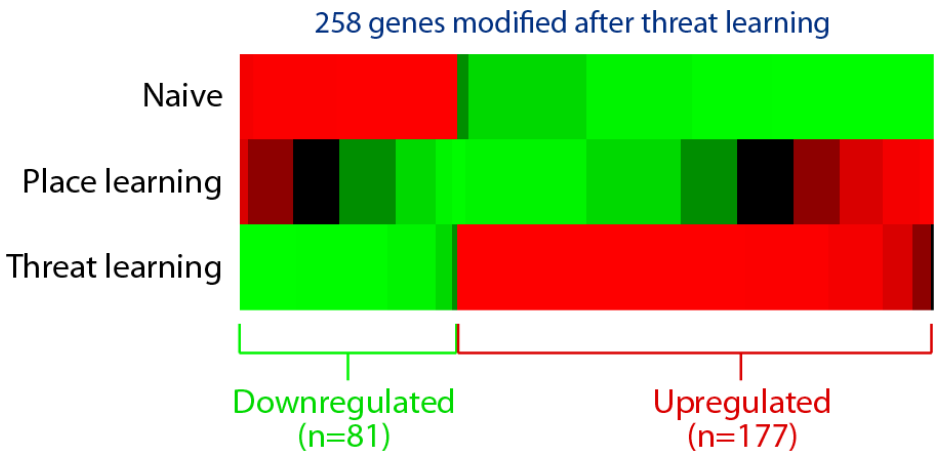
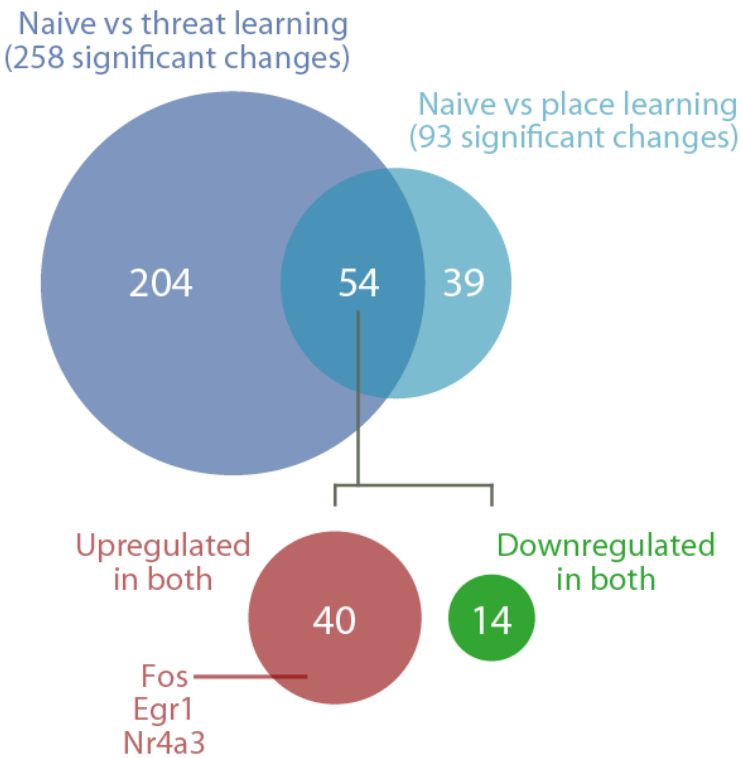


