UBIQUITINATION 16: YOUR EYE AS A CLOCK AND NOT A CAMERA

READERS SUMMARY:

1. IS YOUR EYE A CAMERA OR CLOCK?

2. HOW DOES NEGATIVE FEEDBACK CONTROL RUIN YOUR CLOCK?

3. IF TIMING IS OFF IN YOUR EYE, DO DISEASES SHOW UP OUT OF THE BLUE?

4. ARE CATARACTS AND GLAUCOMA A PREMONITION OF ONCOGENESIS?

5. HOW MUCH ATP DOES PROTEIN SYNTHESIS COST A CELL?

Your eye can be a clock or a camera. A blind man's world is bounded by the limits of his touch and he relies on his timing; an ignorant man's world by the limits of his wisdom; a successful man's world by the limits of his vision and sense of timing. Man is the most complex eukaryote. Therefore he has the most sophisticated time piece in his eye that controls protein turnover. Protein turnover is a synonym for ubiquitin marking.

Eukaryotes spend 80{a7b724a0454d92c70890dedf5ec22a026af4df067c7b55aa6009b4d34d5da3c6} of their total energy budget on protein synthesis. That process is controlled by ubiquitination rates in cells. This is why you need to understand ubiquitin. Once you master ubiquitin you can use that recovered energy to reverse illnesses. Each peptide bond requires 5 ATP to seal the bond. That amount is 5 times as much that is needed to polymerize nucleotides into DNA!! Each protein is reproduced in thousands of copies, which are continuously turned over by ubiquitin to repair wear and tear. Elevations of ubqutin marking are

usually associated with higher blood glucose and ammonia levels.
Medicine today treats the eye as a camera almost exclusively, when its most important physiologic role is as an optical clock. It turns out cataract formation and glaucoma are the best evidence that the timepiece in your eye is no longer working in concert with your gut, skin, or any of your cells properly. When this occurs diseases usually follow. Most people today view elevated blood glucose as a pathologic condition. When the clock in your eye is altered their is now another way to perceive an elevate blood glucose as a clinical sign of elevated ubiquitin ratio's in all proteins.
Glucose is normally fully capable of braking ubiquitin cycling when ubiquitin is coupled to the cell cycle by normal light cycles, but not when it is uncoupled and isolated due to altered light cycles. The reason glucose has this ability because it contain a strong blue light signal in it for the SCN in the eye to provide negative feedback for the SCN. This ability is lost when light cycles are uncoupled from the nitrogen cycle in the eye or gut. When it is isolated, glucose levels go through the roof to stop the PER 1 and PER 2 clock genes from turning over proteins by ubiquitin marking in cells. PROTEIN Turnover is the most energy costly activity a living thing does.

Most view the eye as a camera, but some of us see it as a clock first. HYPERLINK

In my recent webinar series for members on my site, (March through June 2015) I taught you about how the loss of negative feedback control in coupled biologic systems is the sentinel event for aging and disease generation. Moreover, I showed you what happens when you lose it in one side of the coupled event. There I used predator or prey to make the point. If you alter the balance of predator or prey the result is always the EXTINCTION of both animals. I have told you that in aging and neolithic disease generation that NAD^+ becomes altered in

relationship to NADH. The chronic loss of NAD^+ is the critical sign of a loss of negative feedback control of the ubiquitin cycle. Now for how this scales to your molecular circadian clock and your peripheral clock genes (CCG's). This same relationship also exists between the two coupled systems that control the eye clock protein timing mechanisms. When they are drowned in blue light they cause extinction of the gears that control your timing mechanism in every system in your body. Where it occurs first is where diseases manifest soonest.

The current model of the mammalian circadian clock includes two interlocking transcription-translation feedback loops comprised of several so-called "clock" genes and their protein products, which ultimately regulate the transcription of "clock-controlled" genes. These feedback loops consist of positive and negative components. The positive components include the basic helix-loop-helix-PAS domain transcription factors, CLOCK and BMAL1. These transcription factors heterodimerize, translocate from the cytosol to the nucleus, and bind to circadian E-box promoter elements that enhance the transcription of genes encoding the negative components PERIOD 1 & 2 and CRYPTOCHROME 1 & 2. The CRYPTOCHROME and PERIOD proteins feedback inhibit the transcription of the Cryptochrome and Period genes by blocking CLOCK/BMAL1-mediated trans-activation. The second feedback loop involves the trans-activation of the Rev-Erbα and Rora genes by CLOCK/BMAL1. The protein products of these genes compete for binding to RRE elements in the Bmal1 promoter, driving a daily rhythm of Bmal1 transcription and closing the second feedback loop. Rhythmic expression of these clock gene products produces circadian clock outputs by regulating transcription of clock-controlled genes (CCGs). At least some of these CCGs, including aanat, the gene encoding the penultimate enzyme in the melatonin biosynthetic pathway, contain circadian E boxes, which have a core nucleotide sequence of CACGTG and are activated rhythmically by CLOCK/BMAL1. Post-translational regulation, including phosphorylation, acetylation,

ubiquitination, sumoylation and proteasomal degradation are also important in the regulatory mechanisms generating the circadian oscillation. All of these coupled processes become unhinged from light signaling to affect nitrogen, water, and carbon flows in cells to cause many neolithic diseases.

SUMMARY:
Once your SCN timing mechanism goes haywire it is a matter of time before your circadian clock genes in tissues the SCN controls also goes haywire and result in diseases. What will be the ultimate result? EXTINCTION of both sides of the circadian timing mechanism and cancer is the ultimate result. It should be interesting to you that plants do not get cancer. There is a deep reason for this that will be covered in this series. Cataracts, glaucoma, and many autoimmune conditions are earlier appearing neolithic diseases that often pre date oncogenesis because of an elevated ubiquitin rate.

CITES:
1. Herzog ED. Neurons and networks in daily rhythms. Nat Rev Neurosci. 2007;8:790–802.
2. Yamazaki S, Numano R, Abe M, Hida A, Takahashi R, et al. Resetting central and peripheral circadian oscillators in transgenic rats. Science. 2000;288:682–685.
3. Ko CH, Takahashi JC. Molecular components of the mammalian circadian clock. Hum Mol Genet. 2006;2:R271–277.
4. Munoz E, Baler R. The circadian E-box: when perfect is not good enough. Chronobiol Int. 2003;20:371–88.
5. Gatfield D, Schibler U. Proteasomes keep the circadian clock ticking. Science. 2007;316:1135–1136.