The Life Clock and Paley's Watch: The Telomeres

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Abstract

The complex telomere structure eloquently demonstrates an example of a precise mechanism which in numerous ways parallels a mechanical watch time piece. The structure also provides a possible mechanism to explain the wide variations in longevity of humans found in history, specifically those described in the Biblical record. This mechanism may also give us insight into the Biblical fall and the change in longevity that has occurred since.

Introduction

One of the most convincing proofs for the existence of a creator has been the existence of a creation. Eloquently propounded by Saint Thomas Aquinas and other prominent church fathers, this line of evidence was more recently elaborated by William Paley and many others since. Paley compared the intricacy and design of living organisms to mechanical watches. He concluded that it is immediately apparent when one holds a watch that it was designed by an intelligent engineer and built by a skilled craftsman. Likewise, the understanding of biology which was just beginning to develop in Paley's time has helped to convince many persons of the validity of the logic that design proves a designer.

Scientists now recognize that the complexity of a single eukaryotic cell is much greater than was known about most entire organisms in Paley's day. We can now say from our vantage point that the understanding of living organisms in Paley's day, and even in the early 1900s, was primitive compared to today's knowledge. Paley's watch thesis has now been eloquently confirmed, especially in the fields of molecular biology, cell structure and function (Behe, 1996; Senapathy, 1994). Numerous examples of this complexity exist including the cell cycle and telomere system which illustrate both intelligence and design which we only now are beginning to understand.

Telomeres and Telomerase

One of the most promising new research fields is the telomere DNA maintenance system used in all mammals. This system uses telomerase enzymes and accessory structures that catalyze the manufacture of telomeres and also maintain their length and even repair them as needed (Lang, 1998). Telomeres are part of the protective end caps located on both sides of all normal chromosomes. Telomerase is an enzyme that maintains telomere length by adding DNA bases to the chromosome ends and by producing certain telomere structural proteins (Blackburn, 1991). It will be discussed in detail later.

The most critical role of telomeres is to maintain an intact chromosome by preventing degradation of its ends. They also prevent translocation of DNA from one chromosome to another and the formation of ring chromosomes (Haber, 1995; Kipling and Cooke, 1992). If these caps break off or are gradually lost as a result of normal cell division, the chromosome ends can fuse, producing ring chromosomes. Translocations result if a telomere-absent chromosome end attaches to another chromosome and one of the connected chromosomes breaks, leaving part of the telomere-absent chromosome bonded to the other chromosome.

Telomeres also function as a biological clock which helps to regulate the length of the cell's life span by triggering the nondividing state termed senescence after a certain number of cell divisions occur (Bodnar et al., 1998). When senescence occurs depends on telomere length which is usually directly related to the number of cell divisions and not chronological or metabolic time as once thought. Human somatic cells have only 92 telomeres, and other living cells have more or less, depending on the species. One animal, the supposedly primitive *Tetrahymena thermophila*, has 20,000 telomeres (Lewis, 1998, p. 982).

The term telomere was first coined by geneticist Hermann J. Muller (1890 to 1967) and comes from *telos*, Greek for "end," and *meros*, Greek for "part." The modern research on the function of telomeres began with the work of James Watson in the 1970's and Howard Cooke in the middle 1980's (Lange, 1998). Telomerase was first discovered in human cells in 1989 by University of California,

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Received 3 June 1999, Revised 14 July 2000

Davis biologist Gregg Morin (Seachrist, 1995). Since then, a meteoric rise in our understanding of the complexities of this cellular life span control system has occurred.

The Structure of Telomeres

Telomeres in humans and most higher eukaryotes consist of numerous associated proteins and a six-nucleotide sequence (TTAGGG or T_2AG_3) that is repeated from a few hundred up to a thousand times (Shore, 1998). This sequence, with few exceptions, is highly homologous in all eukaryotes examined to date (Clark and Wall, 1996, p. 35). Telomeres also are involved in a wide range of diverse biological phenomena which include influencing both gene expression and DNA replication.

Human germ-line cells contain telomeric TTAGGG/CCCTAA repeats at each chromosome end averaging 10,000 DNA bases (10kb), and telomeres can make up as much as 10 percent of the total genome (Bodnar et al., 1998; Blackburn, 1991). Telomeres also differ "in major ways from other DNA sequences in both structure and function" (Blackburn, 1991, p. 569). For example, the DNA at the extreme ends of some telomeres is not arranged in a double helix but is single stranded. Furthermore, telomeres are guanosine-base rich nucleotides that can bend back to form a hair-pin structure with the complementary cytosine base rich strand and this is evidently necessary for the functioning of telomere DNA.

