Promoting Optimal Results in a Regen Setting

Dr. BT Watts DC CSCS CFMP Pn1

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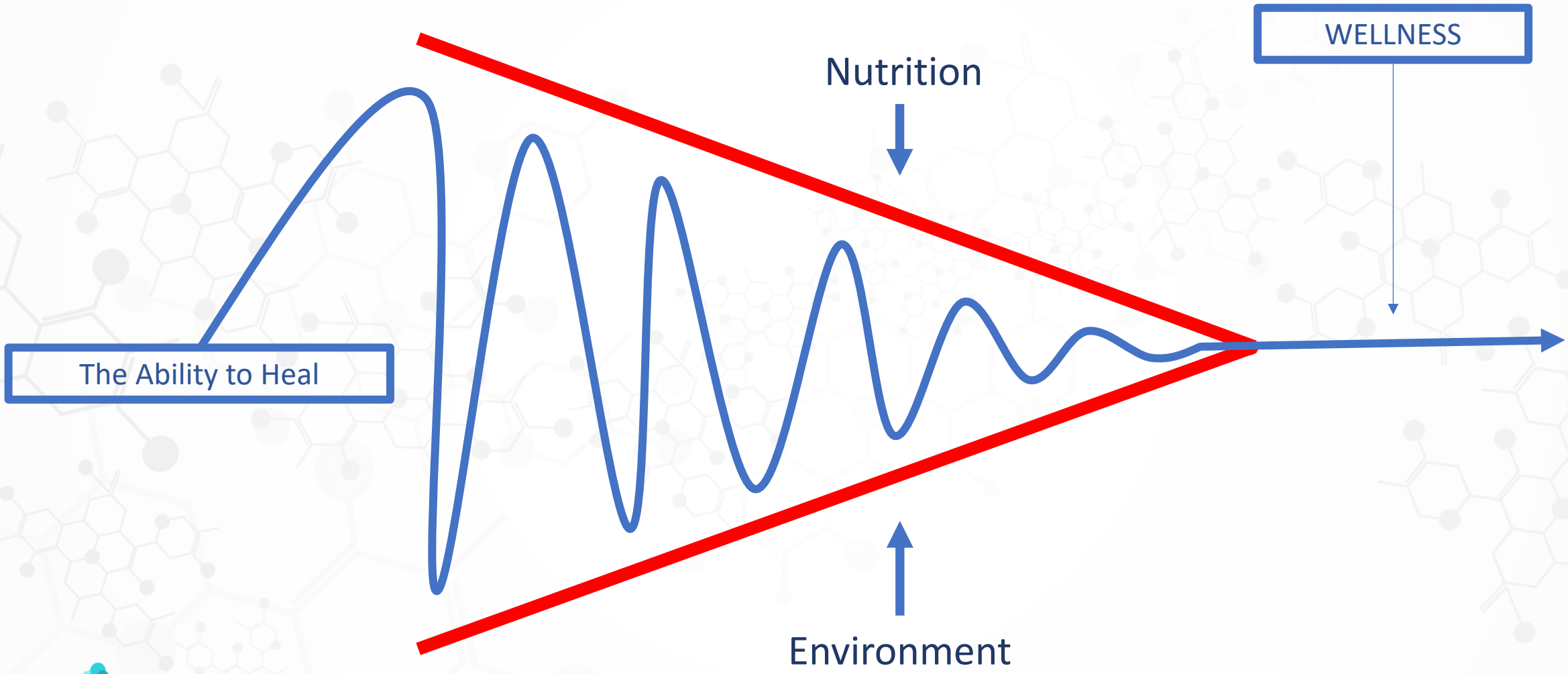
Disclaimer

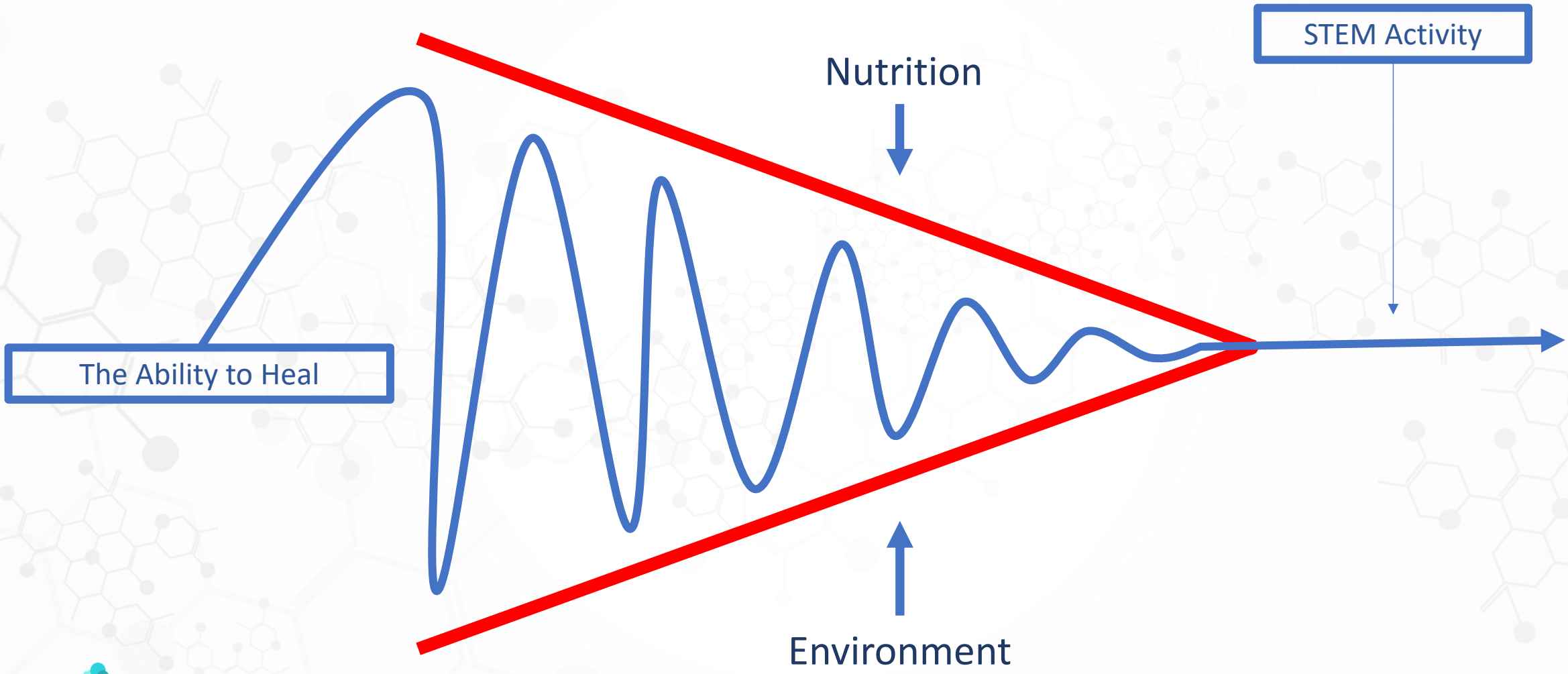
- *Information in this presentation is not intended, in itself, to diagnose, treat, reverse, cure, or prevent any disease. While this presentation is based on medical literature, findings, and text, The following statements have not been evaluated by the FDA.*
- *The information provided in this presentation is for your consideration only as a practicing health care provider. Ultimately you are responsible for exercising professional judgment in the care of your own patients.*

