

# Epigenetics & Telomeres

Additional Slides from Sonoma Community Resilience Collaborative Workshop

# Epigenetics and Trauma

## Epigenetics

- ▶ Which genes are turned on/off, when and where
- ▶ Ecology (environment/experiences)
- ▶ Stress-induced changes in gene expression

## Parental Stress and Children's Genes

- ▶ Parents' stress leaves lasting marks on children's genes
- ▶ Higher stress levels reported by mothers during their child's first year correlated with methylation on 139 DNA sites in adolescents

# Epigenetics and Trauma: Early Life Stress & Gene Methylation in Children

- ▶ Epigenetic changes in the glucocorticoid receptor gene were examined in whole blood from 56 children, ages 11-14
- ▶ Results showed greater methylation within certain regions of the gene in children exposed to physical maltreatment vs. non-maltreated children
- ▶ Specifically, more methylation occurred in regions responsible for numerous biological functions, including healthy human brain development
- ▶ Results highlight molecular mechanisms linking childhood stress with biological changes that may lead to mental and physical disorders

# The Epigenetics of Trauma

- ▶ Researchers observed the effect of childhood abuse on the gene expression profiles
- ▶ Sixty-one individuals met criteria for current PTSD, of which 32 reported a history of childhood maltreatment and 29 did not report childhood abuse.
- ▶ All individuals reported trauma in adulthood
- ▶ Gene expression profiles of PTSD patients with childhood abuse compared to non-childhood abuse were almost completely non-overlapping (98%).
- ▶ Childhood abuse has an influence on biological processes via epigenetic modifications.

# The Epigenetics of Trauma

In a 2014 study, Yehuda observed the effect of Holocaust trauma exposure on the gene expression profiles of adults and offspring

- ▶ Twenty-four-hour urinary cortisol excretion was measured in 35 adult offspring of Holocaust survivors and 15 health comparison control subjects
- ▶ Low cortisol levels were significantly associated with both PTSD in parents and in offspring.
- ▶ Parental PTSD appears to be associated with low cortisol levels in offspring, even in the absence of lifetime PTSD in the offspring
- ▶ In Yehuda's 2015 study, Holocaust survivors and their offspring both showed methylation alterations on the FKBP5 gene
- ▶ These results demonstrated the transmission of pre-conception stress effects resulting in epigenetic changes in both exposed parents and their offspring

Yehuda, R., Bierer, L. M., Schmeidler, J., Aferiat, D. H., Breslau, I., & Dolan, S. (2014). Low cortisol and risk for PTSD in adult offspring of holocaust survivors. *American Journal of Psychiatry*.

Yehuda, R., Daskalakis, N. P., Bierer, L. M., Bader, H. N., Klengel, T., Holsboer, F., & Binder, E. B. (2015). Holocaust exposure induced intergenerational effects on FKBP5 methylation. *Biological Psychiatry*.

# Epigenetics

- ▶ Exposure to traumatic stress in mouse parents altered the miRNA expression, heightened the anxiolytic behavioral activity in response to threats and decreased glucose and insulin tolerance in the next generation
- ▶ Injection of sperm RNAs from traumatized males into fertilized eggs reproduced the behavioral and metabolic alterations in the resulting offspring.

# Epigenetics

## Chronic Stress and DNA Methylation

- ▶ Researchers show that chronic and unpredictable maternal separation induces depressive-like behaviors and alters the behavioral response to aversive environments in the separated animals when adult.
- ▶ Most of the behavioral alterations are further expressed by the offspring of males subjected to maternal separation, despite the fact that these males are reared normally.
- ▶ Chronic and unpredictable maternal separation also alters the profile of DNA methylation in the promoter of several candidate genes in the germline of the separated males.
- ▶ Comparable changes in DNA methylation are also present in the brain of the offspring and are associated with altered gene expression.