Another structure located at the end of the telomere is a protein/guanine "cap" which protects the telomeric ends *in vitro* and may also help to regulate the action of telomerase by preventing both further chromosomal elongation and degradation. The cap is a heterodimer (a unit consisting of two sections), and its units have a molecular mass of 55,000 Daltons (55kD)[1] and 41 kD.

How the Telomere Functions as a Clock

Telomeres are often likened to the plastic tags called aglets located at the end of shoe strings which prevent the shoestrings from fraying in order to extend their useful life. Once all or most of this protective end is lost, the chromosome deterioration process can begin. Each time the chromosome divides, a short section of the telomere end is left uncopied—and the copy is thus shorter then the original—because DNA strands cannot be replicated to the very end by DNA polymerase (Lange, 1998). The reason is that the DNA polymerase must bind to a primer at the 3' end, and new bases cannot be added at the point where DNA polymerase primer attaches to the DNA.

The area where the DNA polymerase attaches to the DNA is called the *primer space* and is necessary to start the DNA duplication process. Consequently, the chromosome end copy shortens with each cell division, and its length serves as a timer which determines the cell's lifespan. The end result is the chromosome shortens with each round of cell division producing a "mitotic clock" that determines how much time will elapse before a cell enters senescence (Lange, 1998).

In the average human somatic cell, the telomeric end loss rate is estimated to be between 15 to 40 nucleotides per year. Consequently, telomeric length can be used to estimate both the past number of cell divisions and the cell's age. When the functional telomere is totally lost, the affected chromosome breaks down and as a result the cell is damaged to the degree that it normally undergoes apoptosis (a process of internally controlled cell destruction). Telomeres that are shortened to a certain point also may cause the activation of a checkpoint pathway system that inhibits cell proliferation (Hartwell and Kastan, 1994).

The Telomerase Structure

Cell death in many animals can be delayed or even prevented by a complex telomere elongation system which replaces the lost DNA and stops the process triggered by telomere loss, allowing the cell to continue to survive (Barinaga, 1996). This elongation system involves the enzyme telomerase. Telomerase is a complex 123 kD ribonucleoprotein that consists of RNA and a protein framework shaped to support a short RNA strand that contains the set of nucleotides complimentary to telomere DNA (Blasco et al., 1995). Telomerase has three main components: a catalytic protein portion that possesses reverse transcriptase activity, an RNA template, and an associated protein called *telomeric repeat binding factor* (Lewis, 1998, p. 981). Comparisons of telomerase with other proteins have shown that the telomerase gene does not resemble any known gene in the existing database. Consequently, identifying it was enormously difficult. This problem has been partly solved by the use of new methods to determine the protein composition and sequence of telomerase (Lingner et al., 1997).

The human telomerase gene was the first mammalian telomerase gene ever cloned (Seachrist, 1995, p. 30). The first two identified telomerase proteins have molecular weights of 80 kD and 95 kD. Analysis of the telomerase enzyme shows that although it does resemble some viral RNA synthesizing enzymes, it is considerably different than *all* other enzymes that synthesize DNA.

[1]A mass of 55 kD is equal to the mass of 55,000 hydrogen atoms.

Two types of telomerase systems exist, one for somatic cells and another for germ line cells. Both are imperative for species survival. If the germline chromosomes were shortened with each cell division, extinction of that animal would soon occur. Actually, while telomeres normally become shortened with age in somatic cells, they often become *longer* with age in some germ cells, specifically sperm cells (Clark and Wall, 1996, p. 36).

Telomerase also completes the assembly of the lagging strand in DNA replication and can in some cases repair broken chromosome ends. As far as is known, all members of the monera kingdom and both germ and cancer cells as well as tumor-derived cell lines that grow indefinitely *in vitro* all continually synthesize telomerase. In higher organisms telomerase activity is shut off in all but germ cells and some blood-forming cells (Haber, 1995). In humans, telomerase production is maintained in only a few cell types, including the *stem cells* located in bone marrow and the testes which use telomerase to produce a life-long production of healthy blood and sperm cells, respectively (Crawford, 1995). Telomerase must also interact with the protein cap located at the DNA ends which may help serve as a regulation system to allow the cell control over its life span in specific situations (Bodnar et al., 1998).

