Trauma and Epigenetics

THE PHYSICOLOGICAL EFFECTS OF TRAUMA

ZACH KAMINSKY PH.D.

DEPARTMENT OF PSYCHIATRY AND BEHAVIORAL SCIENCES

JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE

Passing experience to our children through DNA

Numerous epidemiological studies demonstrate altered psychiatric outcomes in children of parents having experienced disaster or trauma

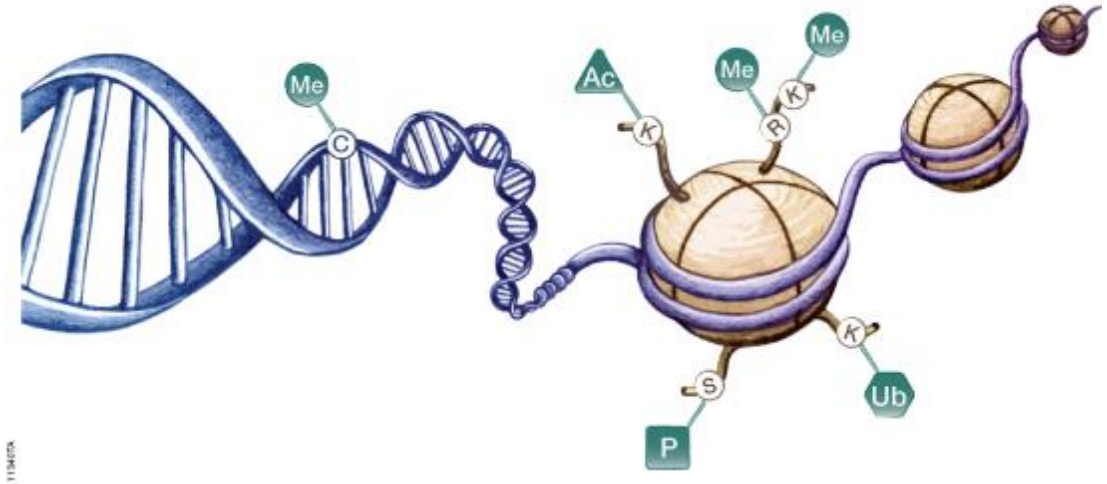
- Dutch famine winter: increased obesity and psychiatric problems in offspring
- Historical Trauma in Native American communities: increased suicide rates in offspring

Evidence suggests these are likely mediate through epigenetic factors

Let’s back up

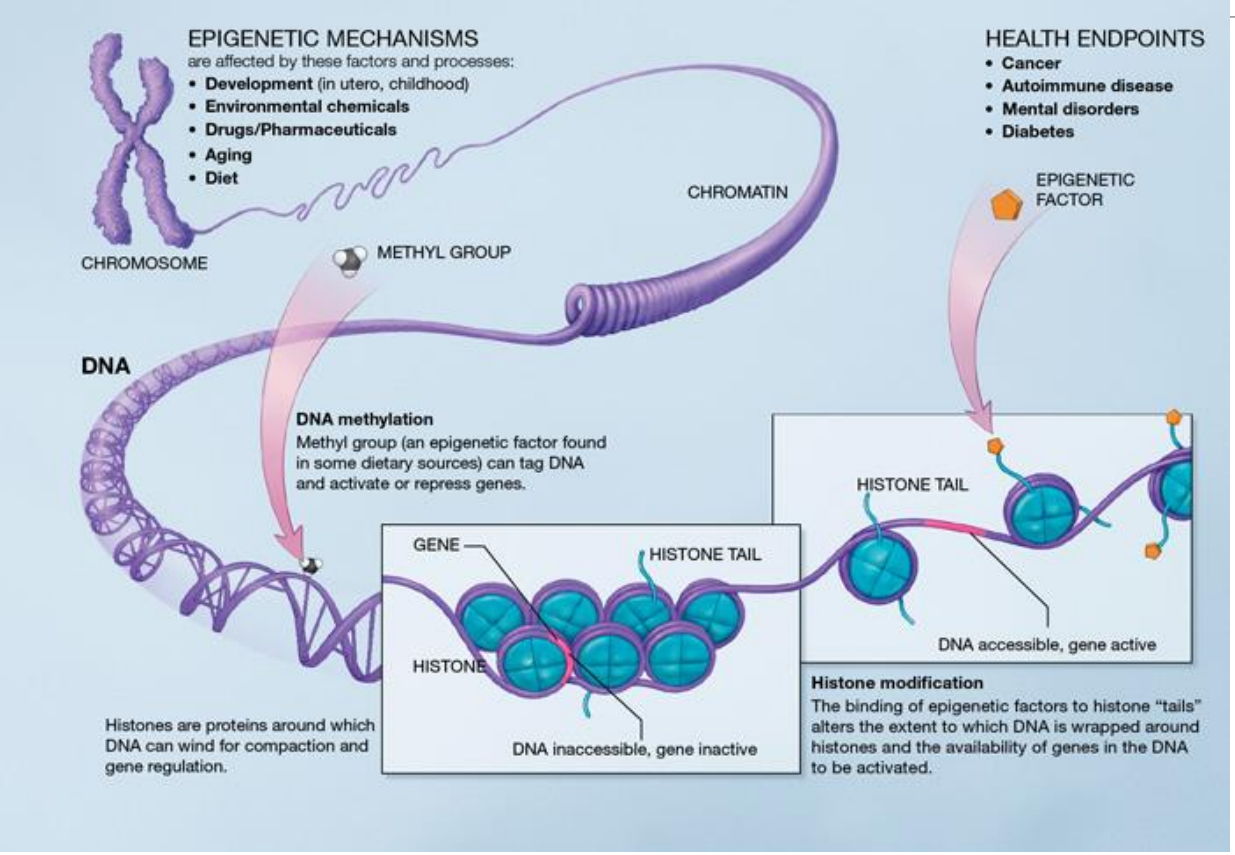
What is epigenetics?