Lifestyle + Genetics = Chronic Health IMPROVEMENT

Protocols



Protocols



Review

Rheumatoid arthritis: From autoimmunity to synovitis and joint destruction

Marie-Christophe Boissier [a, b], Luca Semerano [a, b], Salima Challal [a, b], Nathalie Saidenberg-Kermanac'h [a, b], Géraldine F[illegible] [a, b]

outside the joints. The interactions between genes and environment are crucial in all stages of the disease, involving namely genes from major histocompatibility complex locus, and antigens such as tobacco or microbes (e.g. *Porphyromonas gingivalis*). T and B cells are activated as soon as the earliest phases of the disease, rheumatoid arthritis appearing as a Th1 and Th17 disease. Inflammatory cytokines have a considerable importance in the hierarchy of the processes involved in RA. The joint destruction seen in RA is caused not only by cytokine imbalances, but also by specific effects of the Wnt system and osteoprotegerin on osteoclasts and by matrix production dysregulation responsible for cartilage damage. Both innate and adaptative immunity demonstrated their respective cornerstone position in rheumatoid arthritis, since targeted treatments has been efficiently developed against TNF-α, IL-6 receptor, IL-1β, CD20 B cells and T-cell/Dendritic cell interactions.

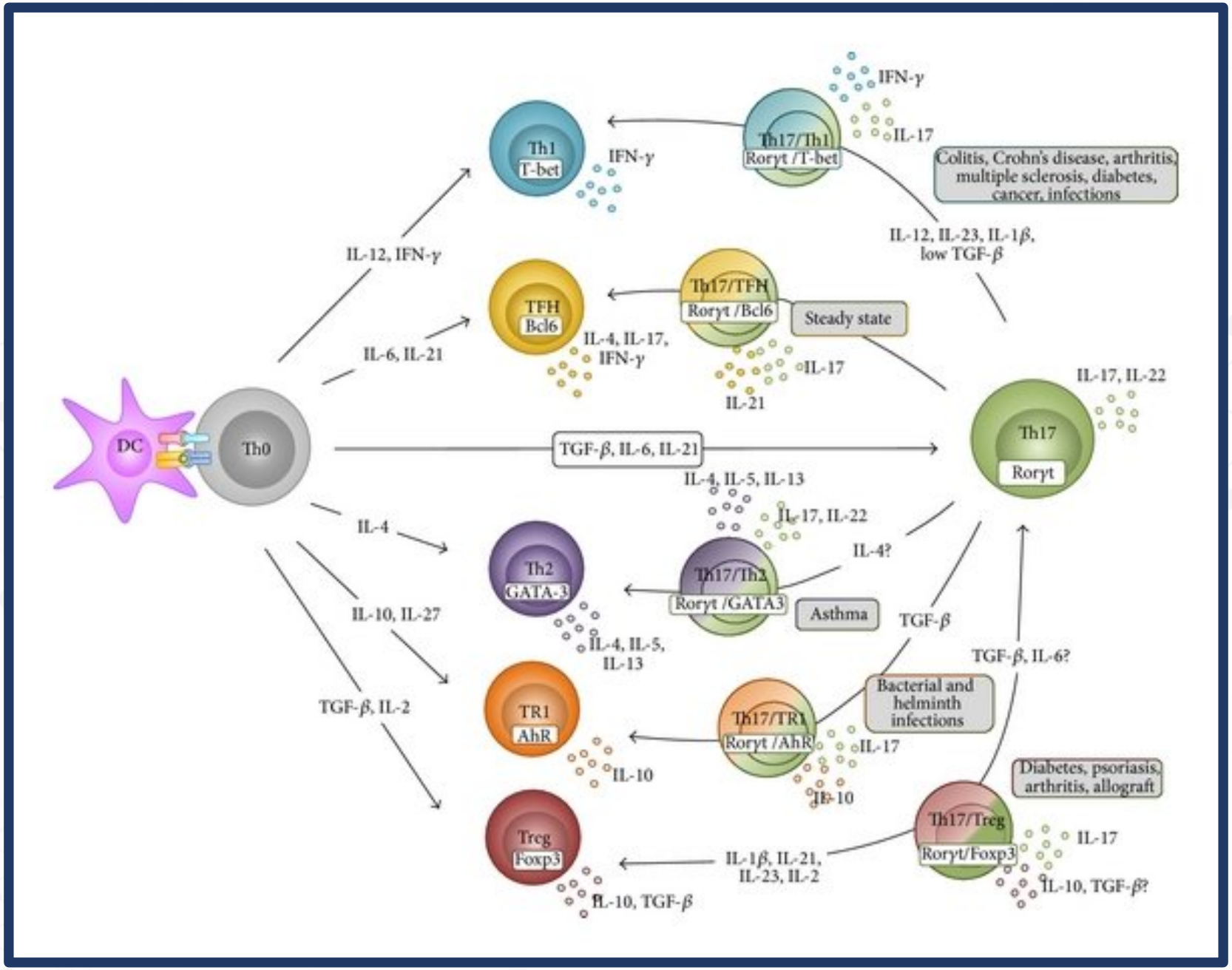
Review > Adv Immunol. 2012;115:45-71. doi: 10.1016/B978-0-12-394299-9.00002-3.