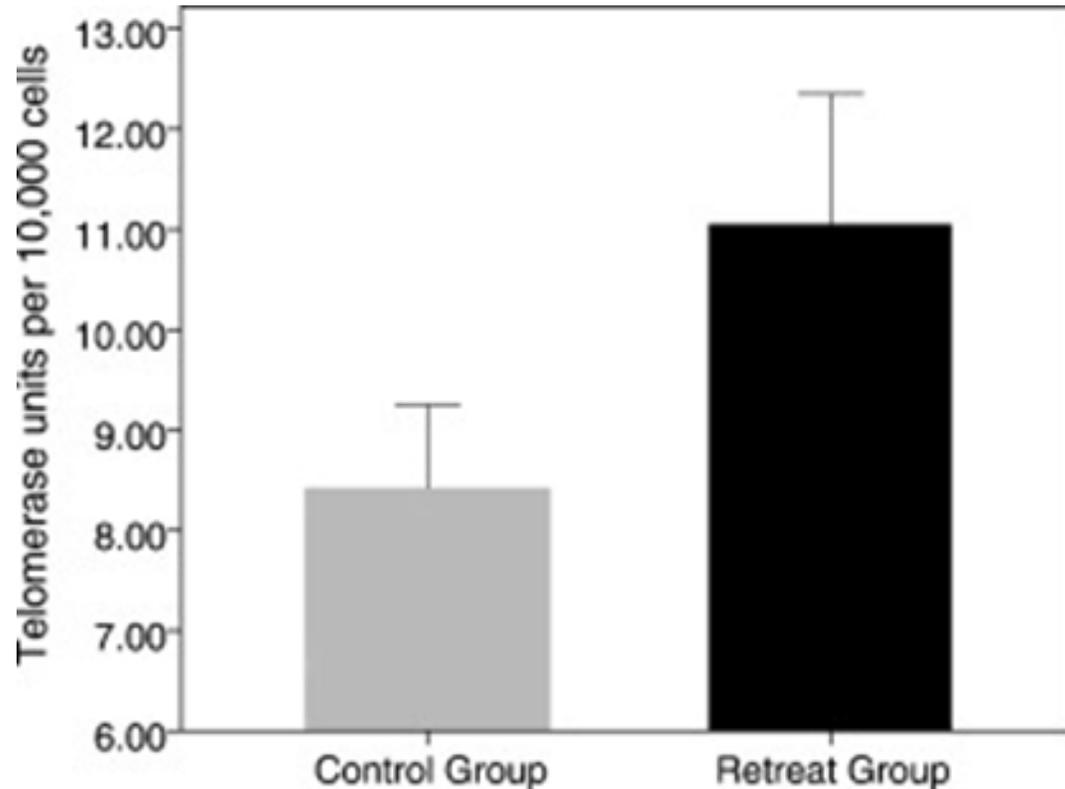
# Epigenetics

## Epigenetic Changes In Twins

- ▶ Bullied twins had higher SERT DNA methylation at the age of 10 years compared with their non-bullied MZ co-twins.
- ▶ Bullied twins also showed increasing methylation levels between the age of 5 years, prior to bullying victimization, and the age of 10 years whereas no such increase was detected in non-bullied twins across time.

Ouellet-Morin, I., Wong, C. C. Y., Danese, A., Pariante, C. M., Papadopoulos, A. S., Mill, J., & Arseneault, L. (2013). Increased serotonin transporter gene (SERT) DNA methylation is associated with bullying victimization and blunted cortisol response to stress in childhood: a longitudinal study of discordant monozygotic twins. *Psychological medicine*, 43(09), 1813-1823.

# Meditation Effects on Chromosomes



- **Telomeres:** “caps” at the end of our chromosomes  
→ *Decreases in length of telomeres associated with many chronic illnesses as well as decreased life span. Greater telomere length may be associated with increased longevity*
  - **Telomerase:** an enzyme that builds up the telomeres preserving healthy cell functioning
- Results of Study
- The retreat group that participated in the intensive meditation training demonstrated a significantly higher rate of telomerase activity
  - Perceived control and Neuroticism were variables found to be influencers of psychological stress. Improvement in these areas, due to the meditation intervention, were links to the positive relationship between meditation and telomerase activity

# The Epigenetics of Trauma

## Why does it matter?

- ▶ Diseases are not primarily attributable to genetics and we have some say over whether we actually get those diseases or not
- ▶ Those same epigenetic mechanisms that were responsible for the disease in the first place, can also be effectively used to fight the disease and promote healing.

**We can use it in a very proactive way to actually enhance our lives.**

# Epigenetics and Mind-Body Medicine

- ▶ Researchers tracked men with low risk prostate cancer who had opted-out of conventional treatment and instead chosen an intensive 3-month lifestyle and nutritional program
- ▶ Treatment: 60 minutes of stress management included yoga, breathing, meditation, imagery and progressive relaxation; a low fat, plant based diet
- ▶ Results:
  - ▶ Improvements in weight, abdominal obesity, BP, and lipid profile
  - ▶ Patients reported significant reduction in psychological distress
  - ▶ **Down-regulation of a set of *RAS* family oncogenes, some of which may be normally increased in tumor tissues**
  - ▶ Significant modulation of biological processes that have critical roles in tumorigenesis, including protein metabolism and modification, intracellular protein traffic, and protein phosphorylation

# Effects of a Comprehensive Group Program of Mind-Body Medicine

- ▶ Researchers tested the effects of a comprehensive mind-body medicine program on long-term practitioners, 8-week retreat participants (short-term practitioners), and control
- ▶ **Results:** 2209 genes were differently expressed in long-term practitioners compared to control
  - ▶ 1561 genes differently expressed in retreat participants compared to control
  - ▶ 433 of 2209 and 1561 genes were shared among long-term and short-term practitioners
  - ▶ Gene analyses showed significant alterations in cellular metabolism, oxidative phosphorylation, generation of reactive oxygen species, and response to oxidative stress in long-term and short-term practitioners