Epigenetics



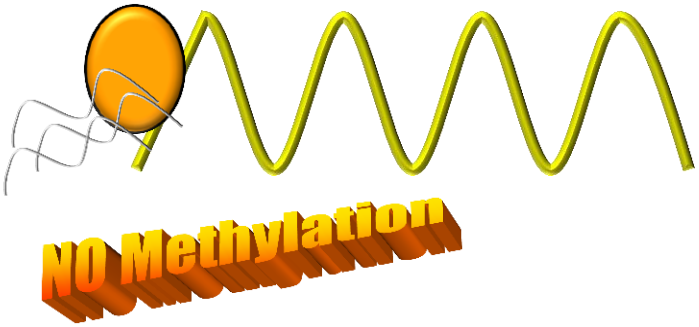
THE CAUSE OF, AND SOLUTION TO ALL OF LIFE'S PROBLEMS

Epigenetics

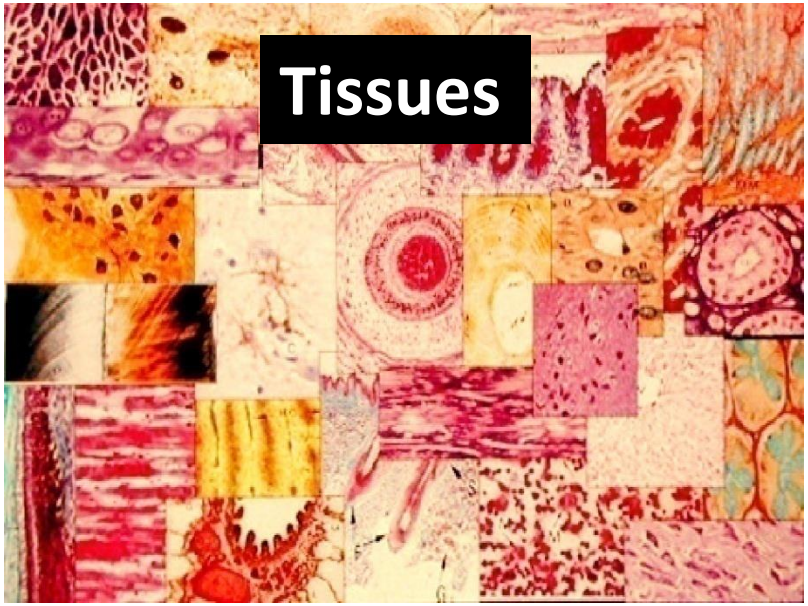


The light switch of DNA

MicroRNA



Epigenetic factors play a major role in biological processes

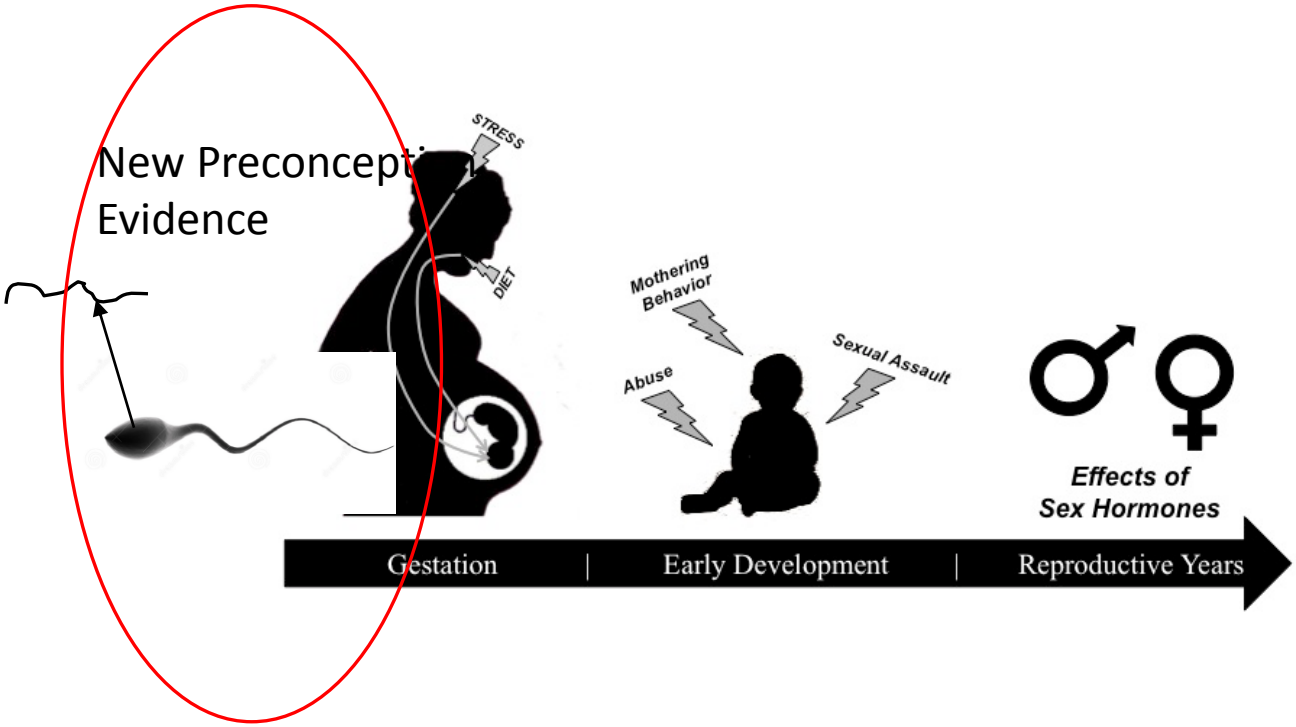


Epigenetic inheritance at the agouti locus in the mouse

Hugh D. Morgan[1], Heidi G.E. Sutherland[2], David I.K. Martin[3] & Emma Whitelaw[1]

Altering life trajectory through experience

The environmental exposures during gestation and later in the postnatal period represent the earliest non-genetically mediated source of variation potentially conferring risk to disease.