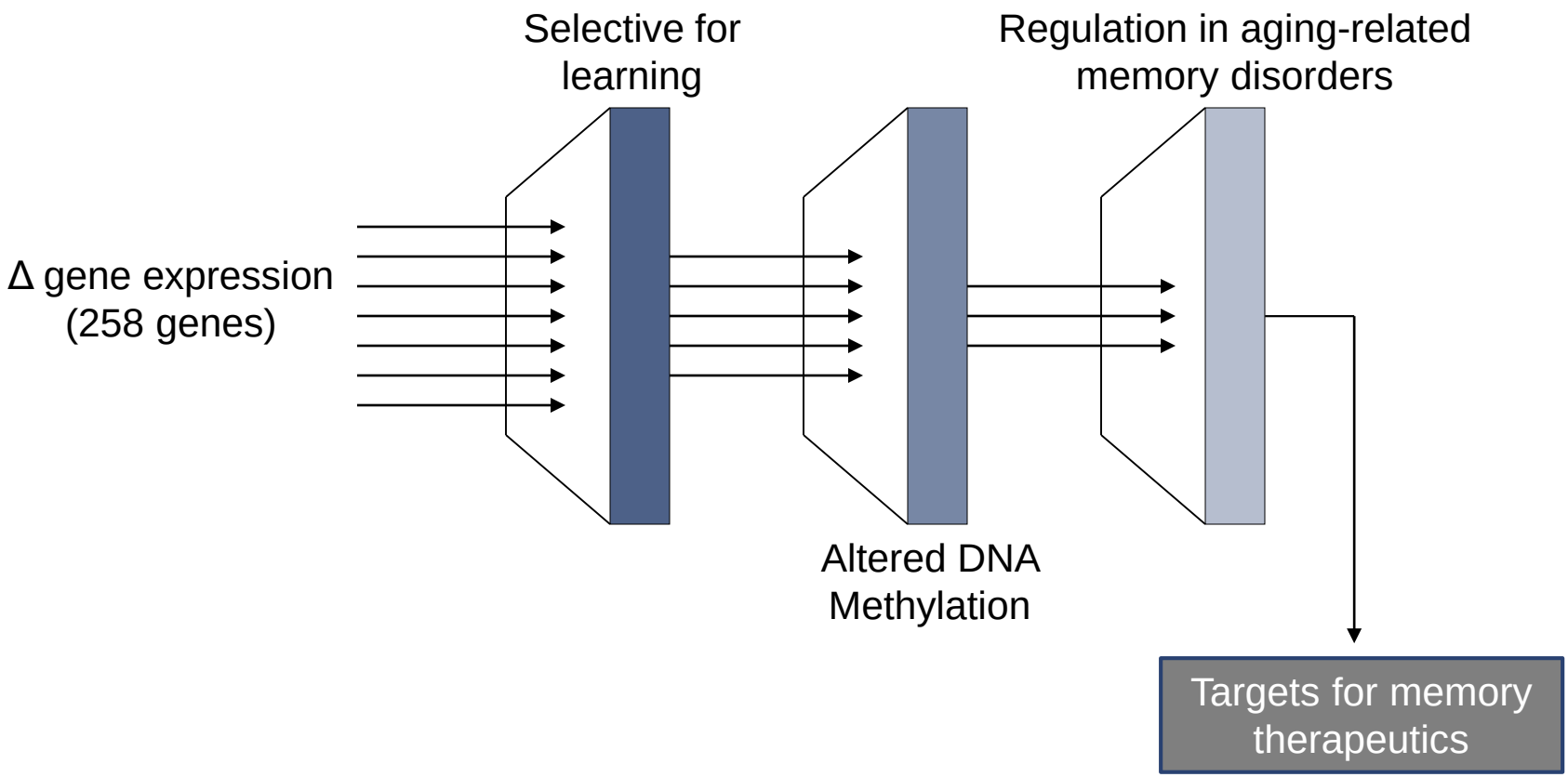

RNA-seq allows for comprehensive transcript analysis and identification of memory-related changes

