Introduction to Symposium: Epigenetics and Home Visiting

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HARC Collaborative Science of Home Visiting Meeting

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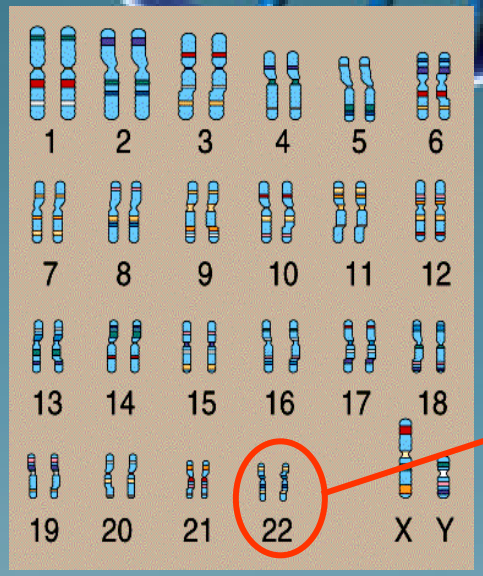
Purpose of the Symposium

- Introduction to epigenetics
- Integration with developmental science
- Relevance to understanding adversity
- Intergenerational risk and resilience
- Examples of studies
- Future applications to home visiting research agenda

Basic Genetics

- Humans have 23 pairs of chromosomes
- DNA with 5 canonical bases (adenine, thymine/uracil, cytosine, guanine)
- Each member of chromosome/DNA pair inherited from one parent respectively
- Chromosomes each contain many genes
- Genes can have many variants
- DNA transcribed → proteins (via RNA)
- More or less …

Schematic and Common Terms



genome

locus

gene

Site

[SNPs within sites]

Transcription/Translation

- RNA polymerase binds to promoter on gene
- DNA strands are pried apart → template strand
- Synthesize mRNA on template strand; zips DNA back as it goes
- mRNA moves from nucleus to ribosome
- Translation via tRNA to specific amino acids (based on 3-unit codons)
- We're all just a bunch of proteins

Stuff Happens

- Mutations across generations
- DNA damage within individuals (chemical and structural processes within cells)
- Repair processes occur when stuff happens
- Repairs are not always perfect
- Details are beyond our pay grade …

Basic Epigenetics

- DNA does not change across the lifespan
- Modifiers of DNA do occur across the lifespan (disrupting DNA structure)
- Multiple non-canonical base pairings; most discussed is 5-methyldeoxycytidine
- Non-canonical bases interact with complex geometric structure of DNA
- Regulate (often silence/dampen) DNA transcription/translation

Telomeres

- Telomeres are found at ends of DNA
- Buffer against stuff happening
- More telomeres indicate more buffering
- Telomeres are reduced during DNA replication/cell division
- Telomere replication can occur (telomerase)
- Implicated in aging and abnormal cell formation (cancer)
- Varies among individuals

How Do We Know any of This in Individuals?

- DNA is in cell nuclei
- Isolate DNA from cells (blood, saliva, other tissues)
- Sequence DNA (identify individual patterns of alleles – gene variation)
- Examine methylation at CpG sites (cytosine followed by guanine → methylation site) via pyrosequencing
- Telomere assays (TRF/QFISH, STELA, etc)