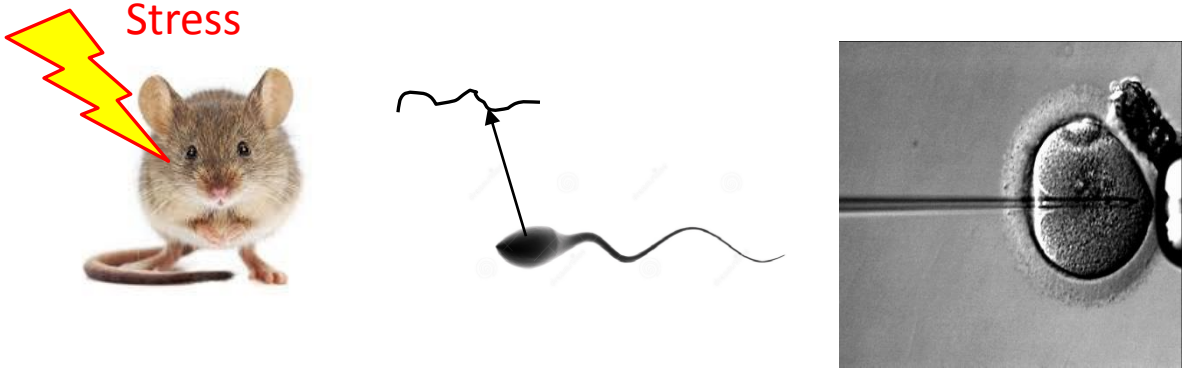


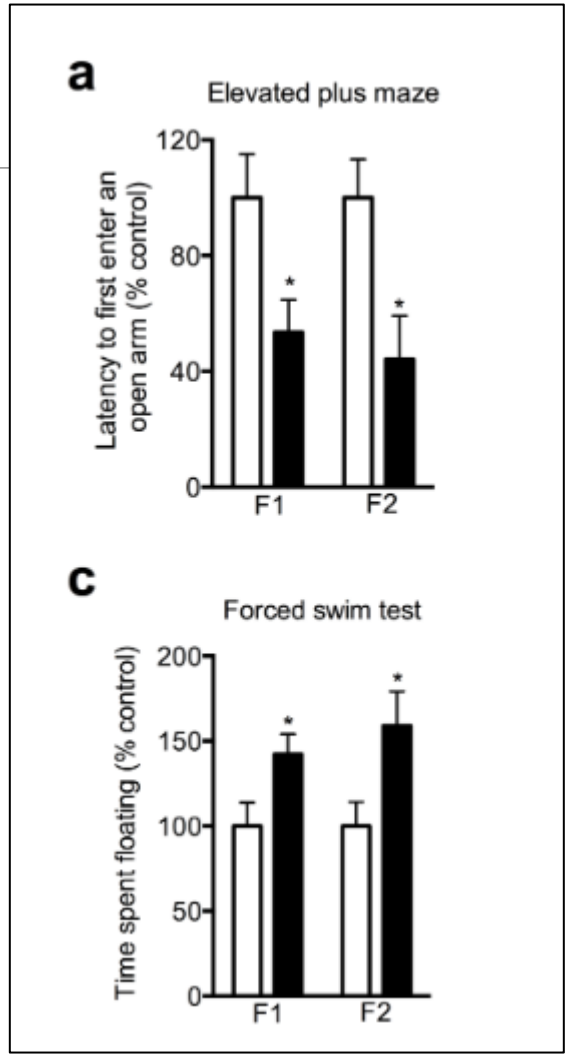
Nat Neurosci. 2014 May ; 17(5): 667–669. doi:10.1038/nn.3695.

Implication of sperm RNAs in transgenerational inheritance of the effects of early trauma in mice

Katharina Gapp[1], **Ali Jawaid**[1], **Peter Sarkies**[2], **Johannes Bohacek**[1], **Pawel Pelczar**[3], **Julien Prados**[4,$], **Laurent Farinelli**[4], **Eric Miska**[2], and **Isabelle M. Mansuy**[1,*]

[1]Brain Research Institute, Neuroscience Center Zürich, University of Zürich and Swiss Federal Institute of Technology, Winterthurerstrasse 190, Zürich, CH-8057, Switzerland [2]Gurdon Institute, Tennis Court Road, Cambridge CB2 1QN, United Kingdom [3]Institute of Laboratory Animal Science, Sternwartstrasse 6; Zürich, CH-8091, Switzerland [4]FASTERIS SA, Chemin du Pont-du-Centenaire 109, P.O. Box 28, CH-1228 Plan-les-Ouates, Switzerland





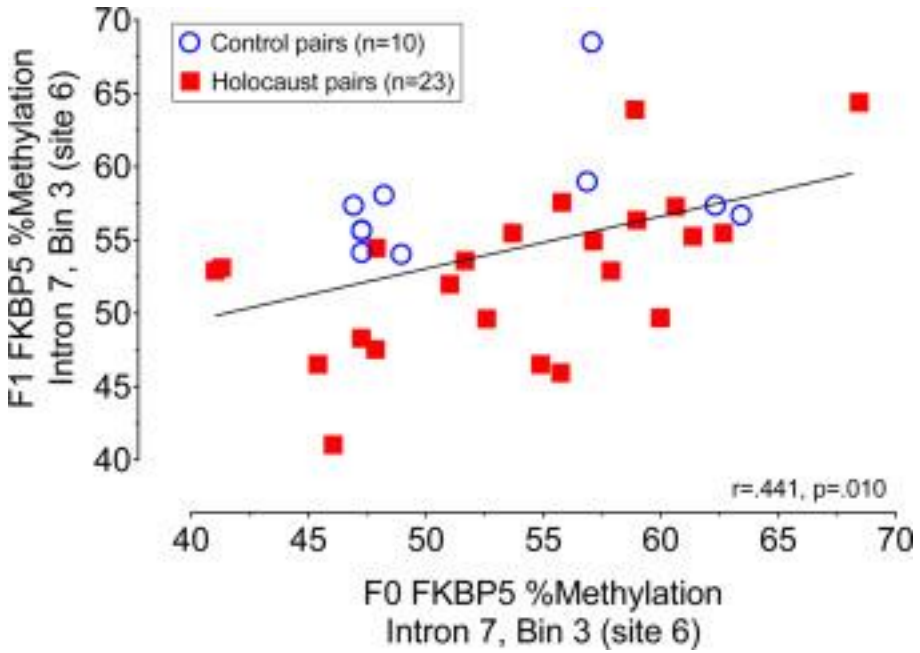


Figure 4. Relationship between original parent generation (F0) and first generation (F1) FKBP5 intron 7 bin 3/site 6 percent methylation. Parent-offspring pairs are represented by red squares for Holocaust survivors (n = 23) and by blue open circles for contro...

Rachel Yehuda, Nikolaos P. Daskalakis, Linda M. Bierer, Heather N. Bader, Torsten Klengel, Florian Holsboer, Elisabeth B. Binder