# » THREAT LEARNING REGULATES *SPECIFIC* GENES IN *SPECIFIC* WAYS

# » THREAT LEARNING GENE EXPRESSION DYNAMICS



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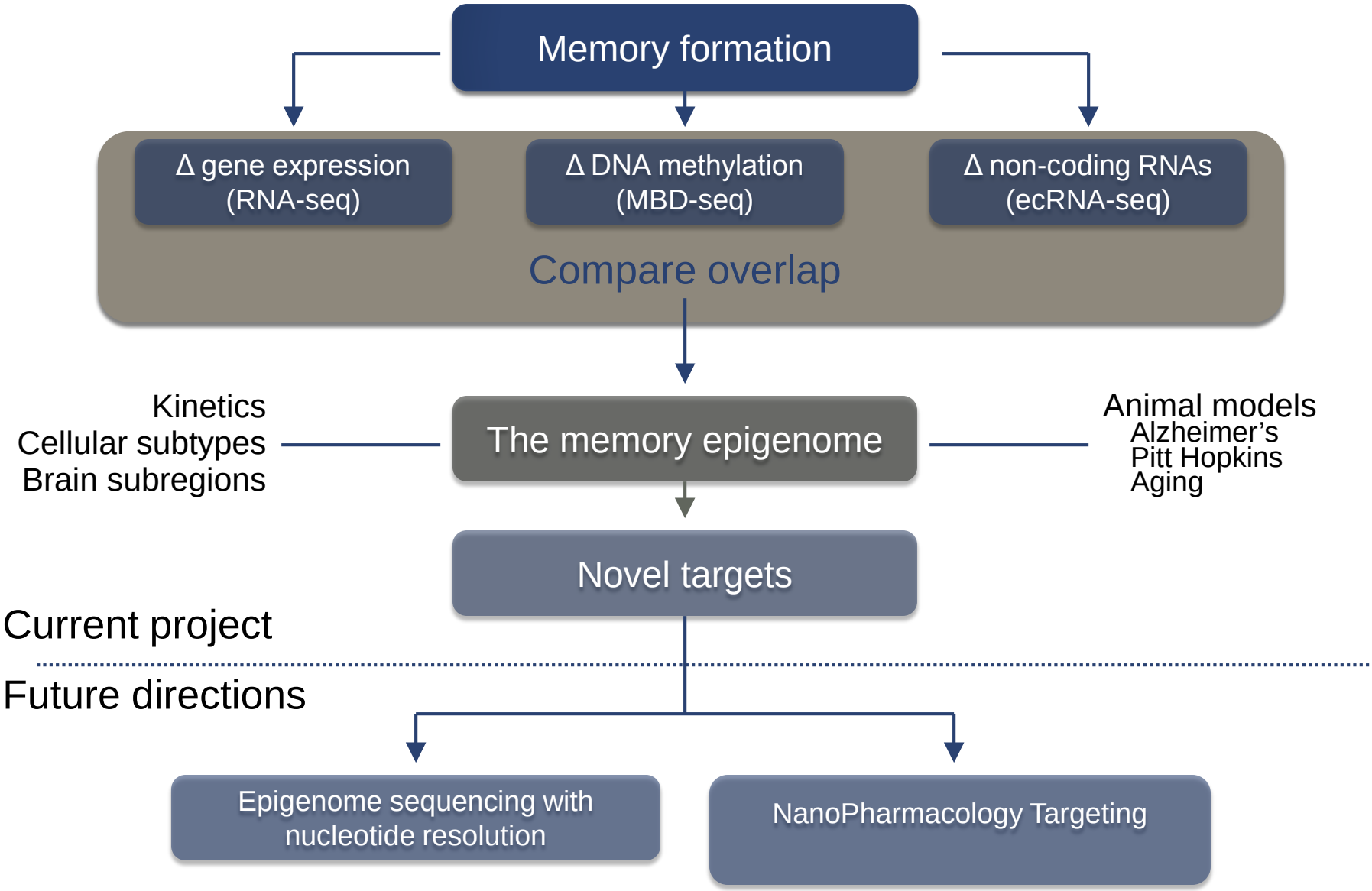
