A proposal: Project "*Homo sapiens liberatus II*"!

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The idea of this project was stimulated by T. Goldsmith's encouragement and approval and was published (without a name defining it) as an operating proposal in a recent work [1].
For the details and the premises, the reading of the entire work is necessary.
Prof. V. Skulachev's strong example has prompted the possible name.

Introduction

Today: Ageing is considered not a physiological event but a mixed set of diseases with age-related increasing frequency and severity. Ageing manifestations are empirically treated for their dysfunctions and in analogy with diseases showing the same dysfunctions. The cures allow often an increase of survival time in conditions of low quality of life.
In future: It is indispensable to acquire the awareness that ageing is something other than a disease and that needs specific measures. It is possible to conceive an ambitious project for the solution of the problem in four steps:

***Step 1* (Duration: at least a decade)**
Parallel pursuit of various targets
a) Widening of the studies on telomere-telomerase system;
b) The same for apoptosis phenomenon;
c) The same for cell turnover of all tissues and its effect on the functions of each organ;
d) The same for the morphogenesis of each organ, in particular for the dentition;
e) Development of genetic techniques for the effective and precise insertion of a genetic sequence in a point of the genome without causing dangerous alterations (Fig. 1-3);
f) Development of genetic techniques for the effective and precise substitution of a genetic sequence with another sequence (Fig. 1-3);
g) Research of possible safe drugs to modify telomere-telomerase actions and/or cell turnover (or other) so that longevity is increased.

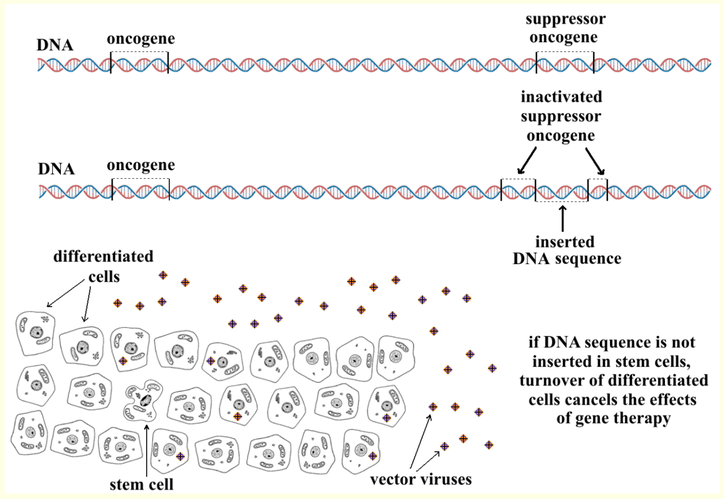

Fig. 1 - Current gene therapy. DNA sequence is inserted in a random position by a vector virus. If an insertion inactivates a suppressor oncogene, this may cause a cancer. The type of vector virus and/or limits in the dose of viruses inoculated may cause the transformation only of differentiated cells and not of the rare stem cells and, consequently, the transitory success of the therapy, because cell turnover gradually substitutes differentiated cells with new cells originated from non-transformed stem cells.

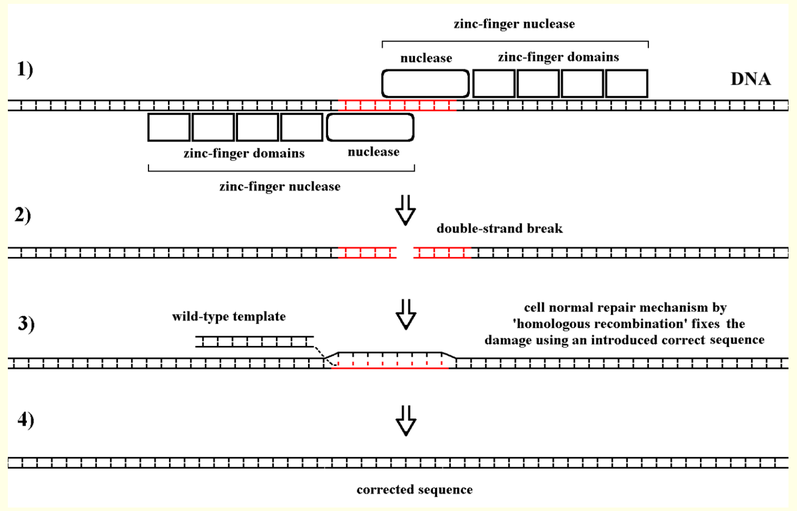

Fig. 2 - The corrected gene is inserted in substitution of the altered gene. With the use of two zinc-finger nucleases, composed of zinc-finger domains (each specific for a particular three-base DNA sequence) and a nuclease (a Type IIS restriction enzyme), it is possible to break DNA double-strand in a precise point with the successive correction by normal cell DNA-repair system by using an introduced DNA corrected sequence [2]. This method appears very promising [3].

