What about “parasite” DNA?

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Abstract

This paper explores “parasite” DNA in light of the recent vaccine based on mRNA.

Recently a number of vaccines have been approved worldwide. The Pfizer vaccine is based on injecting the mRNA of the spike of the virus into the cell. The S spike protein is then construed from the viral mRNA. In turn, immunity can be trained to respond to viruses and eliminate them by recognition of the S spike protein. It is noted that the assumption is that the spike protein itself can do little harm to the cell. So it is a kind of poisoning through large numbers of alien protein that triggers the immunity response. Most likely, the molecular geometry of mRNA vaccine S spike is not exactly the same as geometry of the spike protein of the whole virus. Note this virus blocks the ACE2 receptor and introduces alien whole viral mRNA into the host cell hijacking the ribosome function.

I would like to formulate a question about the genomics of spike mRNA. It takes some introduction to do so.

It is known that RNA can be converted back into cDNA with the use of reverse transcription enzymes. The process is comparable to HIV. However, there are also in the human cells non-viral reverse transcriptase enzymes that accept RNA and make cDNA out of the RNA information. In addition there are retroposons. These endogenous viruses might also produce reverse transcriptase.

As a non-viral example, RNA dependent DNA transcriptase $\eta^{1,2}$ (pol $\eta$) is a reverse transcriptase dedicated to DNA repair. In addition it is noted that there are some indications that the complete SARS-CoV-2 virus can be reversed transcribed and enter the human genome$^3$. Perhaps the latter is not true in the sense of a whole RNA sequence. However, smaller subsequences derived from S spike mRNA can, in principle, be reversed to DNA by reverse transcriptase enzymes, such as pol $\eta$, present in e.g. the skin cells.

Provided the viral RNA sequence is relatively small, there is the possibility that the cDNA of the virus RNA is inserted into the complete DNA and becomes a kind of “parasite” DNA$^4$ that wanders through the genome. Parasite DNA can multiply itself quite a number of times. This wandering and multiplication occurs via a number of times that the parasite DNA is translated back into RNA again. This RNA, in turn, produces cDNA that can be inserted back in the genome at a different position by the activity of integrase enzymes.

A real life example of such a parasitic DNA is Alu DNA. It is based on the 300 nt 7SLRNA$^5$. The back and forth transcription creates a large number (around 900000) of Alu insertions. Most of the Alu DNA is silenced. Note btw here the cost of the effort of the cell to maintain that. The LINE1 Alu elements, however, are active. They can be involved in illness$^6$ and hamper normal cellular processes because the ability to intrude in useful normal transcription$^7$. 
How can the initial spike mRNA turn into DNA and become parasitic. It is known that pol η occurs in the repair of UV broken DNA in skin cells. Absence of this enzyme gives rise to the rare illness xeroderma pigmentosum (XP-V) where the absence of pol η give error-prone DNA repair which turns into malignancies. Therefore, double broken DNA repair is such a possibility to introduce alien RNA information into DNA that becomes part of the genome. Do note that there are other sources of DNA breaking as well. We mention here environmental pollution or radionuclides emitting gamma radiation. Variability under irradiation depends in plants to a great extent to repair of double-strand DNA breaks. Arkhangelskaya, et al indicated a subtle effects concerning double-strand broken DNA in blood lymphocytes and the differentiation in repair in an environment where different magnetic isotopes of magnesium (here $^{25}$Mg$^{2+}$ vs $^{24}$Mg$^{2+}$) are present.

A next point of notice where reverse transcription takes place is with the synthesis of telomeres. Telomeres protect the integrity of chromosomes. Telomerase recognizes the 3'-OH at the end of chromosomes and extends telomeres by using its associated RNA molecules as a template. The DNA repair mechanism is in this way able to distinguish double strand breaks and a telomere ended chromosome. The synthesis of telomeres is a reverse transcription process with the enzyme telomerase.

In a recent study into the effects of COVID-19, a relation was found between severity of COVID-19 disease and a remarkable decreasing length of telomeres. When cells divide and DNA has to be replicated, the telomeres grow shorter as a molecular mechanism of ageing. This could perhaps explain the shortening of telomeres in severe COVID-19. However, it is also possible that parts of SARS-CoV-2 infected mRNA material, hijack the telomerase and use its reverse transcriptase capacity.

After these introductory remarks my question is as follows. If a small (signal) RNA such as 7SLRNA can generate Alu “parasitic” DNA, then how can we be sure that e.g. 300nt subsequences of vaccine (=S spike) mRNA that resembles 7SLRNA, cannot form Alu-like parasitic DNA themselves?

Especially when there are broken DNA strands the pol η repair activity will likely be higher. This polymerase enzyme accepts RNA and turns it into cDNA that subsequently can be introduced in the human genome. There it, theoretically, can become an Alu-like DNA parasite. Furthermore, although telomerase uses its own built-in RNA that also holds an enzymatic function, it could still be so that alien viral RNA can hijack the reverse transcription activity and so destroys the synthesis of telomeres.

The author acknowledges that the here explored possibilities are hypothetical. However, have they been excluded experimentally? On our part we have started an in silico study to identify candidate subsequences of spike mRNA.

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