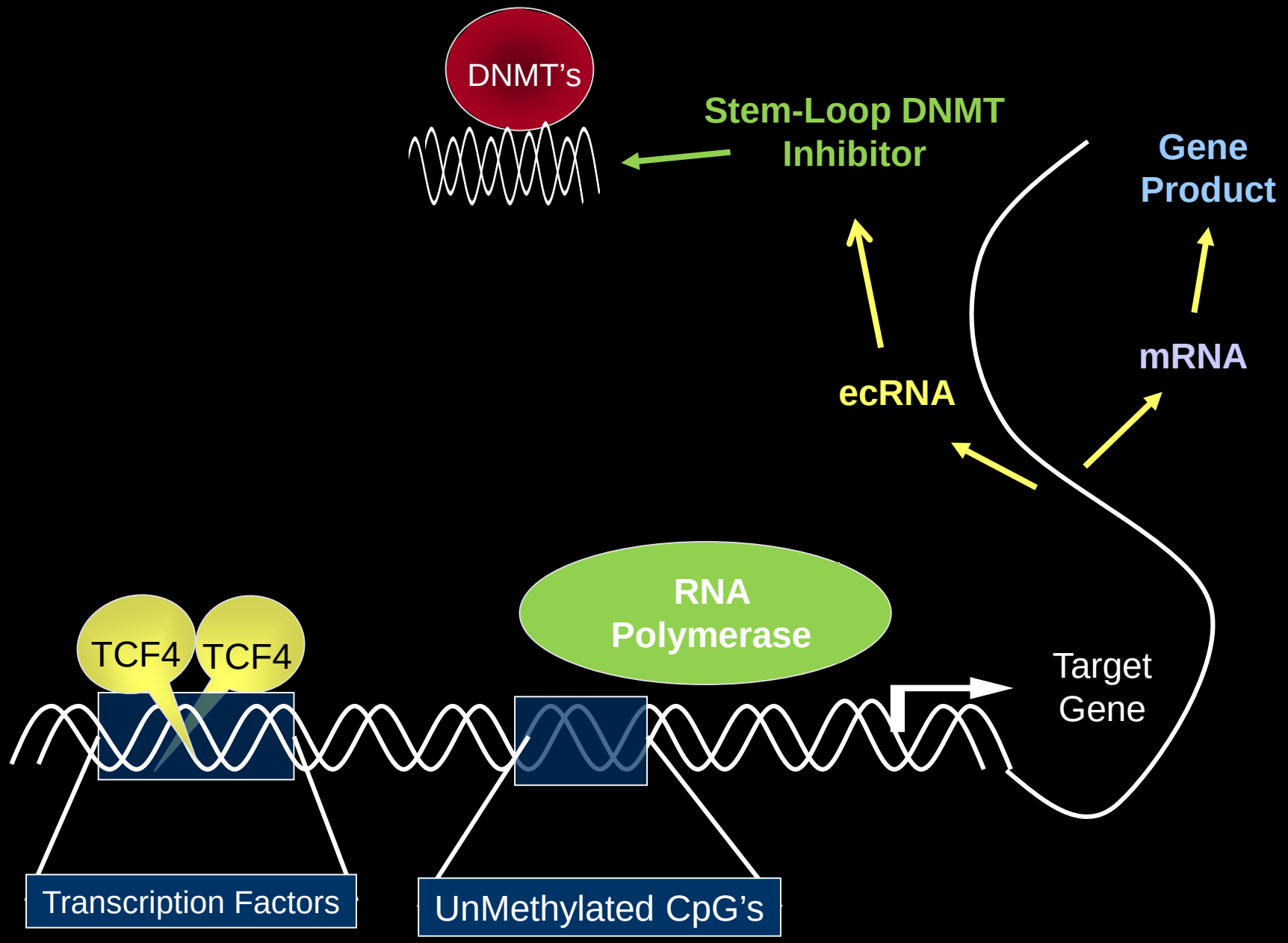
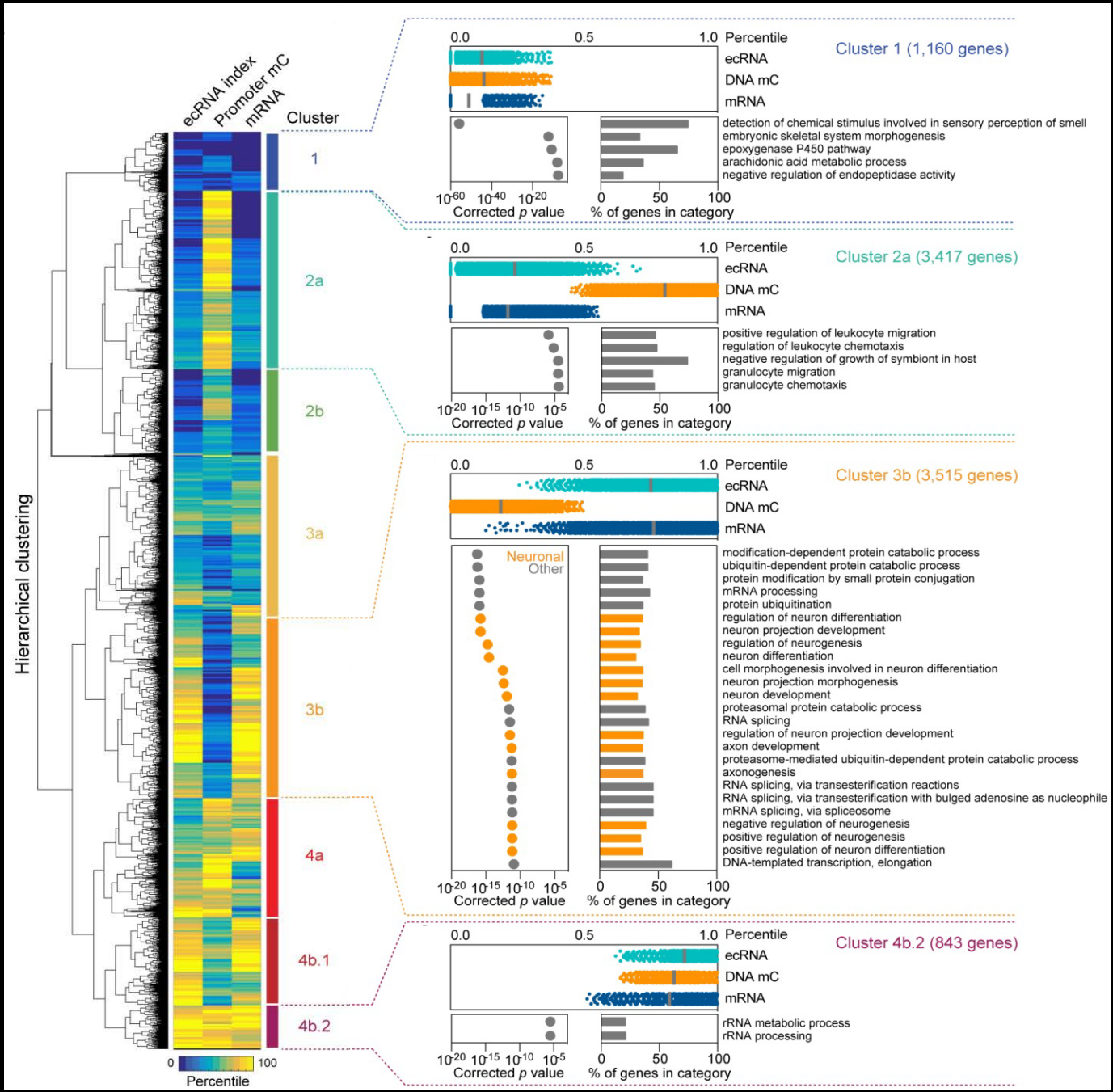