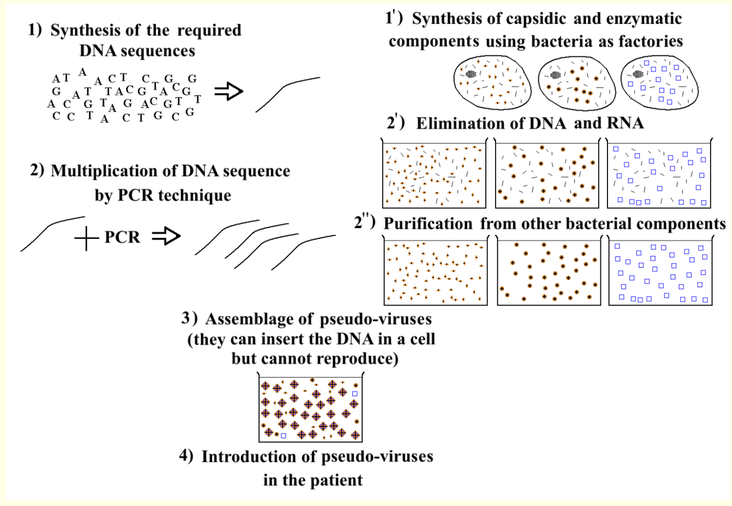

Fig. 3 - Creation of gene vectors (hypothetical scheme). The required DNA sequences (for the specific zinc-finger nucleases, for the gene to be modified, etc.) are created starting from defective viral sequences and from single nucleotides and multiplied by using PCR technique. Capsidic components and enzymes essential for the assemblage and activation of pseudo-virus are synthesised by using transformed bacteria and later eliminating DNA, RNA and other bacterial components. DNA sequence and capsidic and enzymatic components are assembled creating pseudo-viruses able to insert or substitute a DNA sequence in a cell but not to reproduce.

***Step 2* (Duration: at least a decade)**
Parallel pursuit of various targets
a) Experiments on animals of insertion of genetic sequences to modify the modulation of telomere-telomerase system for increasing longevity;
b) The same with techniques of genetic substitution;
c) First applications of the above-mentioned techniques on man for the treatment of severe genetic diseases;
d) First applications of the above-mentioned techniques on man for the treatment of age-related severe diseases such as Age-related Macular Degeneration and Alzheimer's disease (Fig. 4);
e) As with (a) and (b) to obtain multiple dentitions;
f) Experiments on animals of possible drugs with increasing longevity qualities.

***Step 3* (Duration: at least two decades)**
a) First experiments on man of gene therapy (but not on germinal cells) and of possible drugs with increasing longevity qualities;
b) Verification of the results and progressive widening of the experiments.

***Step 4* (Duration: indeterminate)**
a) Possible experimentation and application of gene therapy on human germinal cells;
b) Applications on a large scale of safe and tested techniques and drugs

Fig. 4 – The defeat of Alzheimer's disease by telomerase activation in neuron satellite glyocites will be a plausible preliminary goal to master ageing.

Effects: Increase in the mean duration of life deriving from longevity increase.

Means: For the extreme weight of the argument, the creation of an apposite international agency, adequately funded, could be useful, with the specific aim of controlling ageing and, as a very important corollary, genetic diseases, following the example and the wonderful outcomes of NASA (Fig. 5A-B).

Aging may be mastered, but it is necessary to consider it a function and not a muddled array of diseases: a paradigm change is an essential preliminary!

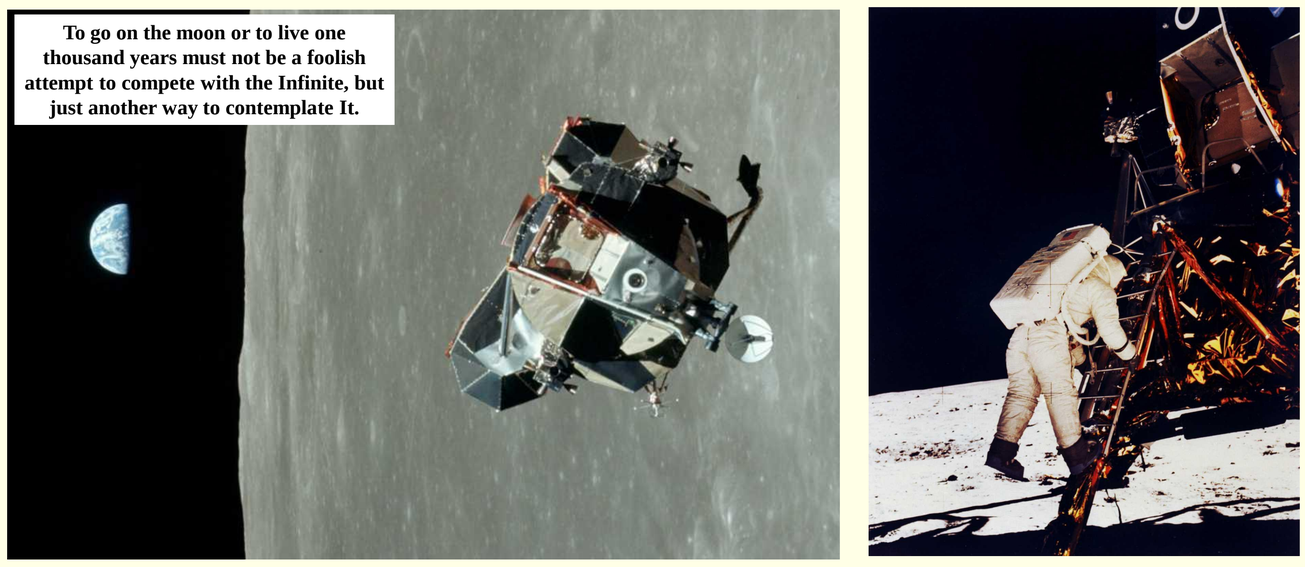

Fig. 5A-B - Moon landing was the aim of an ambitious and complex project that was successful because based on solid scientific grounds and strongly supported both economically and intellectually.

REFERENCES: [1] Libertini G (2009) *Prospects of a Longer Life Span beyond the Beneficial Effects of a Healthy Lifestyle*, Ch. 4 in *Handbook on Longevity: Genetics, Diet & Disease*, Nova Science Publ., New York (with 244 references); [2] Urnov FD et al. (2005) Highly efficient endogenous human gene correction using designed zinc-finger nucleases. *Nature* 435, 646-51; [3] High KA (2005) Gene therapy: the moving finger. *Nature* 435, 577-9.