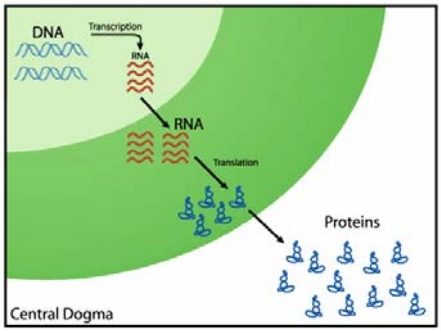
NIST Advanced Technology Program
Gem Report

Fighting Disease with Zinc-Finger Proteins

Sangamo Develops Technology to Turn Genes On and Off



Zinc Finger Proteins (ZFPs) affect cells' DNA. Each cell contains only one DNA molecule. That DNA instructs the cell to produce multiple RNA molecules (transcription). The RNA molecules produce many proteins (translation). Thus, a change in the DNA molecule can have a dramatic impact on cellular activity.

The Challenge—In the 1990s, DNA research held promise for new disease treatment methods. Zinc Finger Proteins (ZFPs) are proteins with finger-shaped folds that can bind with DNA. Sangamo BioSciences, Inc., a biotechnology start-up company, attaches ZFPs to DNA in a sequence-specific manner and cleave the DNA at specific sites. The technology has the potential to detect and alter individual gene mutations, which affect the cell's function and health. In 1996, Sangamo submitted a proposal to ATP to develop high risk therapeutic applications for hepatitis B and HIV/AIDS. The three-year project began in 1997.

The Outcome—The ATP-funded project led to Sangamo's ZFP platform technology, regulating endogenous human and viral genes. Technical success has led to business growth. Sangamo raised $60 million from an initial public offering in 2000 and acquired a competitor firm in 2001. As of 2005, Sangamo collaborates with pharmaceutical partners in developing ZFP Therapeutics. Sangamo is conducting clinical trials to treat numerous diseases based on ZFP technology:

- **Diabetic Neuropathy.** Sensory and motor neuropathy symptoms, including numbness, tingling sensations, and pain, can lead to amputations, especially in diabetics. In 2005, Sangamo submitted an investigational new drug application to the U.S. Food and Drug Administration for SB-509, a novel therapeutic designed to stimulate the regeneration of nerve function. Clinical trials began in 2006.
- **Peripheral Artery Disease.** Three million Americans suffer from heart failure. Sangamo is developing a ZFP that could stimulate the gene that controls blood vessel growth. Clinical trials began in August 2004 and continue through 2007.
- **HIV.** Some people have a natural immunity to HIV/AIDS, because they have a mutation in a receptor gene, called CCR5. Sangamo aims to mimic the mutation that naturally occurs in these immune patients, and the company anticipates beginning human trials in 2007.
- **Other Diseases.** Sangamo is pursuing numerous other disease treatments using ZFPs: diabetes, sickle cell disease, ischemic heart disease (caused by the narrowing of the coronary artery), congestive heart failure, cancer, neuropathic pain, hepatitis B, Wiscott-Aldrich Syndrome and X-linked severe combined immunodeficiency "bubble boy" disease.

Although the technology is still risky, if any one of Sangamo's treatments succeeds and reaches commercialization, it could result in saving thousands of lives.

Partnering Organization:	Sangamo BioSciences, Inc., Richmond, CA
Project Duration:	5/1/1997 – 4/30/2000
Project Cost:	$2.0M ATP cost-share; $0.7M industry cost-share
Project Brief:	http://jazz.nist.gov/atpcf/prjbriefs/prjbrief.cfm?ProjectNumber=96-01-0315
Project Status Report:	http://statusreports.atp.nist.gov/reports/96-01-0315.htm Research conducted February 2006