An enzyme which translates RNA back into DNA is called a *reverse transcription enzyme* or a *reverse transcriptase*. Telomerase functions by using reverse transcription to produce a DNA copy of its RNA sequence and its major protein component called *human telomerase reverse transcriptase*, resembles known reverse transcriptase enzymes (Lange and DePinho, 1999). The telomerase catalyst uses a template to lengthen the telomere. It does this by fusing the DNA made by telomerase onto the 3' terminus of the chromosome and as a result extends the cells lifetime. The strand is then copied to produce a double stranded DNA. This ends the normal cell life span and if the extending mechanism is not damaged or turned off, it potentially confers immortality to the cell (Lingner et al., 1997).

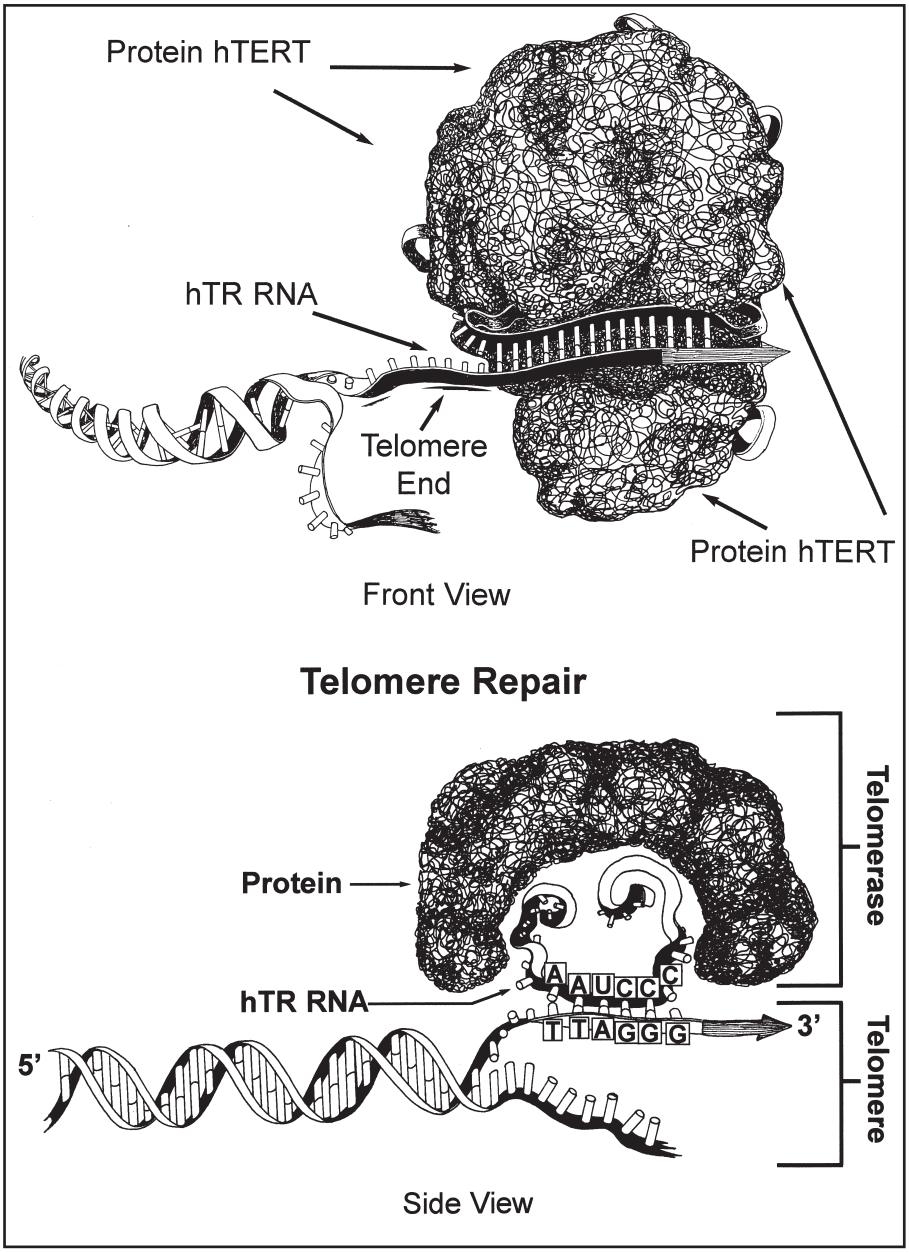

Figure 1. Two views (front and side) of the telomere and telomerase assembly unit. The telomerase enzyme adds new bases onto the end of the chromatin to extend its life. The telomerase is composed of hTERT protein and nucleotides shown in the front view. (Adapted from several sources including Haber, 1995).