Autoimmune arthritis: the interface between the immune system and joints

Noriko Komatsu [1], Hiroshi Takayanagi

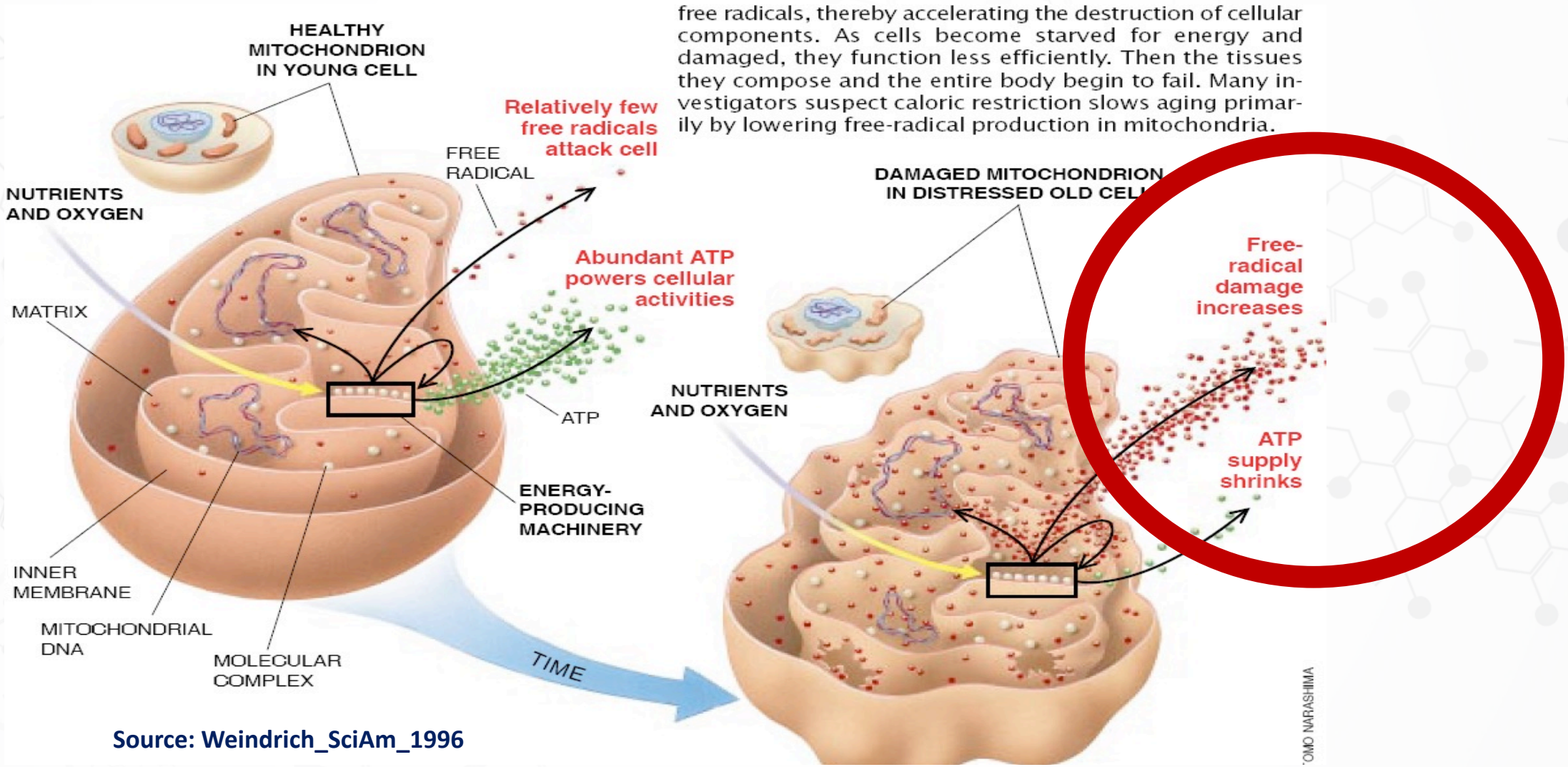
Affiliations + expand

research has shown that CD4(+) T cells, especially IL-17 producing helper T (Th17) cells, play an important role in RA development. However, it still remains to be clarified how the systemic immune response results in the local joint disorders. Studies on animal models of RA have shed light on the importance of the interaction between immune cells and joint-specific mesenchymal cells. In particular, joint-specific mesenchymal cells contribute to the Th17-mediated augmentation of the inflammatory phase in RA by promoting the migration of Th17 cells to the inflammatory joint and then homeostatic proliferation with increase in IL-17 production. In addition, recent progress in osteoimmunology has provided new insights