Executive Summary of *REGEN: Rapid Epigenetic Enzymatic Nuclear Repair*

In human evolution, aging systems chronologically merged as follows: telomere shortening, mitochondrial aging, mutation accumulation, senescent gene expression, targeted somatic tissue apoptotic atrophy, as well as female reproductive tissue- apoptotic-atrophy. Certainly, periodic predation was the most prevalent episodic selection pressure in evolution. Effective defenses to predation that allow exceptionally long lifespan to evolve are shells, extreme intelligence, isolation, and flight. Without episodic predation, aging provides no advantage and as such aging systems will be deactivated to increase reproductive potential in unrestricted environments. While much of the human DNA maybe inactive or actually regulate 3' prime regions to effect transcription, we have been able to identify many important human genes at work and recently identified approximately 30,000 genes in the human genome affected by many environmental elements having strong epigenetic effects. This notion provides the potential of using epigenetic modifiers to repair DNA in humans possibly using first animal models.

In fact according to John Hawks (2014) - **Homo *sapiens*** are biologically predisposed to drink, eat, reproduce, and desire pleasurable experiences. After 30,000 years we are still evolving. Humans have rapidly evolved (e.g. straight black hair, blue eyes and lactose tolerance) are a few examples of recent traits. This is underscored because the switch from hunting and gathering to agrarian – based societies, allowing for enhanced reproduction and the chance for new advantageous mutations. It is likely that in the future our so-called human gene and future generations due to epigenetics for example, will likely be mosaics of past genome. The ability to build skyscrapers and cities suggest that we are different from our closest relative ***homo ergaster.*** While the brain of a chimp based on cognitive tests do as well as young children the human brain size has quadrupled over 4 million years including structures around our reward system.

DNA encodes vital information about cellular content and function. There are only two copies of each chromosome in the cell, and once the sequence is lost no replacement is possible. The irreplaceable nature of the DNA sets it apart from other cellular molecules, and makes it a critical target for age-related deterioration. To prevent DNA damage cells have evolved elaborate DNA repair machinery. Paradoxically, DNA repair can itself be subject to age-related changes and deterioration. Changes in efficacy of mismatch repair (MMR), base excision repair (BER), nucleotide excision repair (NER) and double –stranded break (DSB) pathway usage occur with age. We know now that old organisms have a higher load of DNA damage due to the less efficient DNA repair machinery. MMR is essential for maintenance of repeated sequences, as mutations in MMR genes are associated with a substantial destabilization of microsatellites, and microsatellite instability increases with aging in humans. In fact, all pathways of DNA repair (e.g. MMR, BER, NER, and DSB) become less efficient with age leading to an accumulation of mutations. These aberrant pathways are responsible for a number of premature aging disorders such as Progeria;

Cockayne Syndrome; Werner's Syndrome; Lison Syndrome, radiation syndrome and others. Apoptosis and senescence caused by DNA damage is upregulated with aging, which has been linked to alterations of at least one gene P53 activity but many others.

Most importantly, old organisms are more sensitive to stress. The stress response has been elicited by DNA damage and insulin/IGF1 signaling and stress induced aging augments the DNA repair machinery. Along these lines in this invention we are proposing the novel anti-stress agent N-Acetyl-L-Cysteine in combination of either KB220Z (previously patented) to promote brain dopamine release and affect DNA repair especially radiation induced damage. These effects include but not limited to: promote cellular oxygenation; decreased epidermal tyrosine phosphorylation (EGF); decreased PGE2 synthesis; increased epidermal phospholipases; increased GSH content; and decreased DNA breaks (parent cells, deletions, dicentrics). Other amino acids to combat aging include methionine, cysteine, taurine, tyrosine, lysine, and tryptophan. In this provisional application we are interested in targeting a number of important genes that regulate transcriptional profiling for CNS diseases including both neuropsychiatric and neurodegenerative disorders.

In summary- *This invention concerns methods to accelerate DNA repair mechanisms by coupling thermal elements both hot and cold to hasten and stop ongoing enzymatic processes that influence life-spanning genes along with novel anti-stress molecules which promote brain health through dopaminergic activation as well as induction of hypotonicity reduction, hypochromicity stabilization, hyperoxigenation, cryotherapy, Deinococcus radiodurans, to cause a natural polymerase chain reaction to reverse the aging process (histone blockers) while the individual receives treatment in a specially designed housing chamber allowing for thermal control we call "**Reprogramming Epigenetic Nucleotide Energizing Whole Body System (RENEWS)." We believe that success utilizing this novel technique may have tremendous impact on human health and well-being.***