WHY DO WE SLEEP?

READERS SUMMARY:

1. Why do we sleep?

2. Does sleep control metabolism and cell growth?

3. Do all living things sleep? How long is too long or too little?

4. What are the stages of sleep?

5. Can sleep help prevent degenerative aging diseases and cancer?

6. Is sleep the primordial condition or did it evolve as we did?

Why do we **sleep**? Well, most sleep researchers are losing sleep trying to find that out as well right now! It appears to be an elusive target. What we do know , is that when you don't sleep a lot of bad things happen. Disease propagation is one and psychosis and eventual death are others. Most people don't realize that lack of sleep is deadly for humans, but it clearly is. Sleep appears to most to be a restorative physiologic process. That is what they say now; I am not so sure about this as yet. If sleep is restorative, as they say, what are its targets? We have no idea what the targets really are as of now. What we do know about sleep is that it is incredibly important biologically because every animal has biologic sleep requirements. It seems evolution has strongly naturally selected sleep as a trait throughout all life systems. Since the real answer remains elusive, let's talk about some things we do observe about sleep. Sleep effects every aspect of human physiology that we currently study. Stem cells, immune function, metabolism, energy biogenesis,

cognition, learning and memory for example. It also is intimately tied to metabolism and to **cell cycle function**.

For evolution to work, a cell first must adapt to its environment. So the first thing a cell would see in an earth day is a period of day and night. It also has to eat to make energy and it also has to control its own cellular division. So in essence the **circadian cycle** has to “yoke” to the metabolic cycle and its growth cycle. Evolution apparently agreed with that assessment because we now know it to be true. When it is night time, the cell becomes more reduced chemically and electrically. (A lower redox state like we saw in the mitochondrial series). During a low redox time, cells are usually recycling their components using **autophagy**. During the day while energy is being made to explore the environment, the cell is more oxidized because of increased leakiness of the mitochondria. Another interesting coupling occurs between the circadian cycle with the cell cycle. They are linked via the PER 1 and PER 2 genes. PER 2 directly effects the cell cycle in **mitosis**. Mitosis is the phase in the cell that occurs just before cell division to generate an offspring. The mammalian period 2 gene plays a key role in tumor growth in mice; mice with a mPER2 knockout show a significant increase in tumor development and a significant decrease in apoptosis (levee 19). This is thought to be caused by mPER2 circadian deregulation of common tumor suppression and cell cycle regulation genes, such as Cyclin D1, Cyclin A, Mdm-2, and Gadd45Î±, as well as the transcription factor c-myc, which is directly controlled by circadian regulators through E box-mediated reactions. This means that sleep is tied directly into to cell cycle functioning and directly into cell mediated immunity at some level. It appears that sleep directly effects the chronic diseases of aging and likely plays a role in cancer development.

Our sleep has characteristics that allow us to study it. Sleep is broken into (rapid eye movement) **REM** and (non rapid eye movements) **NREM** patterns. The NREM pattern has three Stages denoted N1, N2, N3. Very little dreaming occurs in any of these stages. N1 stage is characterized by the transition of alpha waves to theta waves on an **EEG**. This is the stage of a drowsy sleep. N2 is a stage where we see sleep spindles and K- complexes. This stage makes up 45-55% of our total sleep. N3 is deep sleep characterized by delta waves. This is the stage where we see sleepwalking, enuresis, night terrors and parasomnias to occur. REM sleep accounts for about 25% of our sleep in adult humans. This is where we dream. It is characterized by a low voltage EEG pattern and paralysis. I guess a general paralysis during REM makes sense in case we decided to act out our dreams as they vividly occur!

Our patterns and depth of sleep decline as we age. As we age, our sleep declines in duration and effectiveness too. As we age, our immune system and cellular metabolism also appear to decline in concert. This is why as we age we gain more fat over muscle and why we face diseases of aging at a more rapid rate. Remember these cycles are all yoked together. Babies sleep 18 hours a day while a supercentenarian sleeps around six hours a night. This is known as sleep degradation. What if we were able to restore sleep in an older person? Could that effect aging and degeneration? I think the answer is firmly yes. I think sleep hold the potential to a lot of human optimization. And that is why sleep has its own levee in the QUILT (levee 28). The reason it is not higher is because we know so little about how it integrates function into metabolism and in the cell cycle. We also know from meta analysis studies on sleep that sleeping too long or too short affects our longevity. If we sleep below 5.5 hours or longer than 9.5 hours consistently we tend to live a short life with disease. Ideal human sleep is around 7.5 hours a night. We

certainly will be exploring why this is the case.

My current belief about sleep is a bit more radical. Think about this for a minute. Did we evolve sleep? Or did we evolve wakefulness? I think sleep is the primordial condition. Think about it for a minute. There is some logic to it. Evolution is based upon finding an environmental niche and exploiting it. A behavior is then naturally selected for according to Darwinian theory. To be active requires wakefulness. In an evolutionary mindset maybe sleep is where we all start and evolution selected us to evolve wakefulness so we could explore our environment. After all, at the dawn of life what did an organism need to do? Think about it. What am I? What do I need to be and how do I preserve myself? It needed to have a sense of self and to distinguish itself from the environment. When you are awake in the environment you have to adapt to the environment, you change. To monitor that change we need to have homeostatic pathways to keep you rooted so that you know exactly what you are up to! When we sleep we cannot evolve to our environment; but, when we are awake, we can perceive changes to our environment. I think wakefulness is a prerequisite for evolution and I think sleep is our primordial condition. This levee is going to be a fun one to explore.