# Epigenetic Regulation by Extra-Coding RNAs



# Hierarchical Clustering Analysis of Neuronal ecRNAs

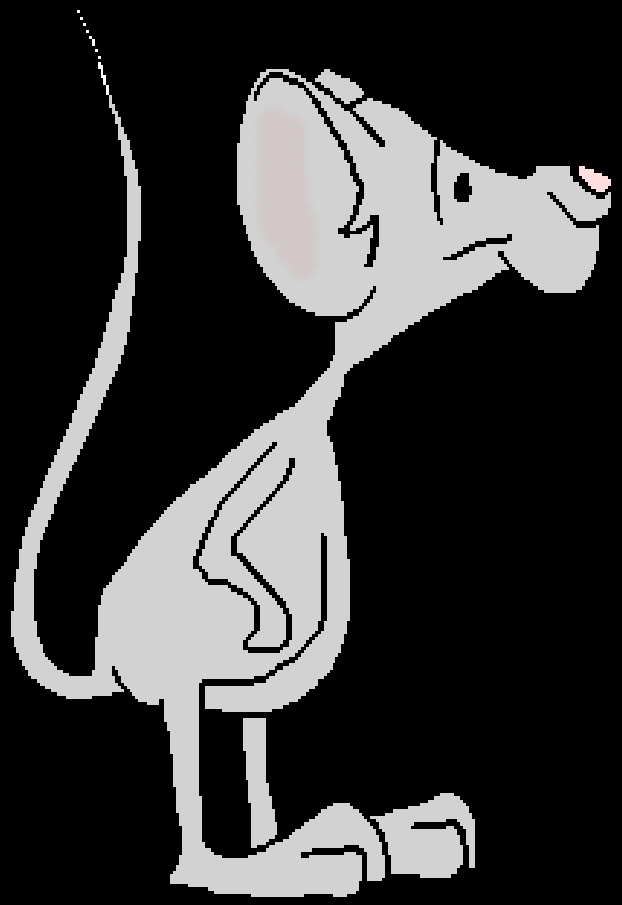


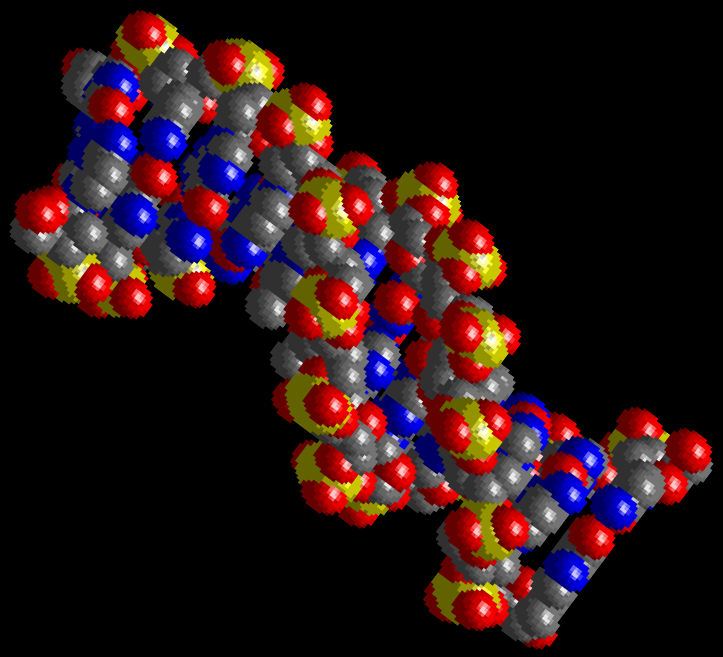
# Reinventing Psychopharmacology

Identifying Novel Memory Targets through Neuroepigenomics

Inventing Cognitive NanoPharmacology

# DNA Sequence-Based Nanotechnology – A Universal Approach That Can Target Any Memory Gene





# Acknowledgements

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National Institute of Neurological Disorders and Stroke