Another protein called the *telomeric repeat binding factor* physically connects to both the RNA template and the reverse transcriptase chromosome end in order that six-nucleotide DNA repeats can be added to the chromosome end. This cellular machinery is essentially a built-in telomere factory that is permanently turned on in certain cells such as gametes and in other cells only at certain times (Lewis, 1998, p. 981).

Telomerase and Cancer

Telomerase is active in all known vertebrates, mostly in germ cells and the early stages of the embryo, and is normally inactivated or repressed in somatic tissue (Sharma et al., 1996). The function of telomeres was first indicated from the finding that a major difference between senescent cells (normal somatic cells) and the so called immortal cells including normal germ or cancer cells was the telomeres (Travis, 1995). The relationship between telomeres and aging was also supported by the discovery that patients with *progeria*, an inherited disease which causes lethal rapid aging at a rate about nine times normal, is caused by defective telomerase. Damage from cell death due to lack of functional telomerase causes a 10 year old progeria patient to physically resemble a 90 year old. Progeria is caused by a deficiency which results in pronounced shortening of the patients telomeres.

Understanding the factors that trigger the production of telomerase is now recognized as critical in a number of fields including cancer (Lange and DePinho, 1999). By assaying telomerase enzyme levels, Kim et al. (1994) found evidence of telomerase activity in 90 out of the 101 primary tumors they sampled, which included 12 different cancer types. This is in contrast to a total lack of telomerase activity in the 50 normal tissues that were examined.

In another study, 98 out of 100 cancer-derived cell lines were found to express telomerase activity, in contrast to none of 22 cell lines that were derived from non-cancerous tissues (Kim et al., 1994). Lange concluded that telomerase-positivity is not a mere side-effect of dedifferentiation or rapid proliferation related to cancer development, but is evidently a *prerequisite* for continued tumor growth (Lange, 1998). Lange and others have also presented evidence that telomere shortening is a major tumor-suppressing mechanism.

Telomerase expression has now been found in approximately 90% of all metastatic cancers including those of the lung, breast, stomach, uterine, and liver and is hypothesized to be a universal factor produced at some time in all cancer cells. Importantly for tumor marker research, it seems likely that *all* tumors contain measurable telomerase activity at some stage in their development, but the telomerase activity in some non-cancerous cells may be too low to measure by current techniques. Background noise must be effectively filtered out before telomerase can be a useful tumor marker. Furthermore, cancer cells do not usually contain *longer* telomeres, but rather do not experience telomere *loss* (Kim et al., 1994).

An example of the use of research on the telomerase as a tumor marker to aid in diagnosing cancer at the early stages, Kinoshita (1997) found of the 45 bladder cancer patients they examined, 36 exhibited telomerase in a bladder washing and the enzyme was found in the urine of patients in over half of the cases they examined.

In contrast to most malignant tumors, some *benign tumors* such as *colonic adenomas* evidently do not express telomerase in levels measurable by current assays, while only 10% of all tissues effected by *benign prostatic hyperplasia* express telomerase. For this reason this enzyme may provide information on the type of, and location of, a tumor (Haber, 1995). This discovery may be critical both for cancer diagnosis and treatment if enzymatic assays can be developed to directly or indirectly detect the presence of cancer cells, and select methods of blocking telomerase activity may be an effective method of adversely affecting cancer cells while having no effect on healthy normal cells.

Compounds have been synthesized which block the action of telomerase, and testing these compounds on humans has now begun. The blocker would disproportionately affect cancer cells, since most normal human cells would be largely immune to a telomerase blocker because they totally lack or contain extremely low amounts of telomerase. One blocker type is an antisense RNA strand that binds to, and thereby inactivates, the telomerase enzyme's RNA. The success of this approach in mice suggests that antisense telomerase RNA can be useful to treat human cancer. A major concern is that the drug may also block telomerase produced by stem cells which are necessary to produce red blood cells. Another promising approach to treating cancer is to produce a means of upregulating telomerase in cancer cells.

Cells can become cancerous without telomerase activity, but sustained growth of the cancer evidently *requires* the constant production of telomerase. Malignant cancer cells normally do not undergo apoptosis, and many even fail to undergo senescence. Telomerase genes can become active by a mutation that damages their control system. An example is damage to the system which inhibits telomerase production also causes loss of regulation, allowing uncontrolled production of the telomerase enzyme.

Telomerase research also has helped investigators to understand why non-cancer cells normally replicate only about 50 times *in vitro* before they die, and why previous efforts to extend cell life have achieved limited results. The number of cell divisions that cultured normal human cells such as fibroblast cells can undergo is highly correlated with the *initial* telomere length. Telomere length is therefore hypothesized to be a major factor that determines cell longevity and may partially account for the normal wide variation in the life span of most of cell types (Haber, 1995). Telomere length also controls when cells enter the senescent or terminal growth arrest state.