Holocaust Exposure Induced Intergenerational Effects on FKBP5 Methylation

Biological Psychiatry, 2015, Available online 12 August 2015

http://dx.doi.org/10.1016/j.biopsych.2015.08.005

Altering life trajectory through experience

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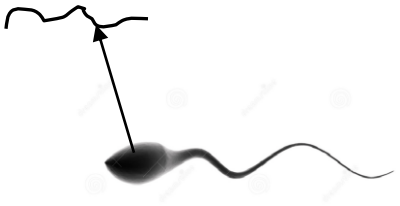
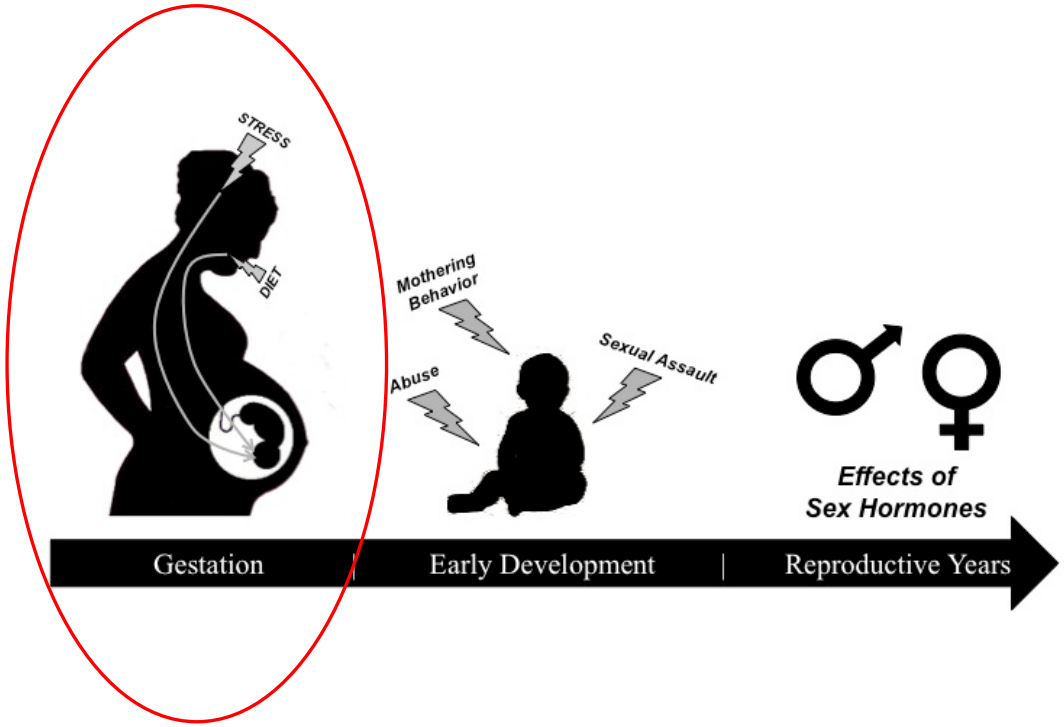
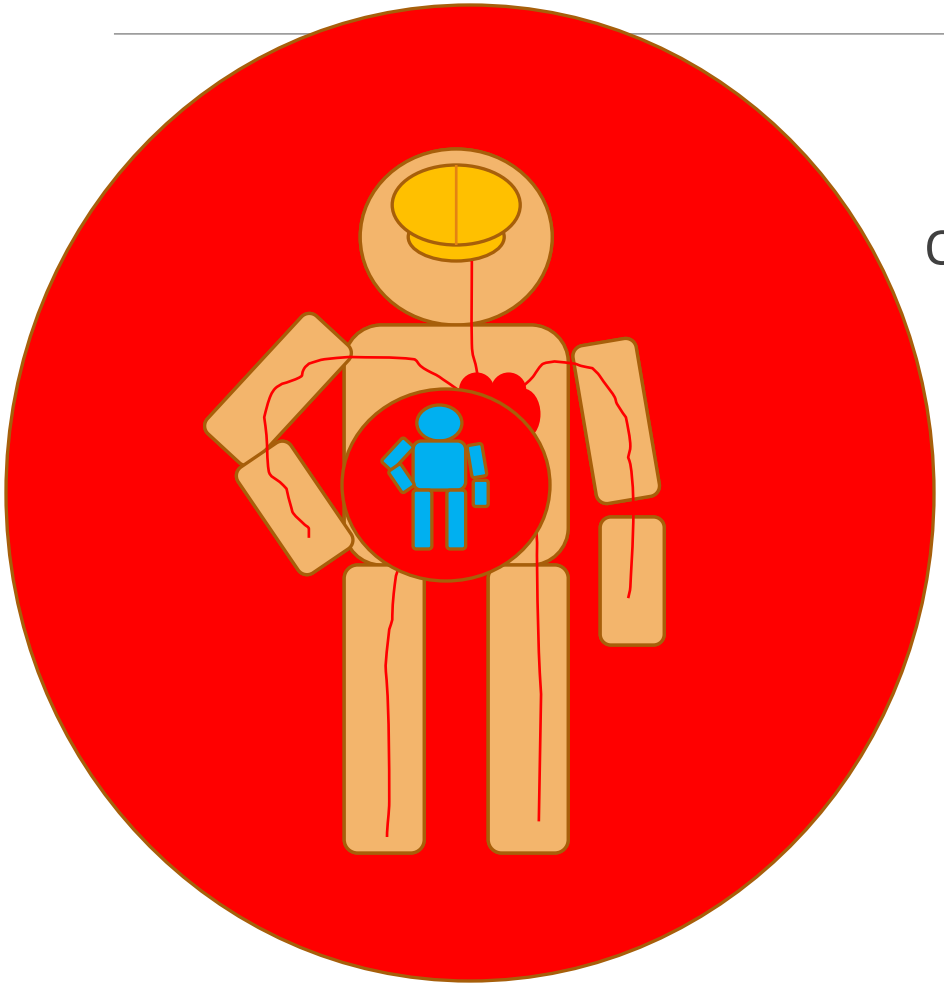
New Preconception Evidence