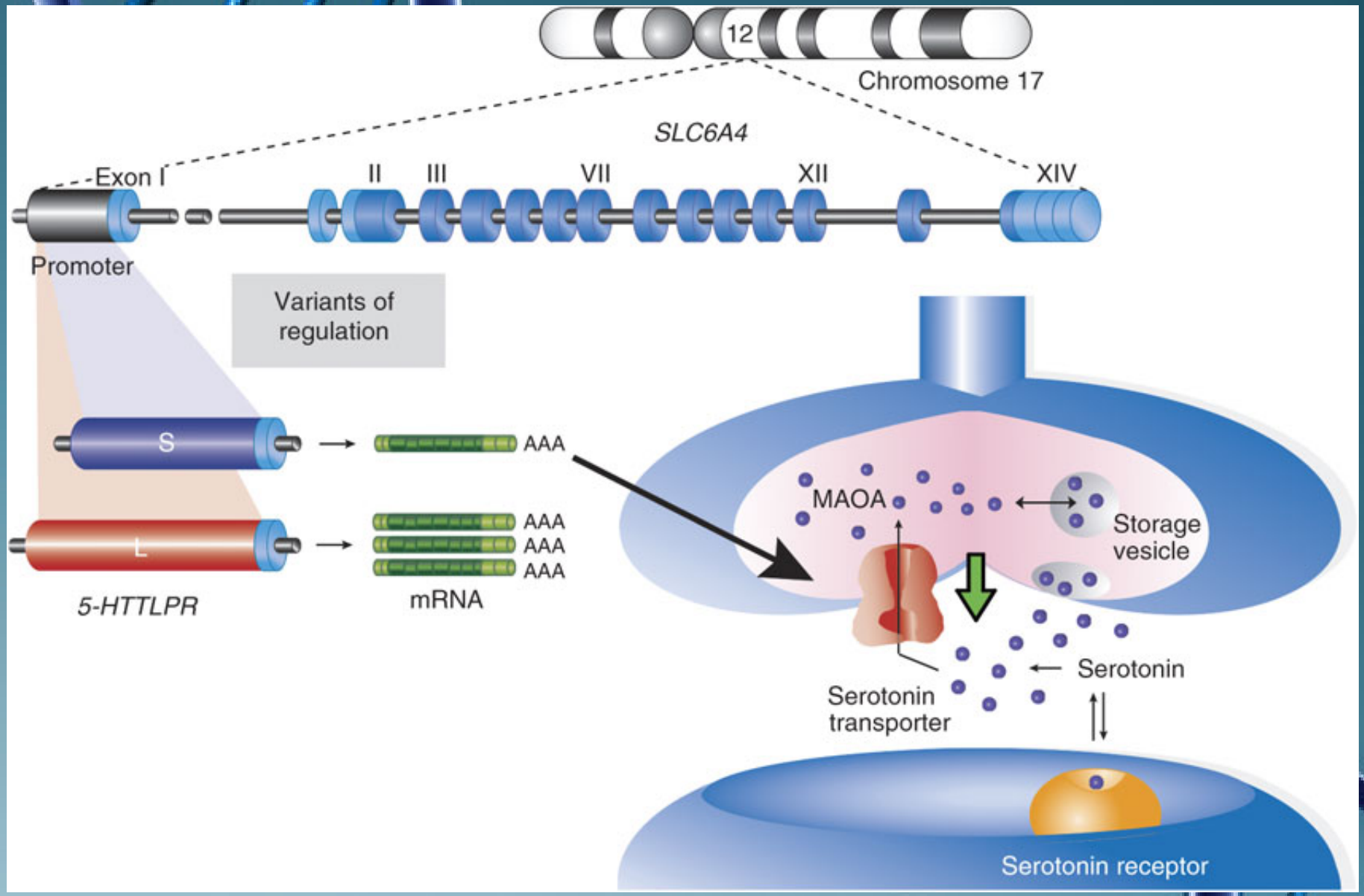
Why Should Home Visiting Researchers Care?

- Stress and adversity set off many chemical responses in humans
- Stress affects methylation of genes (can occur in both directions)
- Stress affects telomere length (generally shortening)
- Genes produce many things affecting behavior
- Cross-generational transmission (?????)

