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'Hot' bacterial viruses shed more light on genetic instability

A number of severe human disorders, including cancer and hereditary neurological diseases, are now associated with genetic instabilities promoted by triple-stranded DNA structures known as triplexes [1–3]. Recently, it has been revealed that triplex-forming sequences are frequently located near mutation hot spots and at breakpoints of genetic rearrangements in mammalian cells. Advancement of our knowledge in the mechanisms of genetic instabilities caused by triplexes may lead to novel therapies [4].

The new insight in this direction came from the latest study of unusual bacterial viruses called thermophages [5], in which triplex-forming sequences have not been found before. These microorganisms were isolated from hot springs of the Kamchatka Peninsula, Russian Far East, and, surprisingly, they have extremely long (~1 μm) tails (Figure 1).

By analyzing the genomes of thermophages, an international group of researchers from academia and the biotech industry, led by Leonid Minakhin and Konstantin Severinov, discovered long polypurine–polypyrimidine sequences with mirror repeat symmetry that can form triplexes. These triplexes happened to be potent blockers of DNA replication by DNA polymerases. Moreover, significantly increased levels of point mutations, deletions and insertions have been detected around the triplex-forming sequences in the thermophage genomes.

Thus, this new study solidly confirms that triplexes may serve as a cause of the fragility of human chromosomes. This study also suggested that thermophages and other viruses may act as vectors in transferring genetic diversity among other microorganisms.

One of the future directions of this study may be to isolate bacteria with the thermophage

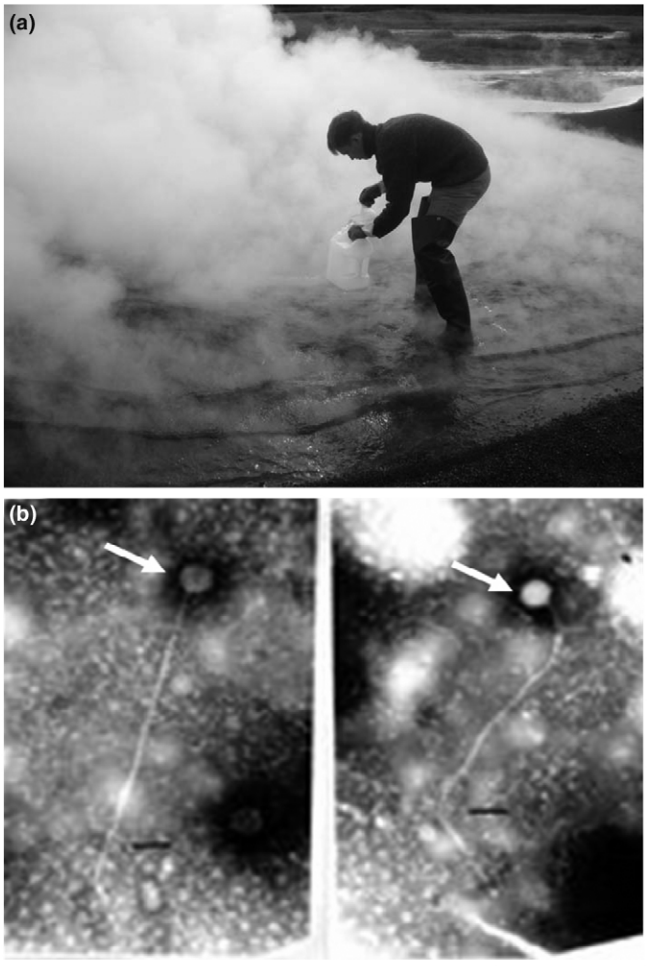

FIGURE 1

(a) The 'hunt' for thermophages: a researcher from Severinov's team collecting environmental samples containing thermophilic microorganisms from one of the Kamchatka's hot springs (courtesy of L. Minakhin); **(b)** Electron micrographs of the two virions of P74-26 thermophage studied in reference [5] that show the icosahedral viral capsid (indicated by white arrows), which is linked to a long filamentous tail. The black scale bar corresponds to 0.1 μm (courtesy of H.W. Ackermann).

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genome integrated into the bacterial chromosome and to use these microorganisms to search for drugs that protect chromosomes from damaging triplexes.

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