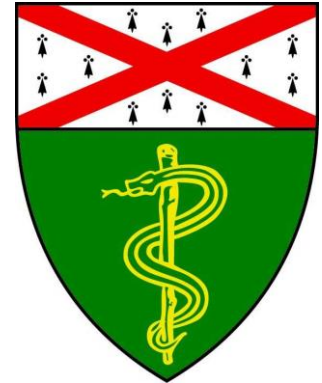


Meditation and T-cell Senescence

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Integrative Medicine

- What is Integrative Medicine
 - ‘Complementary & Alternative’
 - Evidence Based Medicine
 - Less invasive ways of treating disease
 - Changing the experience of the disease
 - Supporting the body’s innate ability to heal itself (placebo/meditation)



What Integrative Medicine Shouldn't be.....

- Anti-vaccine
- Anti-antibiotic
- Anti-conventional medicine
- An 'alternative'
- A panacea for disease
- 'Cutting edge medicine'



| | | Is the Therapy Effective? | |
|------------------------------------|------------|--------------------------------------|-------------------|
| | | <i>Yes</i> | <i>No</i> |
| Is the Therapy non-Invasive | <i>Yes</i> | Recommend | Tolerate |
| | <i>No</i> | Monitor closely or discourage | Discourage |



Brief introduction to meditation

- Consciously directing your attention
- “I’m going to go meditate on that”
- Meditation: meditatum, “to ponder.”
- Practice



A (VERY) Brief history

- Earliest references in Hindu scriptures (5th-6th century)
- Initially developed by Hindus to get closer to God (Brahman)
- Hinduism and Buddhism split
 - Hindu: closer to God
 - Buddhism: Interrelatedness
- Scientific History:
 - Howard Benson
 - **Jon Kabat Zinn**
 - Richard Davidson



Many Different Types

- Transcendental Meditation
- Mindfulness/MBSR
- Forest Bathing
- Guided Meditation
 - Compassion
 - Guided imagery
- Etc. Etc. Etc.



Meditation and the Immune System in Brief

- Most studies (1) pre and post MBSR course (2) Long Term Meditators (30 minutes/day for 2-3 years)
- Inflammatory Markers: Decreased IL-6, increased IL-10, decreased TNF- α
- Transcription Factors and Gene Expression: Decreased NF- κ B in PBMC
- Decreased expression of pro-inflammatory genes (RIPK2 and COX2 with changes in histone deacetylase)
- Cell Counts: Increased CD4+ in HIV patients
- Ig Response: significantly greater influenza titers

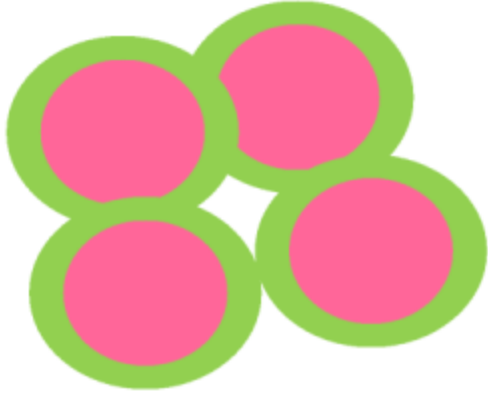


Senescence/Immunosenescence

- Cellular senescence
 - Response to cellular aging (ie human aging) and stress
 - Highly stable cell cycle arrest that is elicited in response to stresses
 - Growth arrest limits replication of old or damaged cells
- Immunosenescence
 - Diminished adaptive immune competence
 - Leads to reduced infection resistance, decreased vaccine response and pro-inflammatory traits

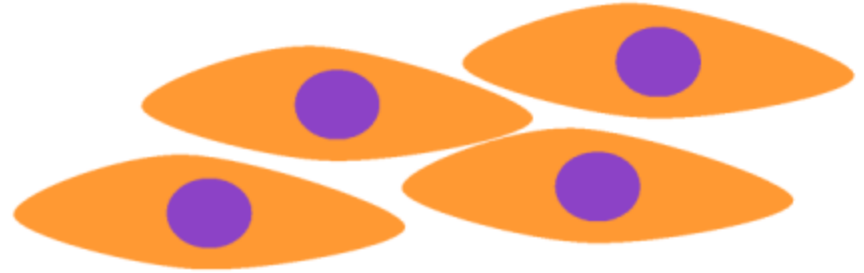


Cell Intrinsic Factors



- Telomere shortening
- Change in cellular phenotype
- Altered differentiation status
- Altered proliferation status
- Defects in homing properties