Gene Products and Behavior

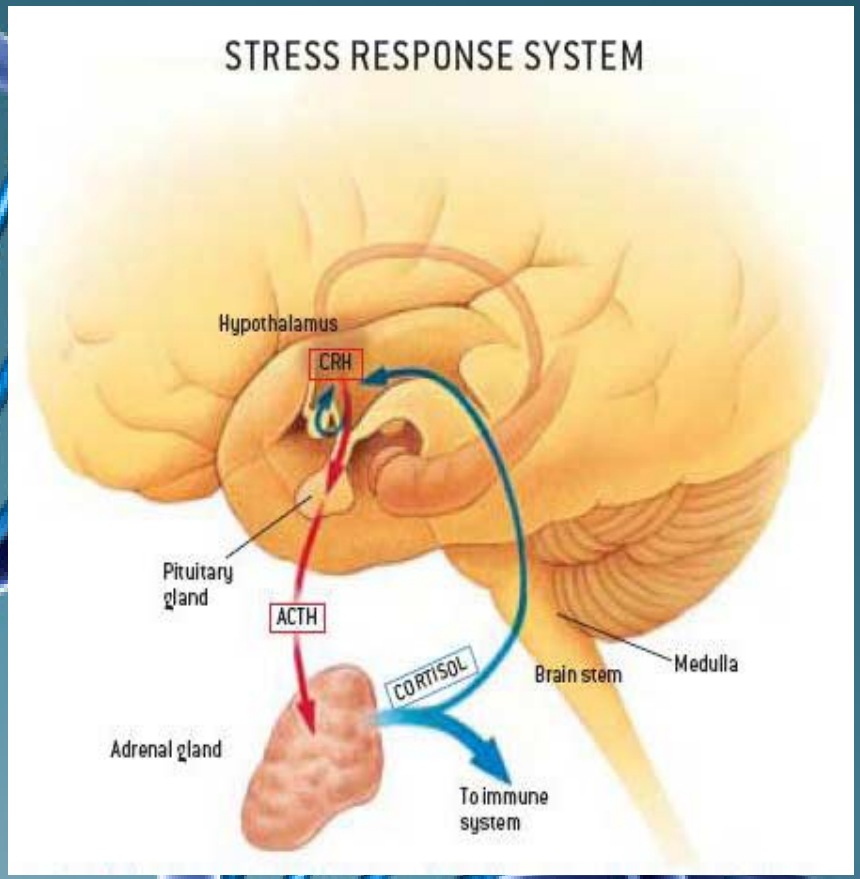
- HPA axis
  [cortisol production, stress response]
- Serotonin [mood]
- Immune system cytokines
  [inflammation]
- Dopamine [movement, reward, attention]
- Neural and non-neural implications
- Promote/inhibit cognitive, regulatory, and social processes + physical health implications