Prenatal Stress

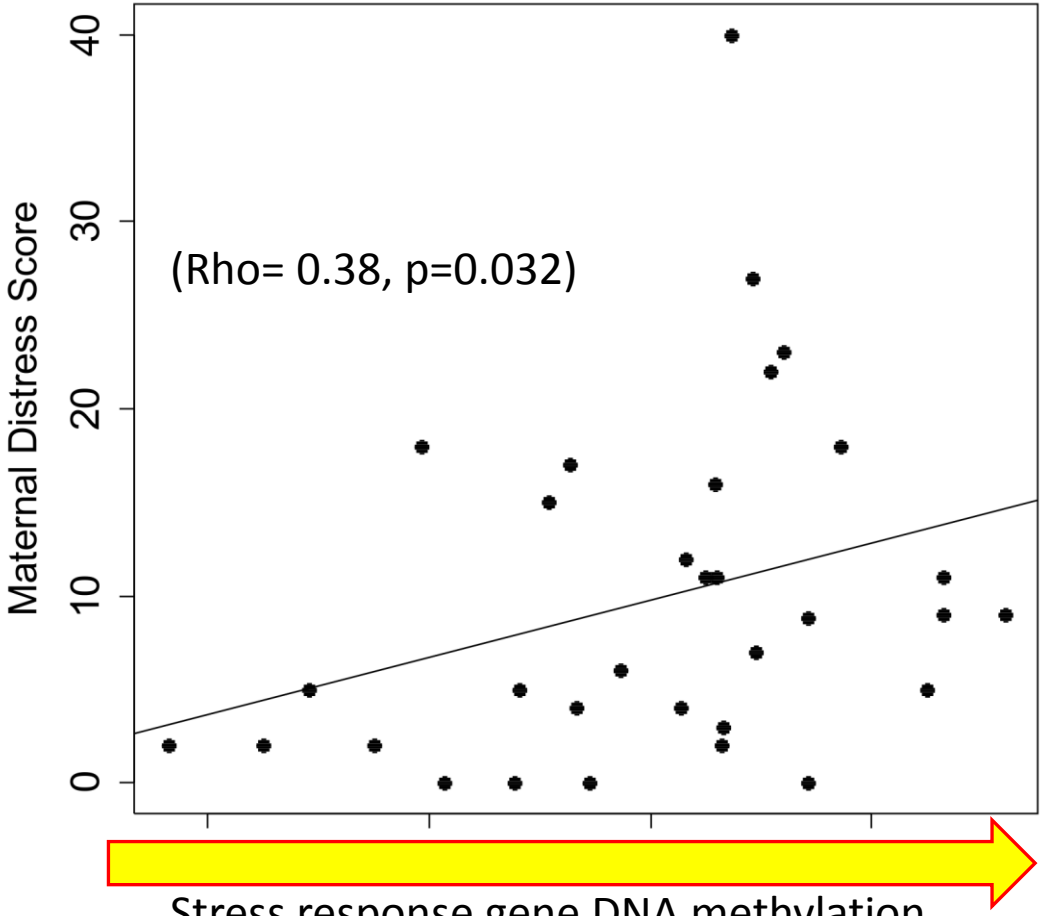


Offspring of depressed mothers:

- Increased ASD rates
- Increased infant stress behavior
- Lower dopamine and norepinephrine
- Lower NICU Network Neurobehavioral Scales (NNNS), an indicator of early neurobehavioral outcome.
- Epigenetic alterations to the stress hormone receptor gene

Maternal Distress = offspring Stress response genes?

GEO # GSE72354: Offspring 13 yr old stress response gene DNA methylation as a function of Maternal Distress during Canada's worst natural disaster



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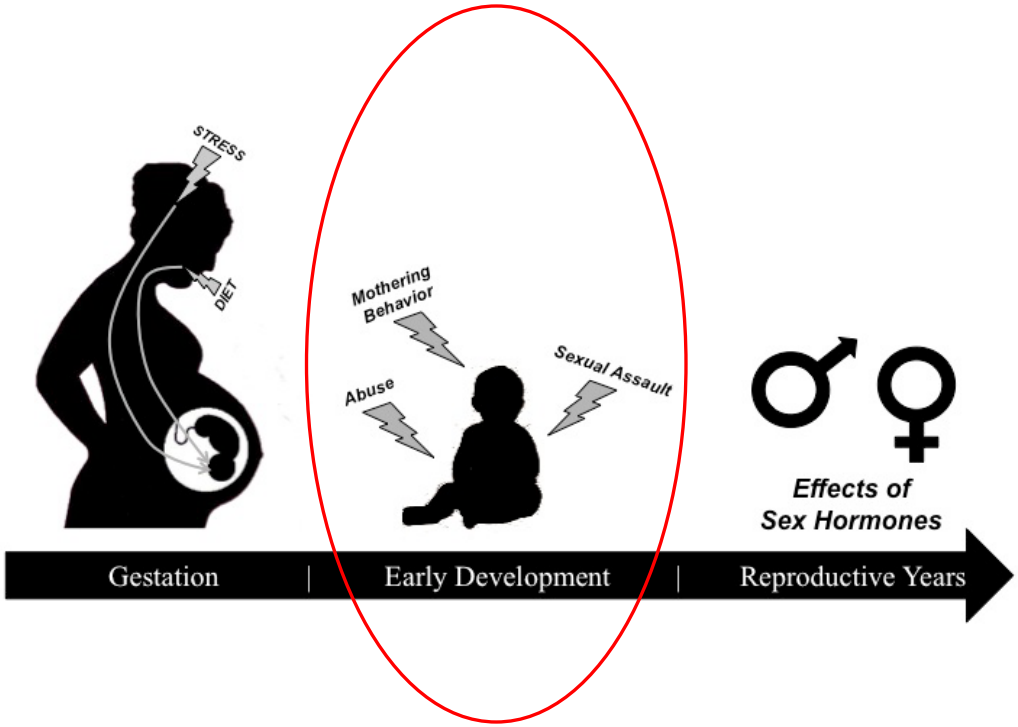