into the pathogenesis of the bone destruction phase in RA. Of note, Th17 cells have been shown to enhance the differentiation of osteoclasts via joint-specific mesenchymal cells. Thus, the interaction of CD4(+) T cells and nonhematopoietic mesenchymal cells in joints plays a key role in RA pathogenesis during both the inflammatory and bone destruction phases. Focusing on this interaction will lead to a better understanding of the mechanism by which the systemic immune response results in local joint disorders and also helps



https://www.researchgate.net/publication/283965918/figure/fig2/AS:329918396289024@1455670083081/Th17-cell-plasticity-T-helper-cells-differentiate-from-naive-T-cells-Th17-cells-are.png

Mitochondria Deteriorate with Stress



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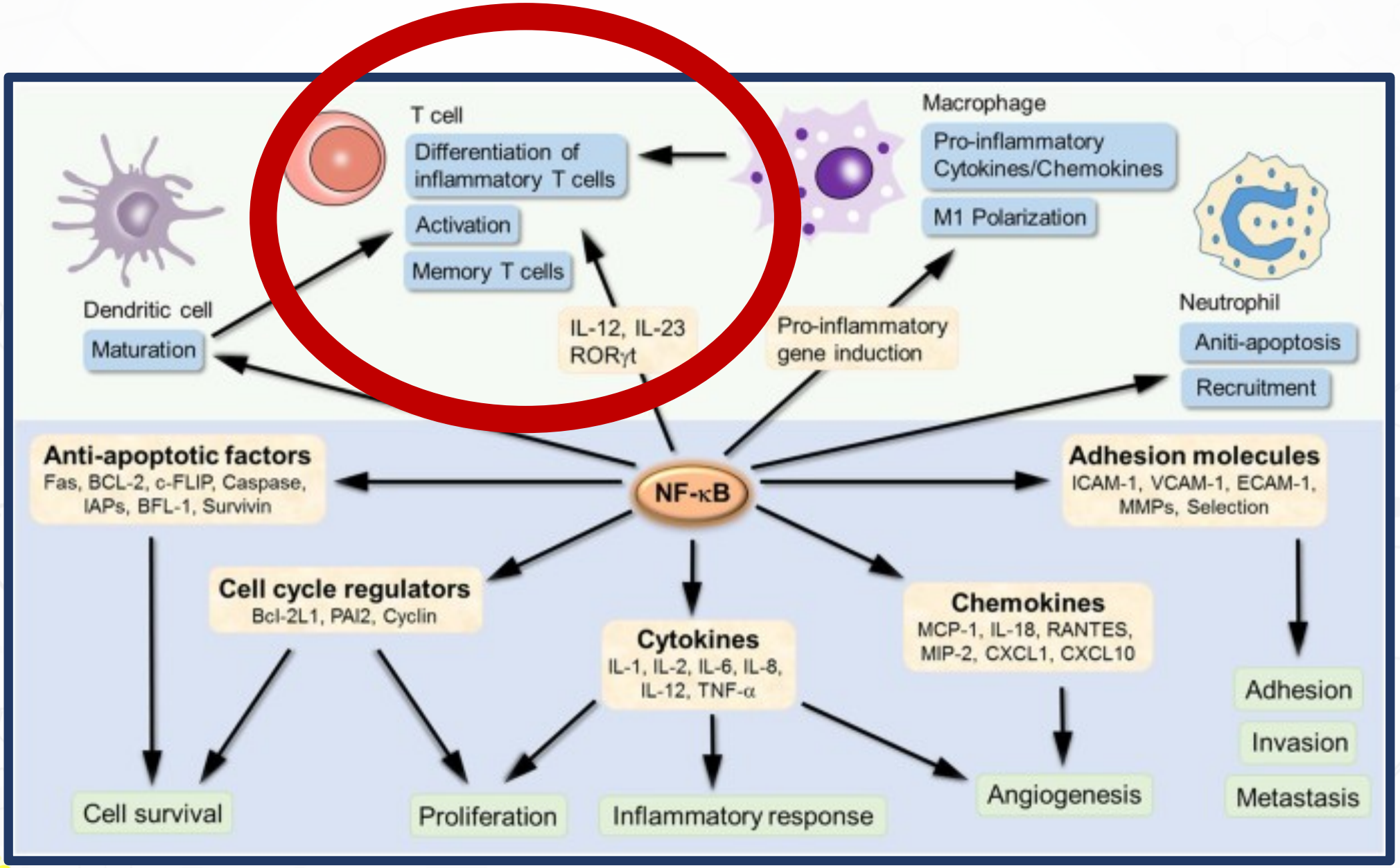
Standard American Lifestyle– All the fires.