Gene Product Example

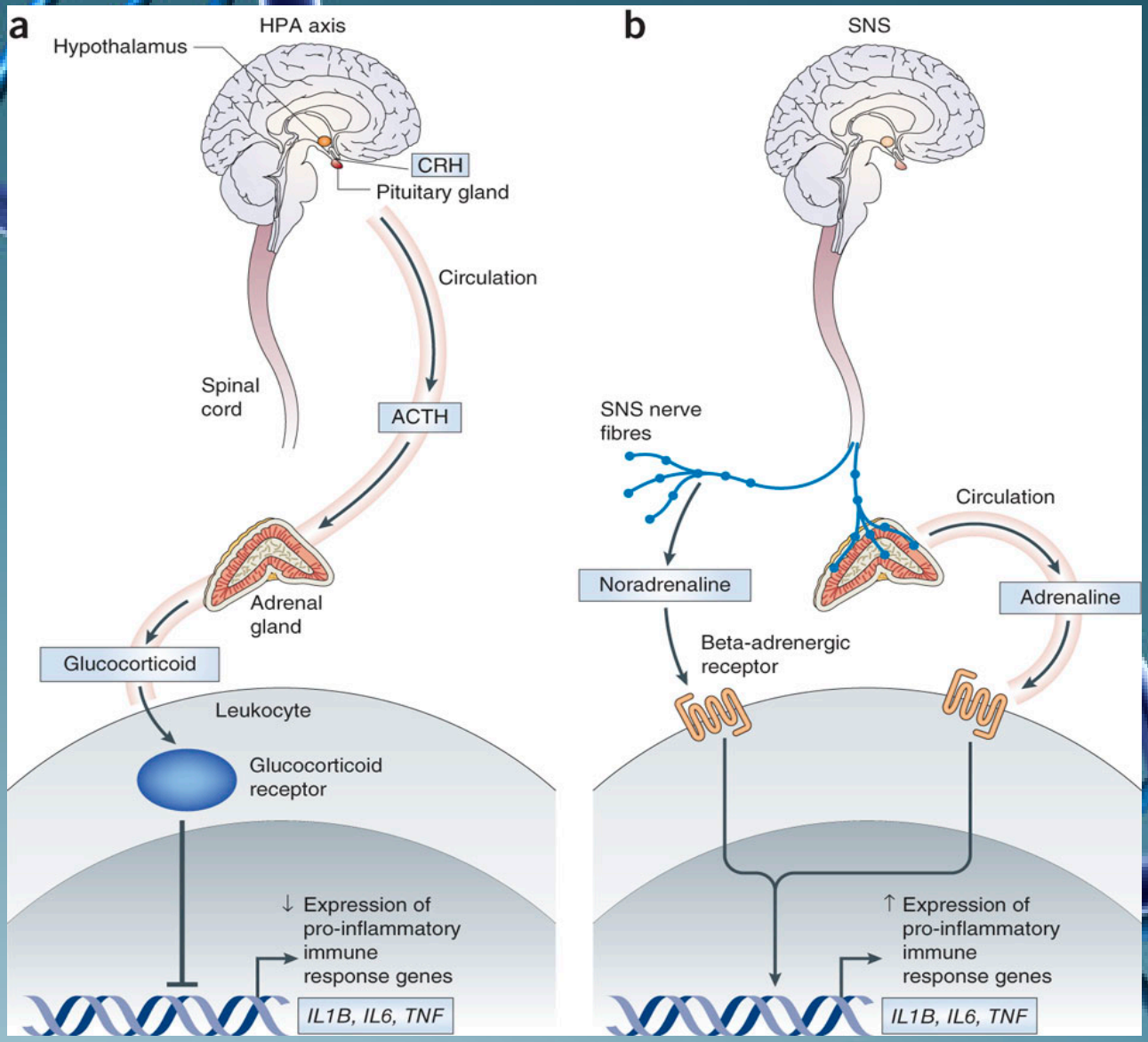


Gene Products and Complex Systems

- $CRHR_1$ (corticotrophin releasing hormone → cortisol)
- NR_3C_1 (glucocorticoid receptor)
- $FKBP_5$ (binding protein)



Effects are Far-Reaching



What Immediate Impact Might This Have on Home Visiting?

- Addressing preliminary research questions regarding epigenetic characteristics in HV cohorts (one example to follow)
- Identifying epigenetic changes associated with HV participation (parents and children)
- Identifying genetic/epigenetic predictors of HV treatment success

What Might the Future Hold for Home Visiting Research?

- Precision home visiting:
  - Identifying who will benefit from HV
  - Tailoring HV approaches to individual families
  - Tailoring HV personnel for individual families
- Development of gene therapies to promote resilience in the face of adversity
- in a galaxy far far away …

Important Considerations

- Epigenetic change is one mechanism for biological encoding of experience – an explanation for enduring behavioral response to stress
- Epigenetic change can be rapid
- Epigenetic change can move in all directions (reversibility)
- This is not genetic determinism – this is a reflection of on open dynamic system

Some Cautionary Notes

- Behavioral science has incorporated only a portion of what is known about epigenetics
- The research is in its infancy; little has been replicated
- Applications to real-life HV need to be thoroughly tested as we move forward
- Good ideas don't always yield effective interventions that help families