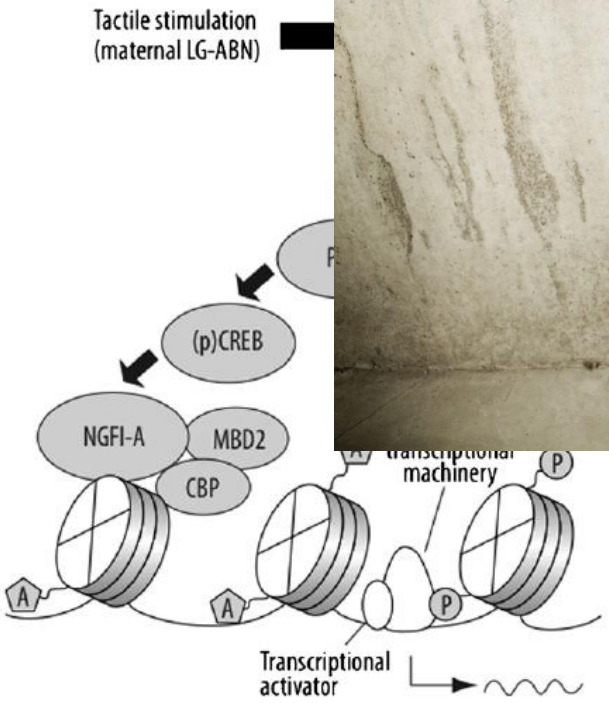
Seminal studies

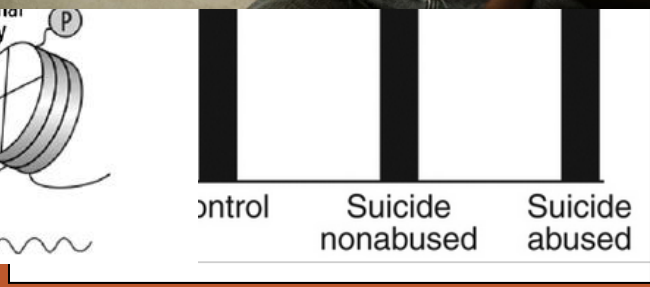
Seminal Studies

Weaver et al., J Neurosci, 2004

McGowan et al., Nat Neurosci, 2009

Maternal Behavior

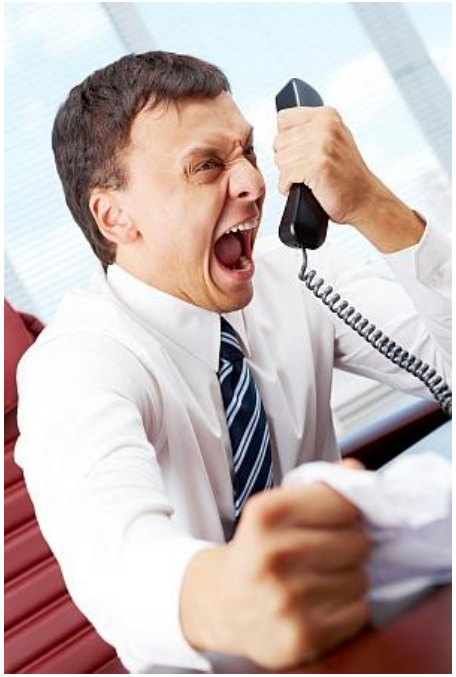




Not just abuse, but lack of parental influence