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PMID: 19242274

Introduction to Stem Cell Therapy

Jesse K. Biehl, B.S., Ph.D. candidate[1] and Brenda Russell, Ph.D., Professor[2]

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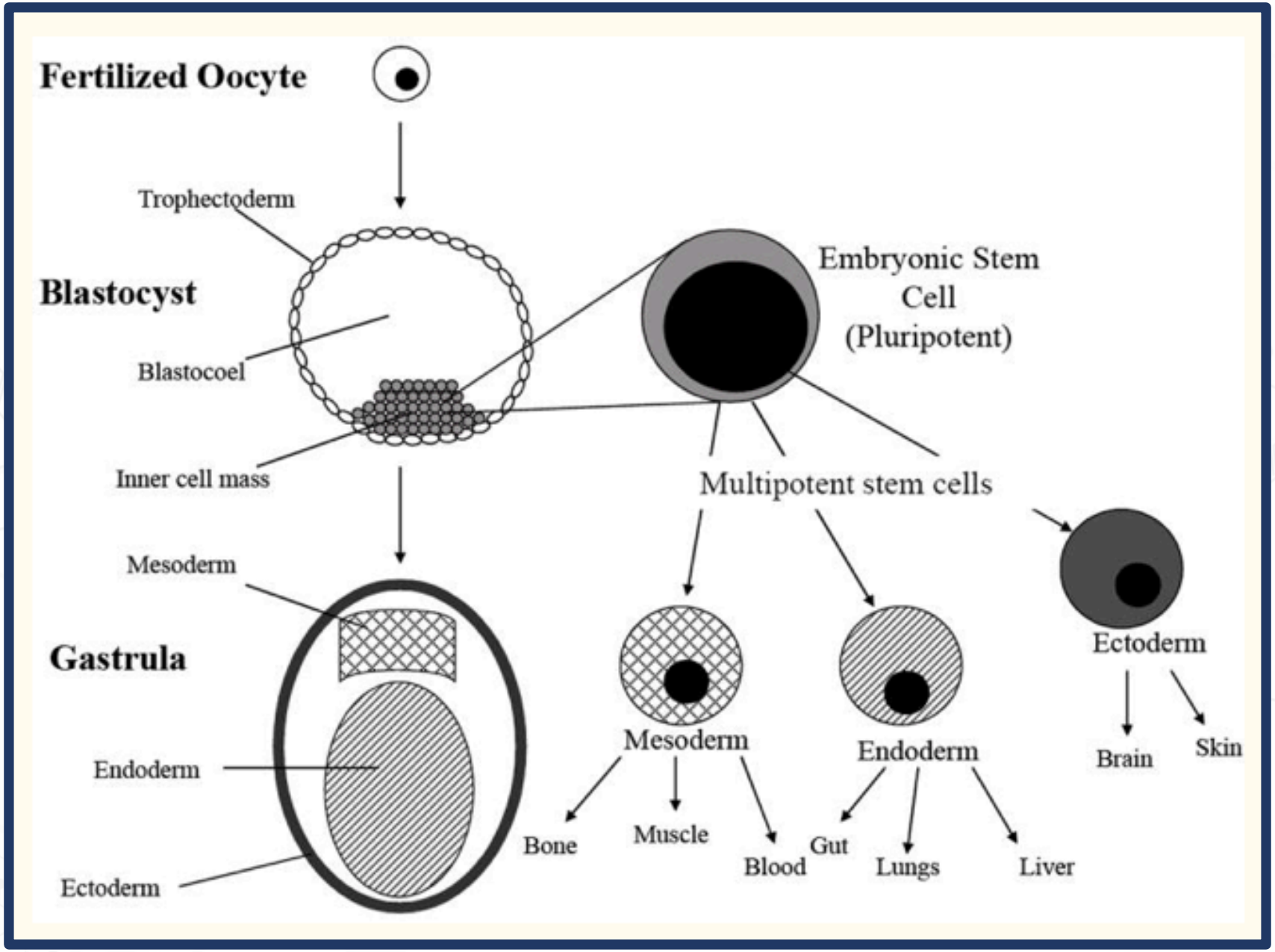
Stem cells have the ability to differentiate into specific cell types. The two defining characteristics of a stem cell are perpetual self-renewal and the ability to differentiate into a specialized adult cell type. There are two major classes of stem cells: pluripotent that can become any cell in the adult body, and multipotent that are restricted to becoming a more limited population of cells. Cell sources, characteristics, differentiation and therapeutic applications are discussed. Stem cells have great potential in tissue regeneration and repair but much still needs to be learned about their biology, manipulation and safety before their full therapeutic potential can be achieved.



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Tissue Eng Regen Med. 2017 Dec; 14(6): 679–698.
Published online 2017 Nov 20. doi: 10.1007/s13770-017-0097-3
PMCID: PMC6171667
PMID: 30603520

Endogenous Stem Cells in Homeostasis and Aging

Ji Eun Lim[1] and Youngsook Son[1,2]

In almost all human tissues and organs, adult stem cells or tissue stem cells are present in a unique location, the so-called stem cell niche or its equivalent, continuously replenishing functional differentiated cells. Those endogenous stem cells can be expanded for cell therapeutics using *ex vivo* cell culture or recalled for tissue repair *in situ* through cell trafficking and homing. In the aging process, inefficiency in the endogenous stem cell–mediated healing mechanism can emerge from a variety of impairments that accumulate in the processes of stem cell self-renewal, function, differentiation capacity, and trafficking through cell autonomous intrinsic pathways (such as epigenetic alterations) or systemic extrinsic pathways.

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Endogenous Stem Cells in Homeostasis and Aging

Ji Eun Lim[1] and Youngsook Son[1,2]

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healthy environment for endogenous stem cells. A variety of epigenetic modifications and chromosome architectures are reviewed as an intrinsic cellular pathway for aging and senescence. A gradual increase in inflammatory burden during aging is also reviewed. Finally, the tissue repair and anti-aging effects of Substance-P, a peptide stimulating stem cell trafficking from the bone marrow and modifying the inflammatory response, are discussed as a future anti-aging target.