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Department of Neurobiology

- Mark Kilgore
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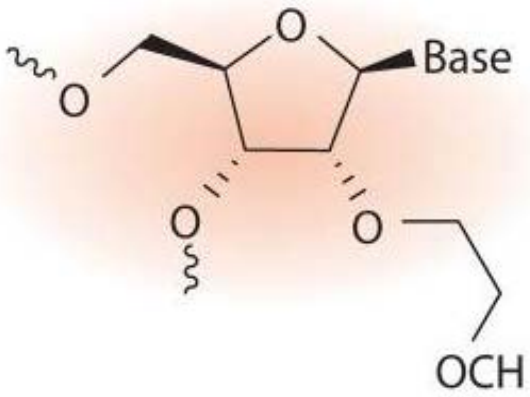
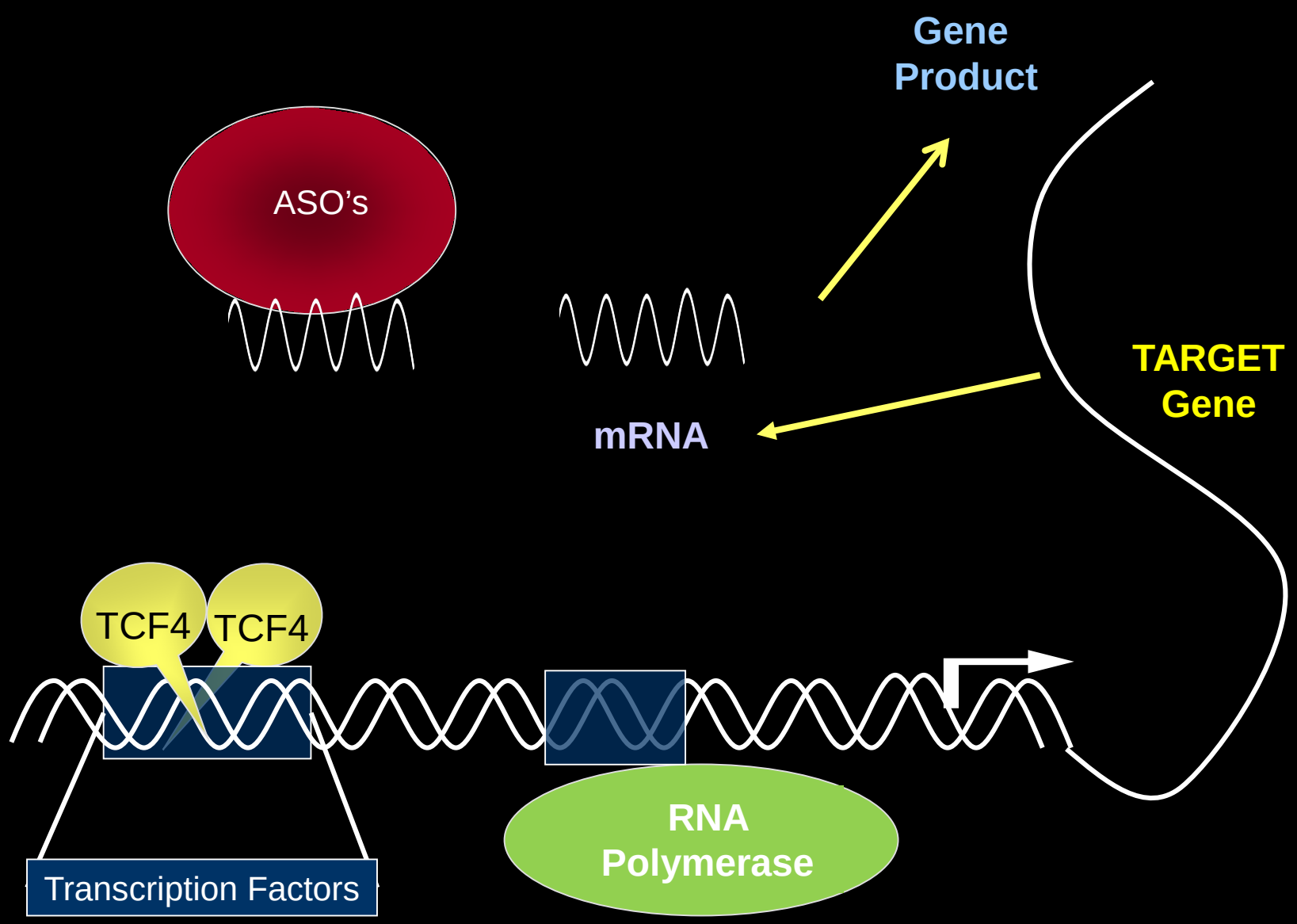
- Garrett Kaas
- Iva Mathews
- Cristin Gavin
- Dawn Eason
- Andrew Kennedy

