CASE STUDY: Telomeres: Fountain of Youth

The ends of eukaryotic chromosomes contain a structure called telomeres. Because of the unique structures of the ends of the chromosomes and the mechanism of action of the DNA polymerases that replicate the DNA (see Chapter 13), the ends of these chromosomes will get shorter with each cell division cycle. However certain cell types express telomerase, which is a specialized enzyme that is used to replicate the ends of the chromosomes. In our bodies, telomerase is not expressed in most cell types, which is thought to give rise to the limited proliferative capacity of our cells. However, telomerase reexpression has been associated with tumors. Based on these observations, please provide your thoughts on the following results.

Questions:

1. Imagine that an enzyme is discovered that selectively shortens telomeres. Its gene is isolated, cloned and transfected into a malignant cell line where it is transcribed and translated. What might happen to the cell line? (Karp test bank #289).

Answer: If the enzyme works properly, it will shorten chromosome telomeres and perhaps eventually stop cell division in at least some of these cells. This might reverse the malignant state and return it to at least a semi-normal state.

2. To probe the function of telomerase, scientists created a mouse model in which the telomerase gene was knocked out. It was particularly surprising that the telomerase knockout mice had no increased or decreased incidence of tumor formation. Why was this surprising?

Answer: Because telomerase re-expression has been associated with tumor cell proliferation, it was assumed that the expression of telomerase gave rise to the immortality associated with tumor cells. Therefore it would have been expected that telomerase knockout mice would be associated with a decreased ability to form tumors in mice. This was not the case, which implies that simple effects of telomerase alone are not sufficient for tumorigenesis.

3. Telomerase is often thought of as the fountain of youth because cells should be forever immortalized if they express telomerase. If this were true, what would you expect to see as a phenotype of the telomerase knockout mice?

Answer: It would be expected that they have a decreased life-span. However this was not observed, suggesting that the telomere length is not directly correlated with cell and organismal viability.
Where can I learn more?