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Reactive oxygen species (ROS) and nitric oxide (NO) could also be important regulators in HSC aging. The accumulation of ROS in aged cells induces FOXO depletion, NF-κB activation, p38-mTOR activation, telomere shortening, DNA damage, and mitochondrial dysfunction [12]. Insulin and IGF activate the PI3K-Akt signaling pathway and phosphorylate FOXO, followed by inhibition of the expression of the anti-oxidant N-acetyl-L-cysteine [28]. After oxidative stress, HSCs increase NO levels, which results in loss of self-renewal, abnormal proliferation, and malignancy [12, 29].

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Endogenous Stem Cells in Homeostasis and Aging

Ji Eun Lim[1] and Youngsook Son[1,2]

Epigenetic changes in aged stem cells

Modifications to DNA/histones and non-coding RNA-mediated mechanisms are epigenetic events that play important roles in the regulation of stem/progenitor cell functions by changing the chromatin structure. Epigenetic changes in adult stem cells are critical during aging because they alter the function, clonal composition, and lineage fate of stem cells which have been regulated by intrinsic and extrinsic epigenetic modifiers. The activating H3K4me3 mark and the repressive H3K27me3 mark are bivalent domains thought to affect developmental gene expression. These bivalent domains also allow timely activation and repression in the absence of differentiation signals [94]. The H3K27me3 mark is essential for maintaining the repressed form of these genes, whereas the H3K4me3/1 mark could lead to activation upon induction of differentiation through external signals.

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Endogenous Stem Cells in Homeostasis and Aging

Ji Eun Lim[1] and Youngsook Son[1,2]

Author

SP is an 11 amino acid neuropeptide secreted from the peripheral terminals of sensory nerve fibers, where it acts as a neurotransmitter or hormone. Subsets of neurons in the central and peripheral nervous systems [162], non-neuronal cells including macrophages and T lymphocytes, immune cells, and bone marrow stroma [163, 164] express SP and other structurally related peptides [165], all of which are encoded by the same gene, preprotachykinin-1 (PPT-1). Moreover, the SP receptor neurokinin 1 receptor is expressed on a variety of non-neuronal cells, such as BMSCs, chondrocytes, osteocytes, osteoblasts, osteoclasts, and mast cells [166–168]. SP mediates pain perception, neuro-immune modulation, cell proliferation, and enhanced proliferation and differentiation of endothelial cells, all of which are expected from its local action: direct nerve innervation and direct cellular contacts [169, 170]. In addition to its local action, intravenously injected SP works systemically to mobilize $CD29^{+}$ stromal-like cells (namely BMSCs) from the bone marrow to the periphery blood, resulting in accelerated wound healing [153–161]. This new function of SP was initially identified as an injury-inducible messenger to trigger an endogenous wound healing mechanism, which recalls BMSCs mobilizing and homing to injured tissue.

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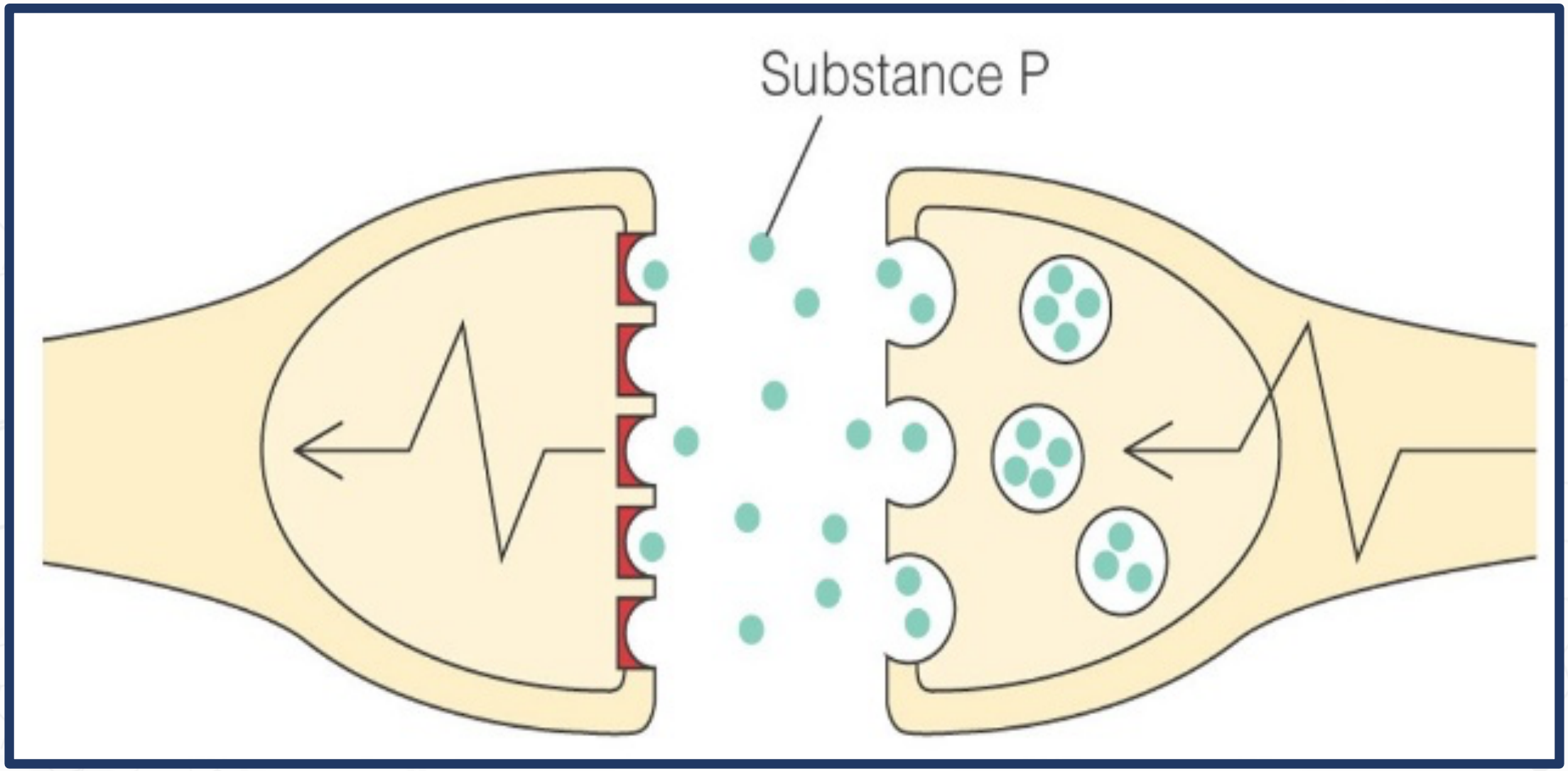
Endogenous Stem Cells in Homeostasis and Aging

