Intracellular telomere length dynamics in human cells

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ABSTRACT

This PhD project was carried out at the Department of Human Genetics, University of Aarhus, and at the Curie Institute in Paris.

Telomeres are DNA sequences located at the end of human chromosomes which serve a protecting function, protecting the cells against genomic instability. Contrary to the rest of the human genome, the telomeres are dynamic structures that shorten during life and it has therefore been suggested that late in life they may loose the ability to protect the chromosomes and therefore have a role in the induction of genomic instability and in the human ageing process.

In this PhD project we have investigated the intracellular distribution of telomere lengths over the chromosomes in human lymphocytes. We have used a fluorescent in situ hybridisation method (Q-FISH) and have thereby been able to quantify telomere lengths on the single chromosome arms.

Our results show that the distribution of telomere lengths over the chromosomes is not random. Rather some chromosome arms have long telomeres and some chromosomes have short telomeres. We find that there are individual specific variations to this distribution and that these variations are similar in twins, thereby indicating that these variations may be inherited. A subsequent study of telomere lengths in families confirmed this possibility, and thereby suggested that if a chromosome with a short telomere is passed on to the child, this chromosome will also have a short telomere in the child, relative to other telomeres on other chromosomes. We also find that a chromosome that has a relatively short telomere at the beginning of life will have a relatively short telomere late in life.

Combining these observations, we conclude that if telomeres have a role in relation to ageing, genomic stability and cancer, inheriting an especially short telomere from a parent may potentially be hazardous later in life.

We thereby also suggest that inheritance of telomere length may possibly explain part of the 25% heritability of lifespan in man.