Drugs that increase telomerase production may also retard the aging process, particularly in vulnerable cells

such as brain cells. Researchers at the University of Texas Southwestern Medical Center have successfully stimulated the production of telomerase in normal skin and retinal cells. Their goal was to reduce disease and cell damage due to the effects of aging (Bodnar et al., 1998). This mechanism already has to some extent been exploited by the utilization of hybridomas, tumor-derived cell lines which can grow indefinitely *in vitro* because they express telomerase, preventing the normal progressive shortening of their telomeres (Kipling and Cooke, 1992).

The Process of Telomere Repair

DNA repair enzymes constantly monitor the integrity of DNA, and rapidly repair any breaks that are discovered. If the telomeres are not properly maintained, DNA repair enzymes can occasionally mistake the ends of chromosomes for broken DNA. As a result, telomeres may be inappropriately joined together or even become fused to genuine chromosomal breaks by recombinational or end-joining mechanisms (Shore, 1998, p. 1818). The result is usually an unstable, dicentric chromosome that can result in transpositions or other abnormalities which can contribute to cancer progression. This is one reason why cancer cells frequently show chromosomal instability resulting in ring chromosomes, telomeric associations, and dicentric chromosomes (Sharma et al., 1996). The complex set of end cap proteins normally protect the chromosomal ends from inappropriately joining, and defects in these proteins can lead to the cascade that results in damaged chromosomes.

Part of the large enzyme required for normal DNA repair is a DNA binding subunit called *KU complex*. A KU protein is a DNA-dependent protein kinase which is a member of the ATM gene family (Shore, 1998, p. 1819). The exact role of this system in various types of cells and organisms has yet to be determined, but KU proteins evidently are key players in the replication and protection of telomeres. The KU protein family and its homologues may also play a role in telomere metabolism, meaning that it may be involved in telomere replication as well as in gene silencing, and evidence now exists that the KU complex is physically bound to telomeres. The KU70 protein and its homologues including YKU70, HDF1, YKU80, and HDF2 are one of several protein families that can bind with high affinity to DNA ends including those that are blunt, overhanging, or hair-pin in structure (Shore, 1998).

As a consequence of telomeric erosion, the telomeric length can be stabilized by activating telomerase to add a hexameric repeat of the sequence 5' TTAGGG 3' to the chromosome ends. Since telomerase production and activity is normally inhibited in healthy cells, researchers are now trying to understand how the cell's telomerase inhibitor system works. This understanding may aid in finding a way to turn off the telomerase enzyme *only* in cancer cells in order to stop cancer cell growth.

Researchers are also experimenting with turning telomerase on or even adding telomerase to normal cells to enable them to live beyond their normal life span. Early experiments indicate that normal cells can continue to divide long past their normal lifespan evidently without any ill effects. The immediate goal is to use the telomerase enzyme to treat certain health problems associated with aging such as macular degeneration or skin ulcers. Recently Bodnar et al. (1998) were able to activate telomerase, resulting in the addition of TTAGGG repeats which artificially elongate telomeres. As a result the growth potential of the cell increased so that it could divide beyond its normal senescence length.

These studies usually add the telomerase gene to the cells which were grown *in vitro*, which produce ectopic expression of telomerase. Lange and DePinho (1999, p. 148) in a summary of the literature concluded that ectopic expression of human telomerase reverse transcriptase could confer immortality on the cells as now occurs with our germ cell line. This approach may also be used to replace cells lost due to injury, degenerative diseases, diabetes, and rheumatoid arthritis. Work is also underway to use this approach to extend the human lifespan to 140, 180, or more years. The results of the preliminary research in this field is now regarded by many specialists as very promising (Feber, 1999, p. 154–155; Lewis, 1998).

Telomere Length Mutations

As noted, the major reason for telomere shortening is because DNA ends cannot be replicated to their terminus by normal DNA polymerases (McEachern and Blackburn, 1995, p. 403). Almost all eukaryote cells can manufacture telomerase which catalyzes the addition of nucleotide repeats on telomeric DNA termini. This process has so far been most extensively studied in yeast. Regulation prevents the telomeric DNA lengths from deviating in *either direction* from the ideal length. A control system consisting of protein and structural support molecules is required both to ensure that the necessary length is achieved and that elongation *beyond* this point does not occur. This is another example of the extreme complexity required to produce the watch-like precision that exists in every cell.