Ji Eun Lim[1] and Youngsook Son[1,2]

monocytes and macrophages to become tissue-repairing M2 macrophages through NK-1R signaling that expresses arginase-1 and secretes anti-inflammatory cytokine IL-10 [172]. Furthermore, SP stimulated the emigration of monocytes from the bone marrow and their infiltration to the injured tissue of a rat with SCI. In consequence, adoptively transferred SP-induced M2 macrophages reached the SCI lesion site and enhanced SCI functional recovery. Collectively, SP could have an integral role in tissue repair by recruiting reparative stem cells from the bone marrow, along with immune modulation systemically, locally, and in the bone marrow stem cell niche. It is a potential systemic factor regulating the proliferation, maintenance, and function of HSCs, BMSCs, and EPCs. Because SP level in the blood is low in diabetic patients and those with chronic cardiovascular disease, its role in the pursuit of successful tissue repair, especially in the case of acute tissue injury, might not be executed properly in the aged and people with those diseases.



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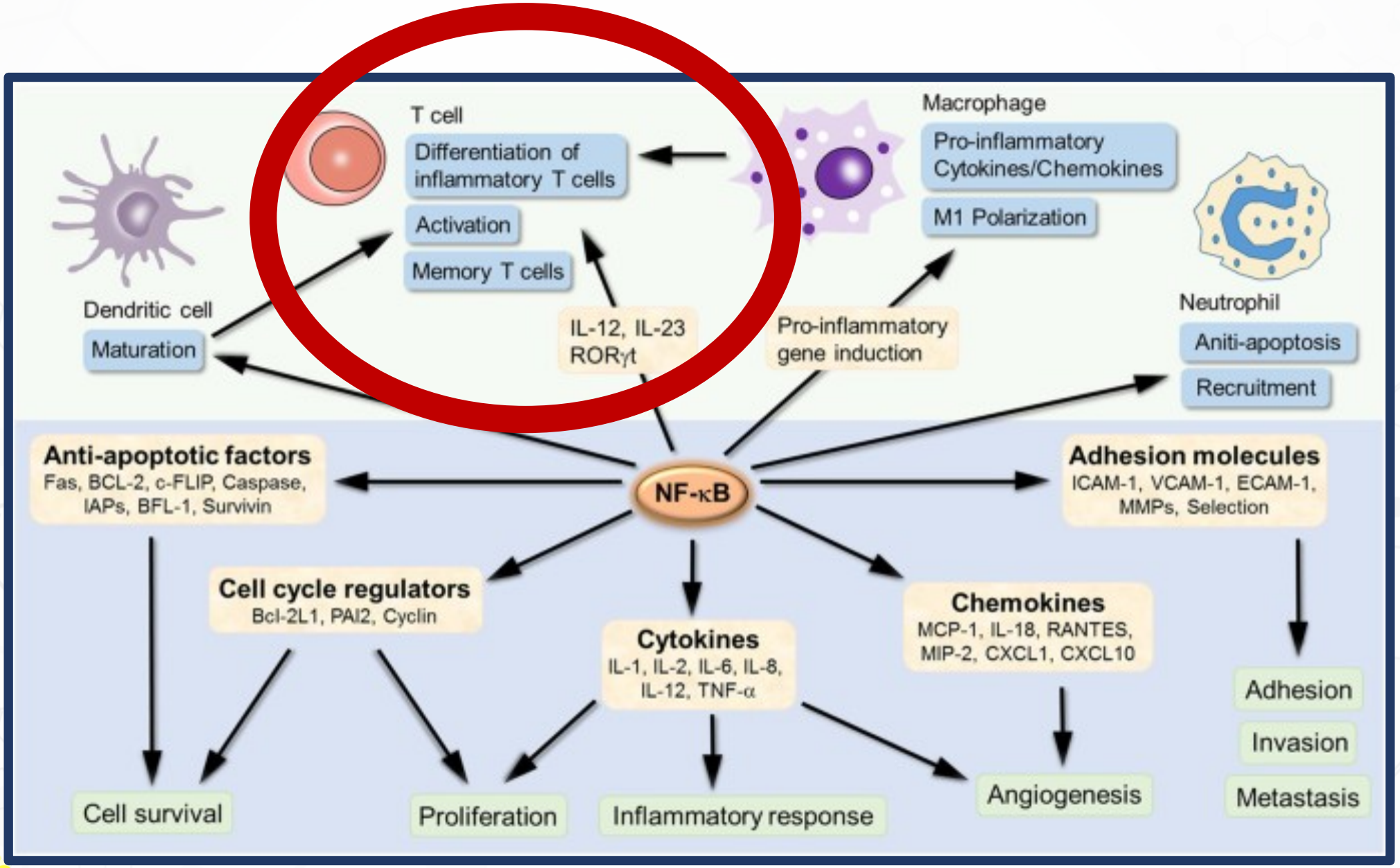
Autophagy and Stem Cells: Self-Eating for Self-Renewal