What’s the consequence of all of this?


SCHOOL BUS
56

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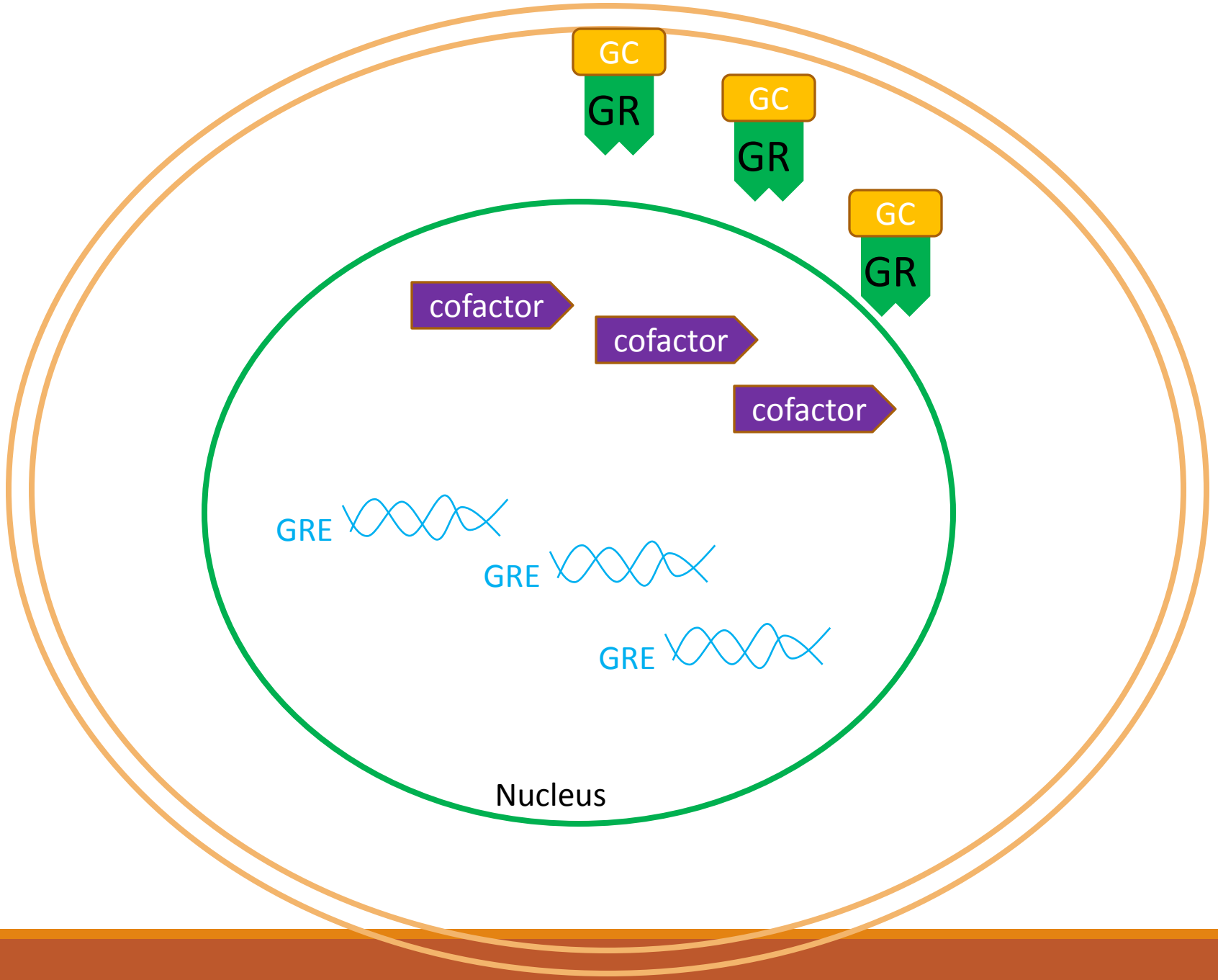
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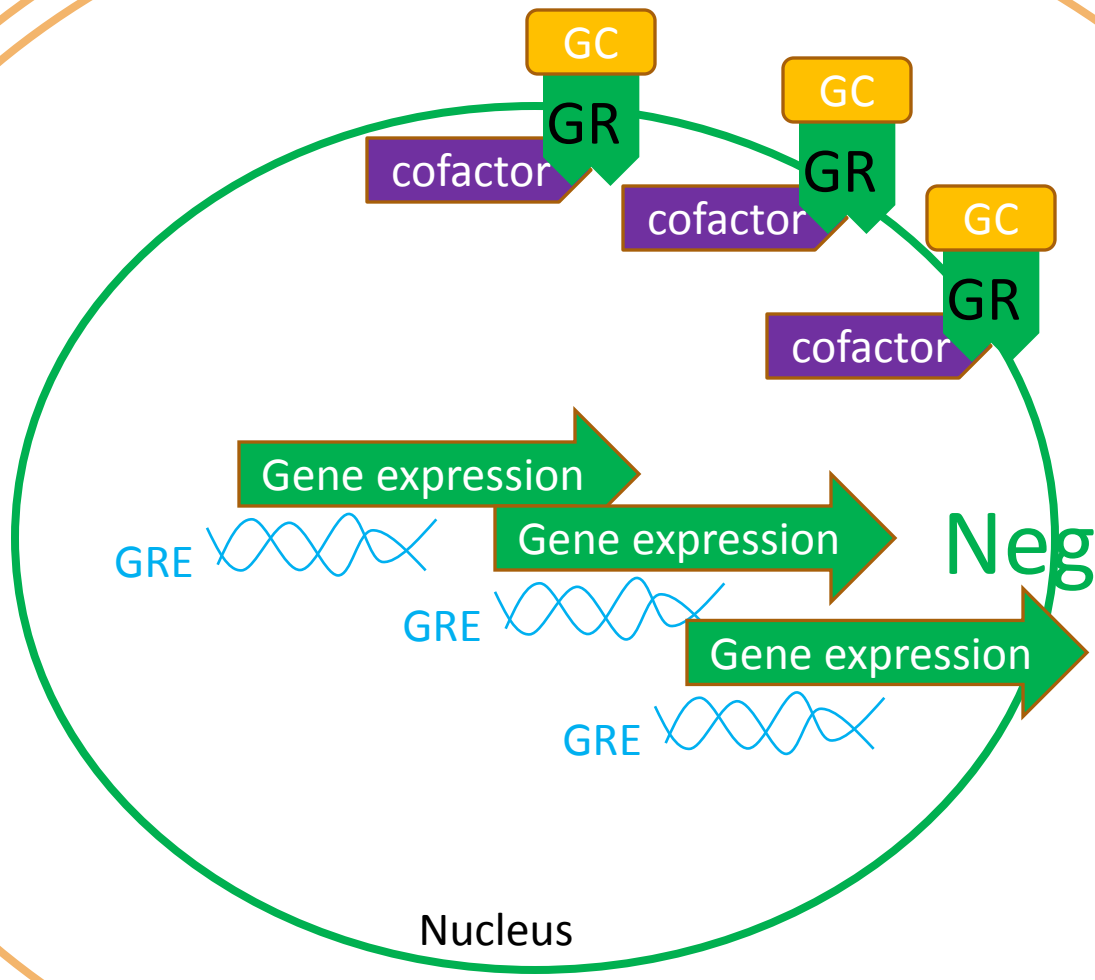
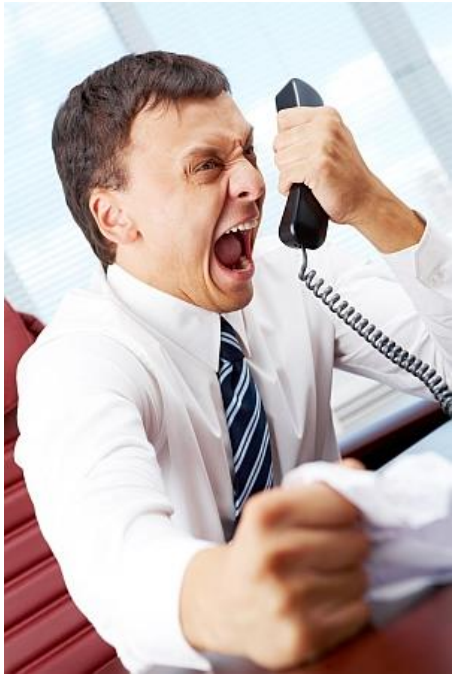