An example of loss of length control is a specific mutation found in the yeast *Kluyveromyces lactic* that results in telomere elongations of up to 100 times beyond normal (McEachern and Blackburn, 1995, p. 403). Some of the many mutations discovered that cause abnormal telomeric elongation cause immediate elongation, whereas others cause elongation *only* after a latent period of hundreds of

generations. Mutations that cause immediate changes directly affect the proteins involved in controlling telomerase activity. Conversely, McEachern and Blackburn proposed that the "genetic time bomb" effect is due to a negative regulation system normally controlled by one or more protein factors that bind to the telomeric repeats.

Along with telomerase that elongates telomeres, an inhibitory double-stranded telomere-binding protein (DS-TBP) is also normally produced. DS-TBP interacts with the terminus specific binding protein to *prevent* the uncontrolled elongation of the telomeres (McEachern and Blackburn, 1995, p. 407). DNA replication also causes a progressive loss of telomeric sequences which *also* causes damage to the genes that produce DS-TBP protein.

Mutations of the DS-TBP regulatory protein can cause both immediate and delayed telomere lengthening. Mutations causing *immediate* telomere lengthening often interfere with the telomere regulatory system located at the DNA terminus. This may cause a change in the DNA sequence, preventing the proper binding of the terminus-specific binding DS-TBP protein. As a result of this change, telomerase is able to bind to the telomere when it normally should not, causing excess elongation.

For the *delayed* elongation phenotype, the telomeric DNA-sequence changes affect the DS-TBP protein binding site. Terminus-specific binding protein is then able to function *only* when a DNA molecule loses a large proportion of its functional DS-TBP. When the wild type DS-TBP's become too few due to loss of telomeric repeats, unregulated telomere lengthening may then occur. As the telomeric terminus is moved progressively away from the region where some DS-TBP remains, normal regulatory interactions become more unlikely, thus favoring a runaway telomeric growth. Another cause of uncontrolled elongation is a disruption of the structure at the terminus of the chromosome which causes it to no longer respond to the inhibition system normally mediated by the DS-TBP system.

Other Mechanisms Used to Maintain Telomere Length

Several other mechanisms exist which can prevent telomeres from progressively shortening. One such system is utilized by certain types of flies and involves structures called *retroelements* which are normally clustered around the telomeres. Retroelements are periodically added to the chromosomes ends, usually several kilobases at a time, preventing telomere shortening. It is not known if a similar mechanism exists in humans. Bacteria avoid the problem of chromosomal shortening that telomere structures are designed to prevent because both their chromosomal and plasma DNA are circular (Lewis, 1998, p. 981).

Implications for Creationism

Paley's thesis is eloquently demonstrated by the complex cell clock system controlled by telomeres. Only a minuscule amount of knowledge about the biological world was known in Paley's day compared to what is known today, and nothing was known about telomeres then. We now realize the level of complexity of the cell exceeds that existing at the gross anatomical level. An estimated over 100,000 different proteins are made by the human body, each which has specific and specialized function(s) and must interact appropriately with all of the other cell proteins. If a protein is altered, it could have adverse consequences for the cell due to causing damage or interfering with other structures. Each one must achieve its own function, and must not interfere with the function(s) of other proteins and cellular processes.

An understanding of telomeres provides a bases for understanding longevity both today and in the past. Claims that it was impossible in the past for humans to live much beyond a hundred years or so are now being seriously challenged, not only by the Scriptural record but also by science. We now realize various reports in the Bible that Methuselah and others lived to be many hundreds of years old are feasible, given that Methuselah was closer to perfection than humans are today. Modern humans are genetically degenerate, but our vastly improved level of knowledge about the biological and physical world has helped us to ameliorate enormously the effects of this degeneration. At some point in history human longevity could have changed as a result of some alteration of the telomerase system.

If Paley had written his opus today, it could consist of hundreds of volumes, and one complete volume alone could be on the telomere system as an excellent example of irreducible complexity. It cannot function until all of its parts are in place. An extensive literature search has found that so far no one has even attempted to speculate on a theoretical scenario regarding how the telomere mechanism could evolve. The system is almost identical in all eukaryotes and shows no evidence of evolution; it either exists in total or another totally different system exists.

