The Gene Therapy Frontier in Aerospace Medicine

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We are poised on the verge of a change in how we view and treat disease that will be as fundamental as vaccination and antibiotics. In October the FDA approved a second gene therapy, just 7 weeks after the first, and its advisory panel has unanimously recommended a third for approval.[1,2,5] The first gene therapy approval in Europe was granted in 2012, and a second in 2016, each supplying a functioning copy of a non-functioning inherited gene to treat a single-gene inherited disorder. The two now approved for use in the U.S. are for treatment of blood cancers; the recommendation is for the first U.S. gene therapy for an inherited single-gene disorder. Gene Therapy Net[4] is currently tracking over 100 clinical trials, and lists over 2400 since 1989. We can expect the pace to increase in response to the stunning advances in the controllability of gene editing, and the successes of these approved therapies.

Will gene therapies have consequences for aerospace medicine? My guess is that they will, and here are just a few reasons why:

1. There will be individuals able to fly (as well as many other things) who otherwise would have been denied by inherited genetic misfortune. In most if not all cases, the original gene and its products will still be expressed in the individual, and may need to be considered in aeromedical determinations. A gene therapy treatment for sickle cell disease, for example, may supply enough healthy hemoglobin to carry oxygen on a parity with wild type genotypes, but with the potential for a remnant of cells which sickle in response to hypoxia, posing a threat to microcirculation. Each therapy, its indicating disease process, and the degree of penetrance of the defective genotype, will need to be considered.

2. Hypoxia induces a host of genetic responses, mediated by hypoxia-inducible factor 1a (HIF-1a). Some research seeks to exploit the frequently hypoxic nature of solid tumors in order to tune genetic constructs such that they are activated by hypoxia. Such a construct is envisioned to circulate freely, only expressing toxicity to cells in the hypoxic milieu within such tumors. The consequences for altitude exposure would be the same, with potentially devastating consequences when all cells are hypoxic.

3. It is highly likely that colorblindness will be amenable to gene therapy.[3] While the squirrel monkey experiments are quite convincing as to the simple fact of color discrimination, we have no idea how the details of natural vs. gene therapy-derived color vision compare with regard to thresholds, resolution, light levels, motion detection, and other aspects of psychophysics of color perception, and how they might interact with the demands of flight.

In a way, none of these things are new, because aerospace medicine has always been "personalized medicine," in the sense of taking the performance of each individual and the demands of each occupation into account. There is comfort in knowing that the basic principles won't change, but there will be some surprises, and there is a reason to invest some thought in this frontier now, before we find ourselves in uncharted territory. But most of all, there is justification for optimism: aviation will be just one of many fields in which humans can expect to perform better and longer than before, thanks to the researchers, clinicians, and regulators who take these advances from concept to practice.

Wishing you and yours peace and joy for the holidays and the coming year.

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