Environmental Extrinsic Factors



- Tissue disorganisation
- Accumulation of different cell types
- Pro-inflammatory environment
- Change in the niche area
(eg ECM, adhesion molecules, chemokine production)



Immune Senescence



T-cell Senescence

- Characterized by
 - telomere shortenings,
 - phenotypic change (loss of CD28 expression)
 - cell cycle arrest
- Proteins p16, p21, and p53,
 - normally inhibit cell cycle
 - accumulated in senescent cells
- Defective killing abilities and the development of negative regulatory functions
- High levels of senescent T cells in older people but also found in younger patients with autoimmune disease and chronic viral infection



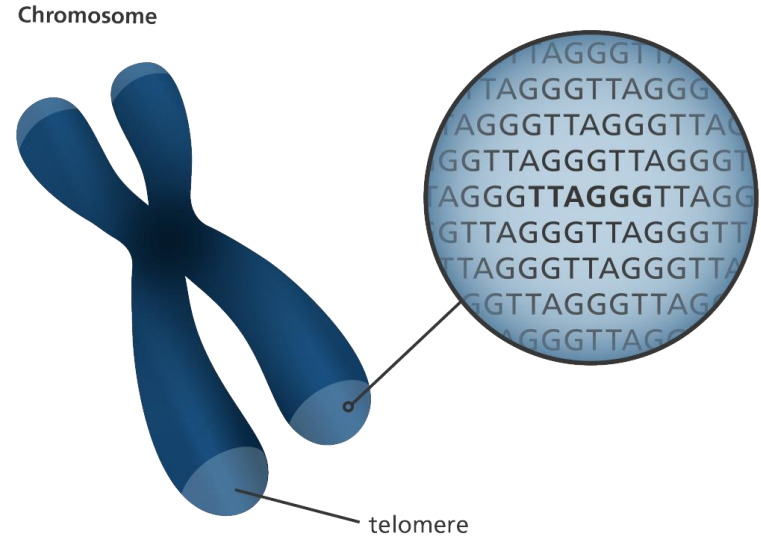
Immunosenescence and Disease

- Increased susceptibility to infection
- Increased cardiovascular disease
- Contributes to neurodegenerative disease
- Contributes to cancer
- Contributes to DM2
- May increase likelihood of autoimmunity



What we know about meditation and cell aging

- Most data comes from telomere length and telomerase activity
- All showed increase telomerase activity
- Increased telomere length in PBMC



CD8+ Cell Aging and use of CyTOF

- Insoo Kangs Lab

- CyTOF: Mass cytometry - uses heavy metal ions
- Allows measurement of 40+ molecules/markers from one tube
- Can be analyzed to show high-dimensional relationships of individual molecules
- Used CyTOF to analyze markers CD8+ cell aging



Findings

- CD8 cell markers of senescence
 - Decreased CCR7
 - Decreased proliferation
 - Decreased CD27 expression (naive cell marker)
 - Decreased CD62L (cell adhesion molecule)
- IL-7 receptor alpha (low vs high) CD8+ EM T cells revealed an age-associated signature linked to influenza vaccine response in older adults



Plan

- Recruit participants in MBSR course as well as long term meditators.
- Compare CD8 senescence markers pre and post 8 week MBSR course
- Compare CD8 senescence markers in long term meditators versus healthy controls



Markers

- CD4/CD8 ratio
 - TREC
 - Telomere Length
 - Telomerase activity
- CD8 Markers:
 - CD57
 - CCR7
 - CD27
 - CD62L
 - IL-7ra
 - CD52
 - CD45RA/RO
 - Tbet
 - PD1
 - Granzyme B
 - Perforin



Thank You

- Insoo Kang MD
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- Suzanne Cassel MD, PhD
- Deborah Levinson



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Anergy vs Exhaustion vs Senescence

- Anergy
 - Naive T-cells
 - Induced hyporesponsiveness with low IL-2 production
 - Low co-stimulator or high co-inhibitory stimulation
 - Induced tolerance (protects from AI dz)
- Exhaustion
 - Effector T cells
 - decreased cytokine expression and effector function,
 - Occurs when T cells are chronically activated at sites of chronic inflammation (cancer, chronic infection etc)

