COMMEMORATIVE LECTURE

Telomeres and Telomerase

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Thank you first for the very kind introduction. It's indeed a great pleasure and a privilege to have the opportunity to address you.

Today I would like to tell you about a special part of the chromosomes that carry all our genetic information in the cells in our bodies. This special part is called the telomere, and it is the end of the chromosome. I will also talk about telomerase, which makes telomeres in cells. Telomeres and telomerase profoundly affect how the chromosome does its job, which is not only to contain the genes of our genetic blueprint (and the blueprints of all organisms), but also to stay in one piece, thus ensuring the faithful transmission of the genetic information from cell to daughter cell and from generation to generation.

If you look deep inside the center of a cell that is about to divide in our bodies, you see objects that look like sausages. Together, these make up our genetic blueprint. The sausages look double because each is a newly replicated chromosome. When the cell divides, it sends one copy of the chromosome to one cell and another copy to the other cell, ending up with two cells. Crucially important for this process are the telomeres, which can be visualized by a molecular probe specific for telomeres.

What are telomeres good for? Figure 1 shows a cell in the process of dividing to become two cells. This is what has to happen in all of the cells in our bodies as we grow from beginnings to adulthood, and also even when we are adults. Many cells in our bodies keep dividing, self-renewing themselves. Examples are cells in our hair follicles, our skin, the lining of our intestine, and our immune system, which is needed to fight off invading pathogens. All these cells keep on self-renewing through much, if not all, of adult life, and these cells therefore have to keep dividing.

Figure 1 shows just one chromosome at the top, and this chromosome, as mentioned above, has to replicate itself and then be correctly partitioned into the two cells. The white circle in the center of the chromosome is called the centromere, and there can be only the one centromere for each chromosome. I won't go into the technicalities, but you can't have more than one centromere in a chromosome, because if you do, they get into a fight and break the chromosome, with bad results.

Also I have indicated the telomeres at the tips of the chromosome. These specialized tips of the chromosomes have a number of different functions. For example, for reasons we really don't understand, they localize the chromosomes and hold them in special places in the nucleus.

Second, as I will describe in some more detail later, the telomeres are necessary to completely replicate all of the DNA of the chromosome. And then, when the chromosomes, pulled by the centromeres, start to move apart to go into the two new cells, the telomeres also have to separate in a timely fashion.

Analogies have been made about what a telomere is like, but this my favorite: we can think of the telomeres being like those little plastic tips on the ends of your shoelaces. If you don't have that plastic tip, the shoelace end becomes frayed, and the shoelace doesn't do its job properly. Similarly, a telomere is like a little plastic tip. It keeps the end of the chromosome from getting frayed and not doing its job properly.

Figure 2 shows you one example of what happens when a telomere doesn't do its job properly. On the left is indicated the situation for a cell with normal (or wild type) telomeres; these replicated chromosomes can pull

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