Gene Therapy (2008) 15, 807

www.nature.com/gt

EDITORIAL

Introduction to AAV Vector special issue

Gene Therapy (2008) **15,** 807; doi:10.1038/gt.2008.62

The genetic code is the system that organisms use to store and encode information required for life. The cellular molecular machinery transfers the genetic information from DNA or RNA genomes into translatable messenger RNA and proteins. The triplex code is familiar to all biologists and utilized by gene therapy researchers. Marshall Nirenberg, a post-doctoral researcher at the National Institutes of Health, envisioned the basis for the genetic code in the late 1950s and by 1965, determined the RNA code for each amino acid. In 1968, Marshall Nirenberg was awarded the Nobel Prize for Medicine or Physiology.

In 1967, at a Research Corporation Award Dinner (republished in Science 1967[1]), I spoke of 'genetic surgery' and the potential benefits and challenges that genetic manipulation presented to mankind. It is with a great deal of interest and enthusiasm that I have watched the emerging field of gene therapy developing over the course of the last 30 years. Pioneering researchers at the National Heart, Lung and Blood Institute, where our work deciphering the genetic code was conducted, played a major role in the birth of the field of therapeutic gene transfer and have continued to make important contributions that have allowed the field to bloom and prosper.

The possibilities seemed limitless when the genetic language of cells was determined about 45 years ago. The development of recombinant DNA methods in the 1970s by Paul Berg, Stanley Cohen and Herbert Boyer, and Hamilton Smith enabled the manipulation of cellular genes and the production of human proteins in genetically modified prokaryotic species. The scientific, medical and commercial values of recombinant DNA technology are indisputable and many potential applications have yet to be discovered. Genetically modified mammalian cells were achieved by chemically transferring genetic material, initially as discrete pieces of DNA and then as plasmids, into cells and selecting for stable integration. Subsequently, applying similar DNA transfer technologies to mammalian ova generated transgenic animals. Thus, the technology has progressed from biochemical experimentation to creating new genetically modified forms of life. The next logical progression of gene transfer technology was to use genes therapeutically in human beings.

A central tenet of the gene therapy field is that by using a virus (or other) vector to introduce a foreign gene into a cell, it would be possible to alter the cellular genotype and produce a new phenotype in a predictable way. Early successful gene transfer studies were based on cell culture experiments and demonstrated rescue of cellular phenotypes by expression of exogenous DNA that encoded corrective proteins, confirming the central dogma. Now that preliminary studies are completed, researchers have expanded their efforts to the issues of systems biology—of altering cellular metabolism, cellular signal transduction, cell cycle progress and cellular differentiation.

The papers in this volume describe progress, history and current salient issues in the field of gene therapy. They present a current picture of where we stand in closing the gaps between basic and clinical research. The field of gene therapy may not only advance knowledge concerning therapeutic gene transfer, but presents the prospect of exploring normal cellular processes in the context of the total organism.

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Reference

1 Nirenberg MW. Will society be prepared? *Science* 1967; **157**: 633.