One theory of telomerase/telomere evolution includes the idea that telomeres originated in early eukaryotes from retrotransposons which were supplied by a retrovirus, and that the unusual *Drosophila* telomeres reflects a relatively recent transposition of retrotransposons to somatic cells that preferentially inserted at the chromosome ends (Eickbush, 1997, p. 911). One of many major problem with this theory is "How did the chromosome ends protect themselves until this fortunate event occurred?" Another method must have existed, and this retrotransposon event must have occurred very early in evolution because the telomere system is evidently uni-

versal in eukaryotes and prokaryotes. Furthermore, retrotransposons are a complex system and parsimony would rule out convergent evolution to explain their similarities. Eickbush concludes that among the many problems with this theory include:

> In order to support this origin of telomerase, it would be necessary to show that non-LTR retrotransposons date back to the origin of eukaryotes. Resolving the ultimate origin of reverse transcriptases will be difficult because of the low level of sequence identity among polymerases. In the meantime, the discovery that the catalytic subunit of telomerase is a reverse transcriptase fuels the argument that retrotransposons have had major influences in shaping the eukaryotic genomes (1997, p 912).

Furthermore, telomerase is necessary for survival and research has found that removing the telomerase gene compromised:

> chromosome stability and the integrity of cells that normally divide often. Their telomeres became shorter than normal, their chromosomes broke, and some nonhomologous chromosomes fused to form translocations. The animals' fertility plummeted, reproductive organs shrank, and highly proliferative tissues, such as testis, spleen, and bone marrow, degenerated. These results therefore confirmed that telomerase is important for maintaining highly renewable tissues (Lewis, 1998, p. 983).

The earliest cells were believed to have circular chromosomes which would have confirmed immortality on them. This finding argues against macroevolution because the telomere system is a complex system which usually *ends* the life of each cell, and eventually the life of the entire organism. It would not confer increased but a *decreased* fitness and a shorter reproductive life span for the animal. Consequently, this system would not be selected for but would rather be selected against. If the whole purpose of life is to produce the next generation of genes, as argued by Dawkins (1976), why would a complex mechanism exist to cause the end of the gene? And when the telomerase system is damaged as occurs in cancer, the end result is also the end of the gene line.

Some evolutionists argue that the telomere system usually does not affect the cell until after the animal's reproductive age is over. This is not entirely true because a longer life span would allow evolution of a longer reproductive life span (Kipling and Faragher, 1999, p. 191–193). Many cells are destroyed early in life by this system and in many cases it would not confer a survival advantage to the organism. Nor would it contribute to the survival of those cells which it destroyed. Evolution cannot explain the origin of this telomere mechanism, but intelligent design can: it is a designed mechanism which controls cell longevity for metamorphosis, developmental changes, and alterations. When damaged, it contributes to cancer and certain other diseases.

Acknowledgements

I wish to thank Bert Thompson, Ph.D., Wayne Frair, Ph. D., John Woodmorappe, M.A., and professors Rena Trautman and Rod Bias for their comments on an earlier draft of this article.

References

Behe, Michael. 1996. *Darwin's black box*. The Free Press, New York.

Blackburn, Elizabeth H. 1991. Structure and function of telomeres. *Nature* 350:569–73.

Blasco, Maria, Walter Funk, Bryant Villeponteau and Carol W. Greider. 1995. Functional characterization and developmental regulation of mouse telomerase RNA. *Science 269:1267–1269.*

Cooper, Geoffrey. 1995. *Oncogenes*. Jones and Bartlett, Boston.

Crawford, Dorothy. 1995. A Plug for cancer's fountain of youth. *New Scientist* Sept. 9, p. 11.

Cummings, Michael R. 1988. *Human heredity: Principles and issues*. West Publishing Co., New York.

Day, Stephen. 1995. Just obeying orders. *New Scientist* 146(1979): 26–30.

Dawkins, Richard. 1976. *The selfish gene*. Oxford University Press, New York.

Eickbush, Thomas. 1997. Telomerase and retrotransposons: Which came first? *Science* 277:911–912.

Ferber, Dan. 1999. Immortalized cells seem cancer-free so far. *Science*, 283:154–155.

Haber, Daniel. 1995. Telomeres, cancer, and immortality. *New England Journal of Medicine* 334(14):955–956.

Hartwell, Leland and Michael Kastan. 1994. Cell cycle control and cancer. *Science* 266:1821–1827.

Hartwell, Leland H. and Ted A. Weinert. 1989. Checkpoints: Controls that ensure the order of cell cycle events. *Science* 246:629–633

Hunt, T. 1994. Cell Cycle in *The encyclopedia of molecular biology*. Ed, John Kendrew. Blackwell Science, Oxford. pp. 161–166.

Kim N.W, M. A. Piatyszck, and K. R. Prowse, et al. 1994. Specific association of human telomerase activity with immortal cells and cancer. *Science* 266:2011–2015.