Negative Feedbac



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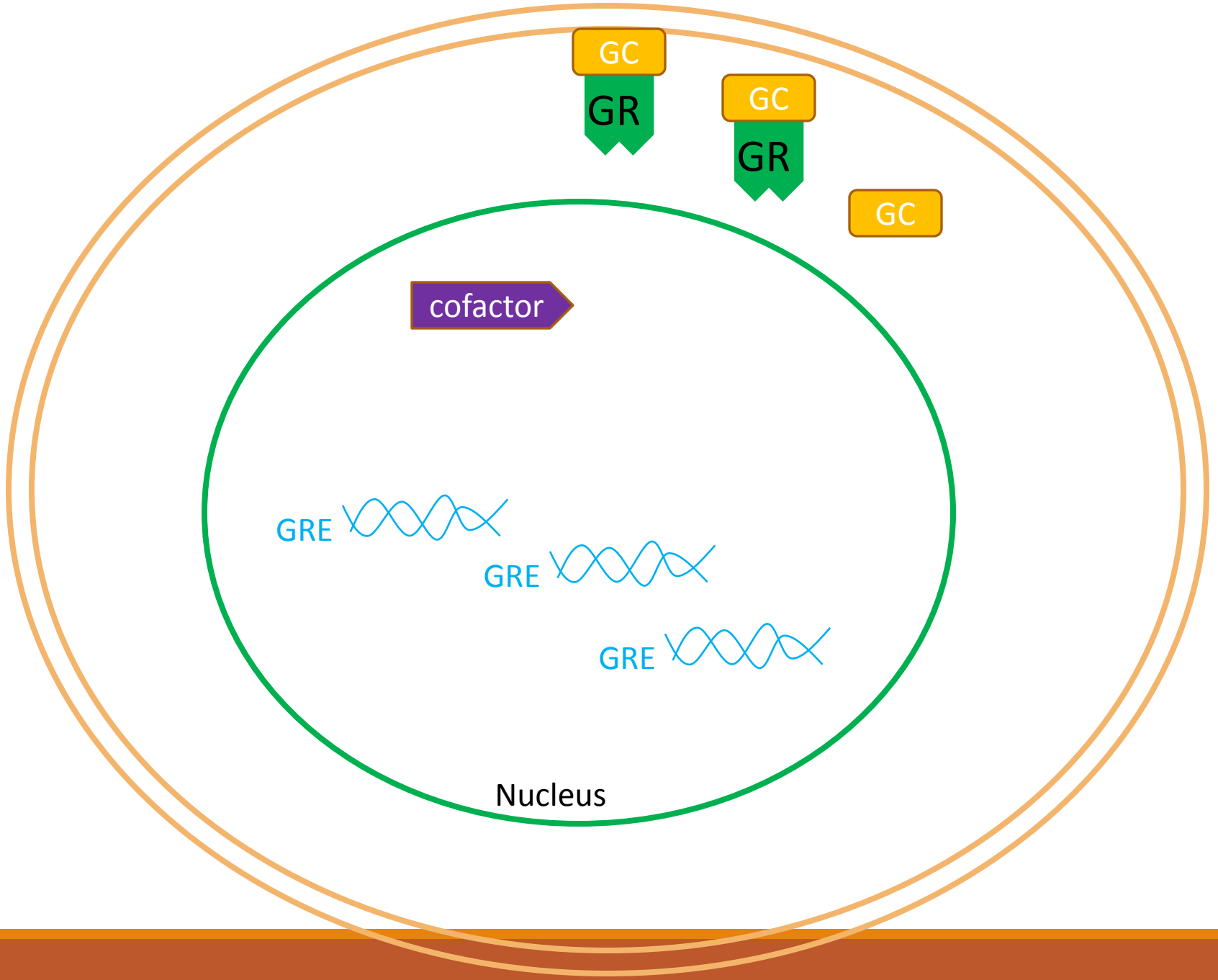
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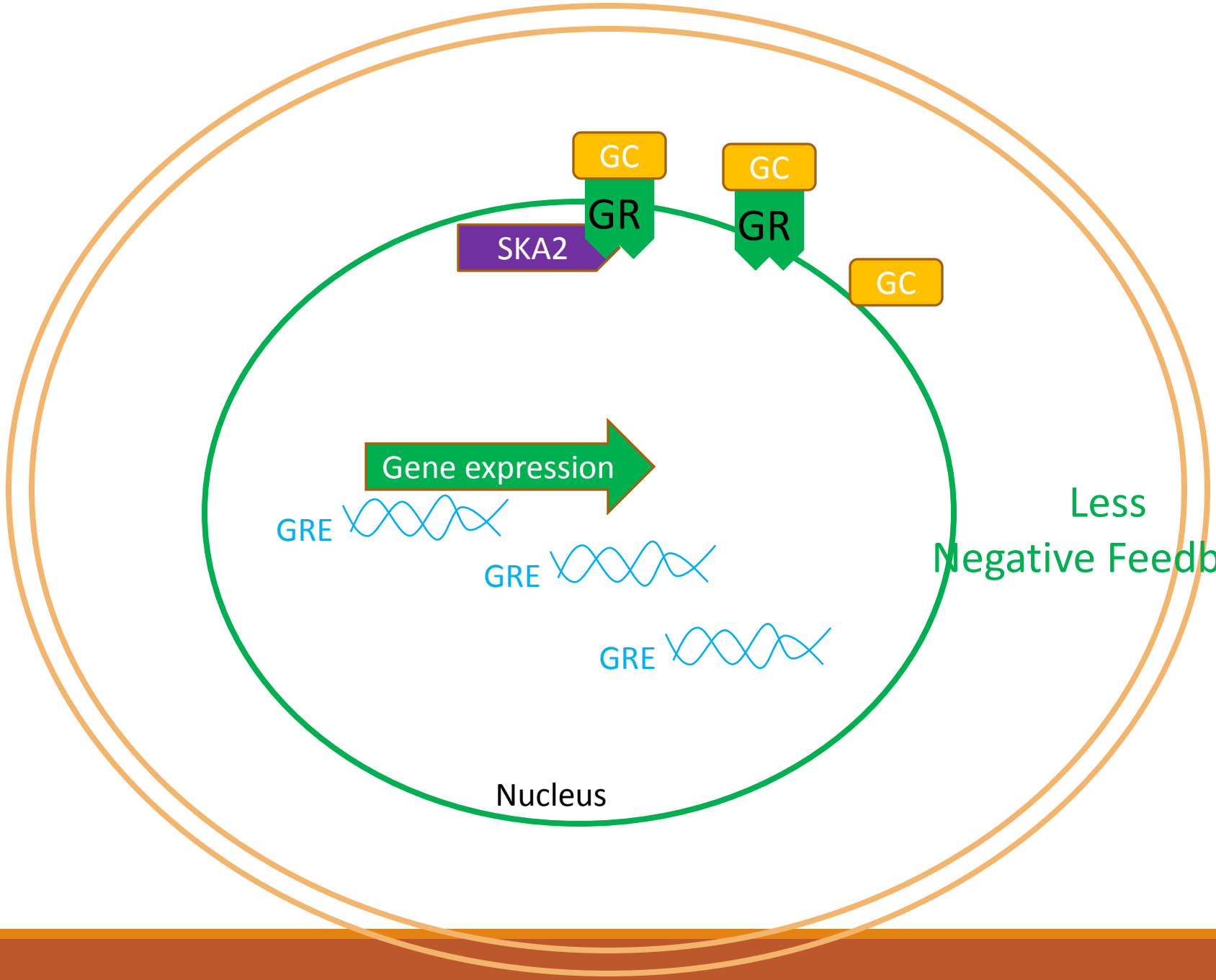

Less
Negative Feedback


SCHOOL BUS
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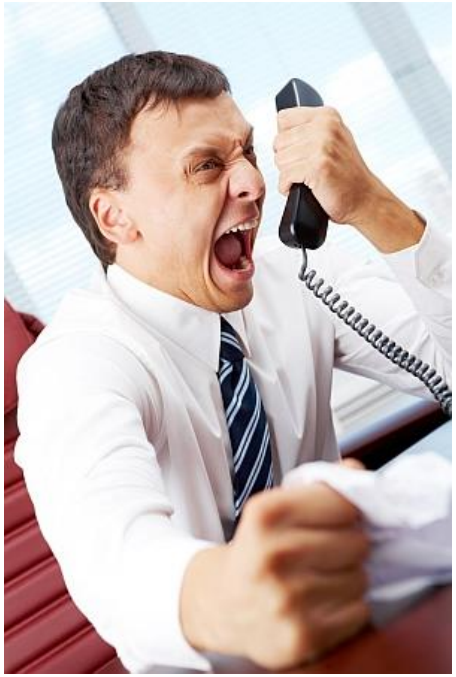


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Why are our genes doing this to us?

Answer: Evolutionary Biology

Lives to pass on genes

The Research Domain Criteria (RDoC) proposal: mental disorders as dysfunctions of brain circuits

"Against the backdrop of lingering discontent with the DSM and ICD, in 2009 the **National Institute of Mental Health (NIMH)** initiated a bold initiative to transform the current framework of psychiatric classification and diagnosis into an explicitly biological system (Cuthbert, 2014, Insel et al., 2010 and Sanislow et al., 2010).

Rather than base psychiatric diagnosis on presenting signs and symptoms, as do the DSM and ICD, RDoC strives to anchor psychiatric classification and diagnosis in a scientifically supported model of neural circuitry.

Specifically, **RDoC** conceptualizes mental disorders as dysfunctions in brain systems that bear important **adaptive implications**, such as systems linked to reward responsiveness and **threat sensitivity** (see also Harkness, Reynolds, & Lilienfeld, 2013)" (Scott et al., Behavioral Research Therapy, 2014).

Break the cycle

Trauma centered interventions are necessary to break the cycle of epigenetically inherited risk and associated deleterious consequences.