Natasha C. Chang*

Department of Biochemistry, Faculty of Medicine, McGill University, Montreal, QC, Canada

Historically, autophagy has been viewed as a non-selective housekeeping process that is upregulated during conditions of nutrient deprivation to provide the cell with an alternative source of energy. Our understanding of autophagy has evolved and increasing evidence demonstrates that autophagy is an active program that controls the metabolic status of the cell. In stem cells, autophagy is emerging as an important mechanism for the homeostatic maintenance, function and survival of long-lived stem cells. Autophagy can also influence cell fate decisions through its ability to influence mitochondrial content, energy production, and epigenetic programming (summarized in Table 1). Particularly in the context of aging and degenerative conditions that involve the decline of stem cell regenerative capacity, autophagy plays key roles in protecting stem cells against cellular stress and is transpiring as a viable target in regenerative medicine.



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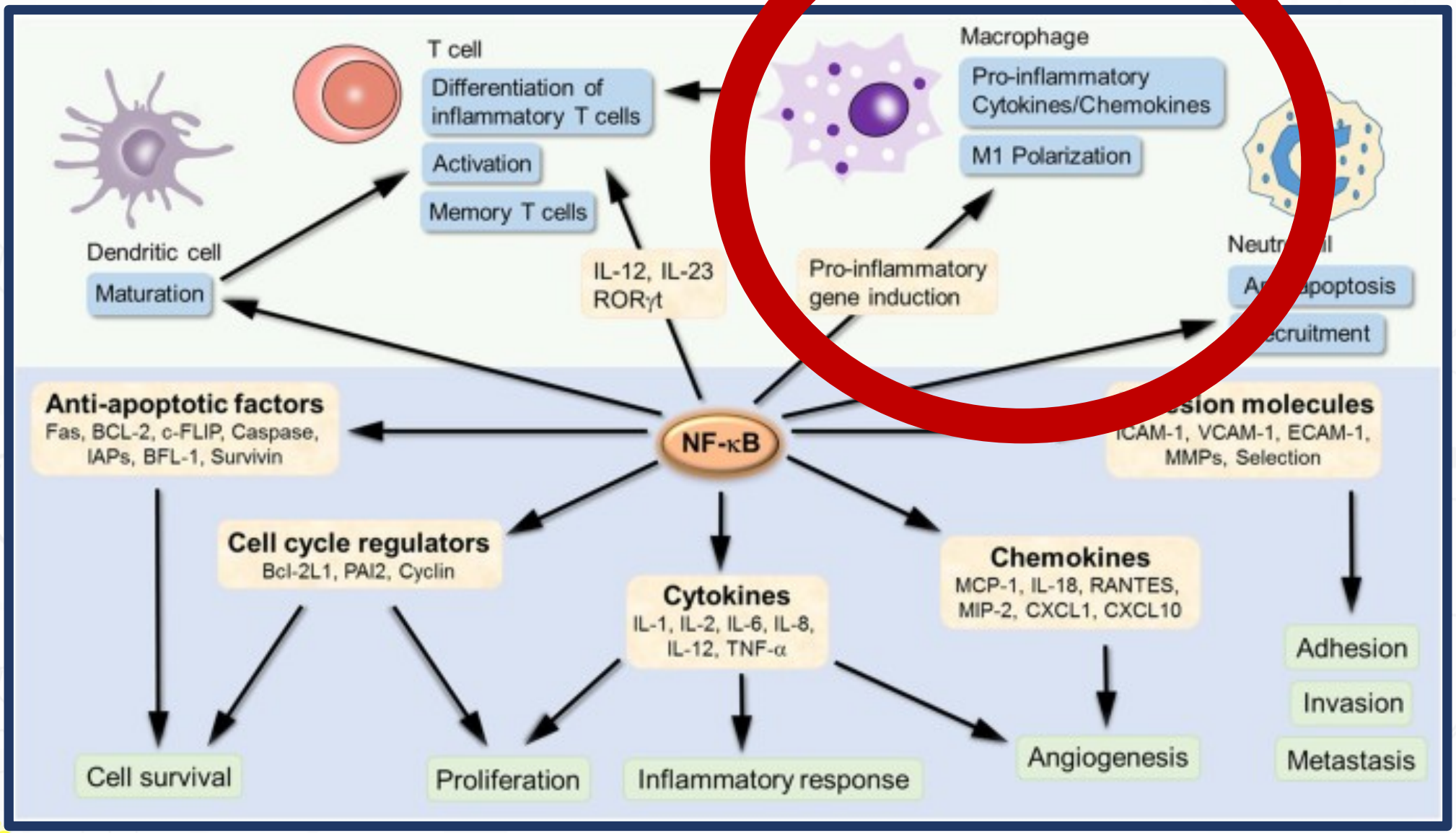
2 Types of Inflammation: Repetitive Use – 1 fire.

Standard American Lifestyle– All the fires.



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Biogenetix Regenerative Support Kit.

Biogenetix: 833-525-0001

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