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Editorial comment

Are we close to the clinical development of novel drugs targeting telomeres and telomerase?

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Approximately five years ago telomerase was first proposed as an attractive target for novel anticancer drugs. The protein maintains chromosomal integrity by adding TTAGGG repeats into chromosomal telomeres and is active in approximately 90% of human neoplasms. In most human somatic cells, the progressive loss of telomeric DNA during each round of cell division triggers senescence. Telomerase has a key role in the maintenance of telomeres and in the immortalisation of cancer cells. It is proposed that cancer cells can be induced to go into senescence by inhibiting telomerase activity.

In this issue of the *European Journal of Cancer* [1], Dr. Lloyd Kelland (Antisoma Research Laboratories, St. Georges Hospital Medical School, London, UK) reviews the concept of telomerase as a target for cancer therapeutics. His article focuses on compounds affecting telomerase/telomere maintenance that are under development as potential anticancer drugs. He outlines current knowledge in our understanding of possible strategies to target telomeres and telomerase. In addition, compounds that have been studied at the preclinical level and that are likely to be investigated in clinical trials in the near future have been examined in detail.

He highlights that G-quadruplex ligands are a class of compounds that appear to be of particular interest as *in vivo* data has shown that they are active anticancer drugs. They have the ability to bind selectively to G-rich sequences of DNA, such as telomeres, and fold into four-stranded intramolecular structures. The binding of G-quadruplex ligands appears to disrupt the function of telomeres leading to rapid senescence and/or apoptosis. As for many other novel anticancer drugs with specific mechanisms of action, there are attempts to discover and validate markers of activity to be used for monitoring the results of phase I–II studies testing these compounds.

Dr. Kelland's paper considers the rationale for the clinical development of telomerase-directed compounds and provides a critical view of potential drawbacks to the development of this novel class of compounds. We may be closer than we think to the development of clinically relevant agents targeting telomerase and we eagerly await further progress in this field.

Reference

1. Kelland LR. Overcoming the immortality of tumour cells by telomere and telomerase-based cancer therapeutics-current status and future prospects. *Eur J Cancer* 2005;41 [this issue].

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