Kipling, David and Howard J. Cooke. 1992. Beginning or end? Telomere structure, genetics, and biology. *Human Molecular Genetics* 1(1):3–6.

Kipling, David and G. A. Faragher.1999. Aging or hardly aging? *Nature* 398:191–193.

de Lange, Tina and Ronald DePinho. 1999. Unlimited mileage from telomerase? *Science* 283:947–949.
Lewis, Ricki. 1998. Telomere Tales. *BioScience* 48(12): 981–985.
McEachern, Michael and Elizabeth H. Blackburn. 1995. Runaway telomere elongation caused by telomerase RNA Gene mutation. *Nature* 376:403–409.
Paley, William. 1839. *Paley's natural theology*. Harper Brothers, New York.
Seachrist, Lisa. 1995. Telomeres: Cancer research. *Science* 268:29–30.
Senapathy, Periannan. 1994. *Independent birth of organisms*. Genome Press, Madison, WI.
Singleton, Paul and Diana Sainsbury. 1989. *Dictionary of biochemistry and molecular biology*, Second Edition. John Wiley and Sons, New York.
Travis, John. 1995. End games;Tips of chromosomes may contain secrets of cancer and aging. *Science News* 148(22):262–264.
Wang, X.W, H. Yeh, L. Schaeffer, R. Roy, and V. Moncollin. 1995. p53 modulation of TF11H associated nucleotide excision repair activity. *Nature Genetics* 10:188–195.
Weinberg, Robert A. 1995. The retinoblastoma protein and cell cycle control. *Cell* 81:323–330.

Book Reviews

The Star of Bethlehem by Michael Kidger
Princeton University Press, Princeton, NJ. 1999, 306 pages, $23

There is a long list of possible natural explanations for the Star of Bethlehem:
- A comet, perhaps Halley
- A conjunction of planets
- Venus
- Nova or supernova explosions
- An occultation of a star or planet by the moon
- A single meteor or meteor shower
- A hoax

Author Mark Kidger is an astronomer working in Spain. He presents a good Biblical description of the Christmas Star, taken from Matthew 2. He concludes that the Lord was born between 7 and 5 BC, and most probably around March – April, 5 BC Kidger thoroughly analyzes each of the natural star explanations. There is much detail given on ancient observations, calendars, dates, and traditional stories.

In Kidger's final conclusion, the Christmas story involved four separate celestial events: *First*, in 7 BC there was a triple conjunction of the planets Jupiter and Saturn. That is, as these planets *wandered* through the night sky, they approached each other three times, once to within a distance of two moon diameters, or one degree. This took place in the constellation Pisces the fish, of special interest to Jewish people. Kidger suggests that this conjunction first alerted the magi to something special about to happen. *Second*, 6 BC brought another conjunction, this time between Mars, Jupiter, and Saturn. This planet gathering was again in Pisces, although this time spread across 8 degrees of sky. For comparison, the open side of the Big Dipper bowl is 10 degrees. *Third*, in 5 BC the crescent moon passed close to Jupiter, as it frequently does. Kidger suggests that this near occultation convinced the wisemen to start packing for the journey! *Fourth*, also in 5 BC, for good measure, a nova or erupting star appeared in the predawn Eastern sky between the constellations Aquila and Capricorn. Stars rise about two hours earlier each month due to the earth's orbital motion. If the magi arrived in Jerusalem after a two-month trip, the nova would now rise four hours earlier, placing it high in the southern sky. Since Bethlehem is located about five miles due south of Jerusalem, the nova led the seekers to the house where the Christ child was.

Some novas repeat their energy outburst periodically. Kidger suggests that such a recurrent nova might eventually be identified in the Aquila – Capricorn region. He names one possibility, *DO Aquilae*, a very dim star of apparent magnitude 18. Kidger predicts that we someday may be able to detect a growing cloud of gas around this star, with a radius in light years equal to the timespan since 7–5 BC Then "the case of the Star of Bethlehem genuinely would be closed and our star identified" (p.275). Present technology does not allow such a measurement.

What are we to think of this hybrid description of the Lord's star? It is very interesting, but probably a futile effort. As William Canton wrote in 1899, "Regarding the character of the marvelous star, speculation has exhausted itself in fruitless conjecture."

I was disappointed at Kidger's doubt that Matthew actually wrote the gospel named for him. Instead Matthew, "may have been one of its sources; some of the rest of the story came from written accounts, some came from the very early Christian oral tradition" (p. 5). The author struggles to understand what led the wisemen to travel to Jerusa-