# Targeting Genes with ASOs

Antisense Oligonucleotide Targeting

# Genetic Knockdown by AntiSense RNAs



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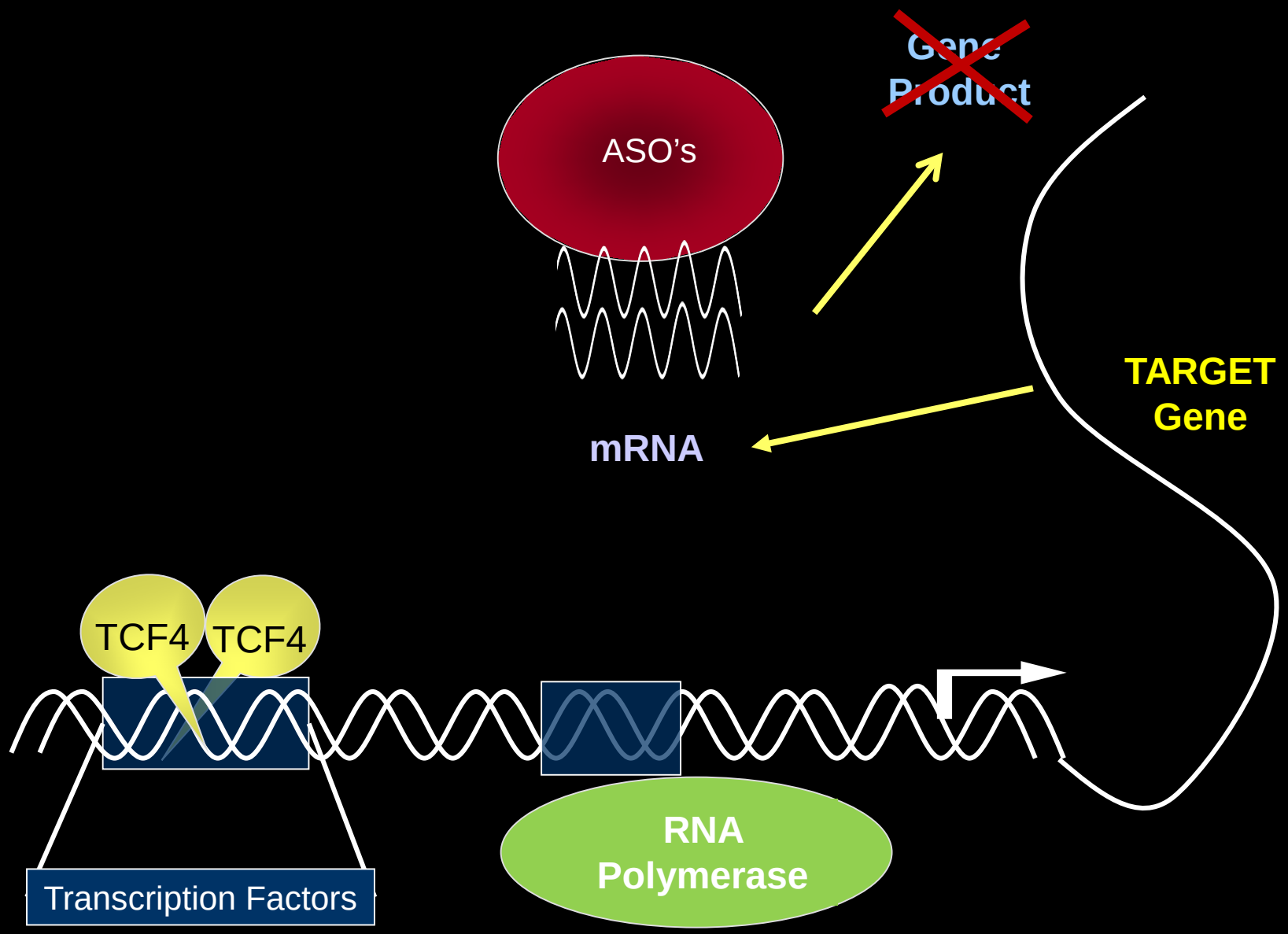
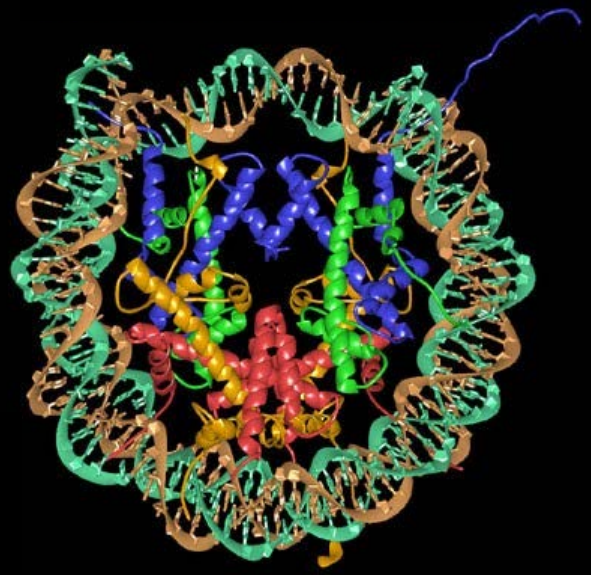


# The Molecular Basis of Long-term Memory

- **Epigenetic mechanisms are involved in memory formation**
- **Manipulating specific gene targets may provide a new avenue for ameliorating learning disabilities and memory dysfunction**

# By Manipulating the Epigenome We Can:

- **Enhance Memory Formation (HDACi)**
- **Block Memory Formation (DNMTi)**
- **Erase an Existing Memory (DNMTi)**



# Reinventing Psychopharmacology

- **Current Target/HTS/Chemical Libraries Approaches Are Not Working**
- **Epigenome-Wide Association Studies for Novel Target Identification**
- **Utilize “Biologics” – Antisense Approaches, miRNAs**
- **Nanotechnology-based Delivery – e.g. Nucleic Acid Nanoparticles**

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