

# SPEEDING GENE THERAPIES

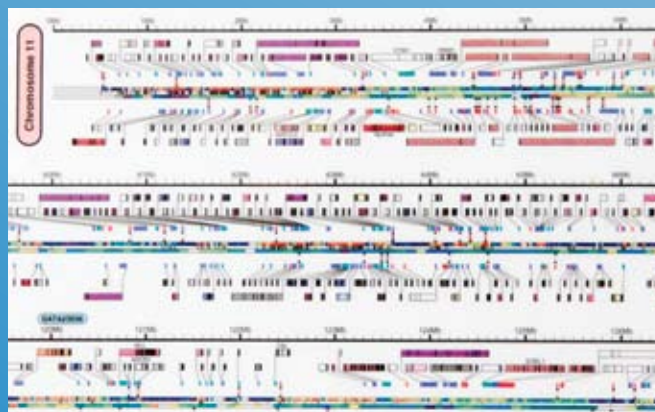
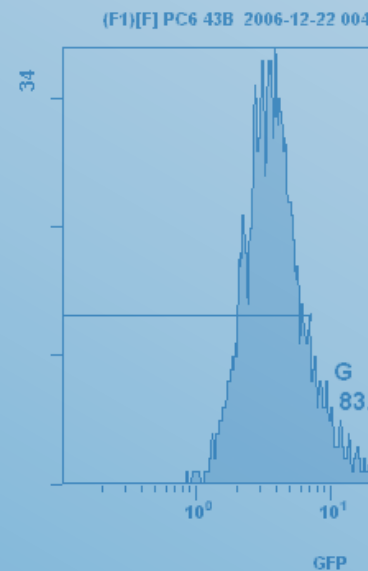
## NATIONAL GENE VECTOR LABORATORY

The most powerful weapons against cancer, diabetes and other serious diseases cannot be seen. They are genes — bits of DNA that can be delivered to wayward cells, fixing problems at the source.

Gene therapy holds huge potential for future cures. But refining these genetic tools, manufacturing them in quantity and getting them into clinical trials is a major challenge on all fronts: technical, analytical and regulatory.

The National Gene Vector Laboratory (NGVL) at City of Hope is helping make it happen. Located within the Center for Biomedicine & Genetics (CBG), the NGVL is the first large-scale facility for manufacturing biological therapeutics at an academic research center in the United States. Here, promising new genetic and cellular agents created by researchers can move into production rapidly, so that they can be entered into clinical trials without delay.

The two-story, 20,000-square-foot CBG facility was built in 2000 with the purpose of creating an unlimited array of novel therapeutics. Led by Larry A. Couture, Ph.D., the CBG currently produces islet cells that treat type 1 diabetes, monoclonal antibodies that fight cancer, engineered T-cells for immunotherapeutic clinical trials, cancer vaccines, viral vectors for gene therapy against HIV, and hematopoietic cell products to treat blood disorders. Process development is also beginning on two types of recombinant proteins, similar to the way City of Hope achieved a breakthrough in the development of synthetic human insulin nearly 20 years ago.



Lower left:  
Larry A. Couture, Ph.D., City of Hope

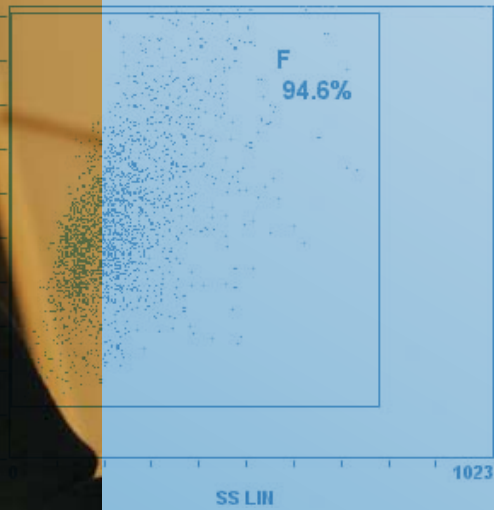
Center:  
City of Hope manufactures  
investigational novel therapeutics for  
researchers around the country.

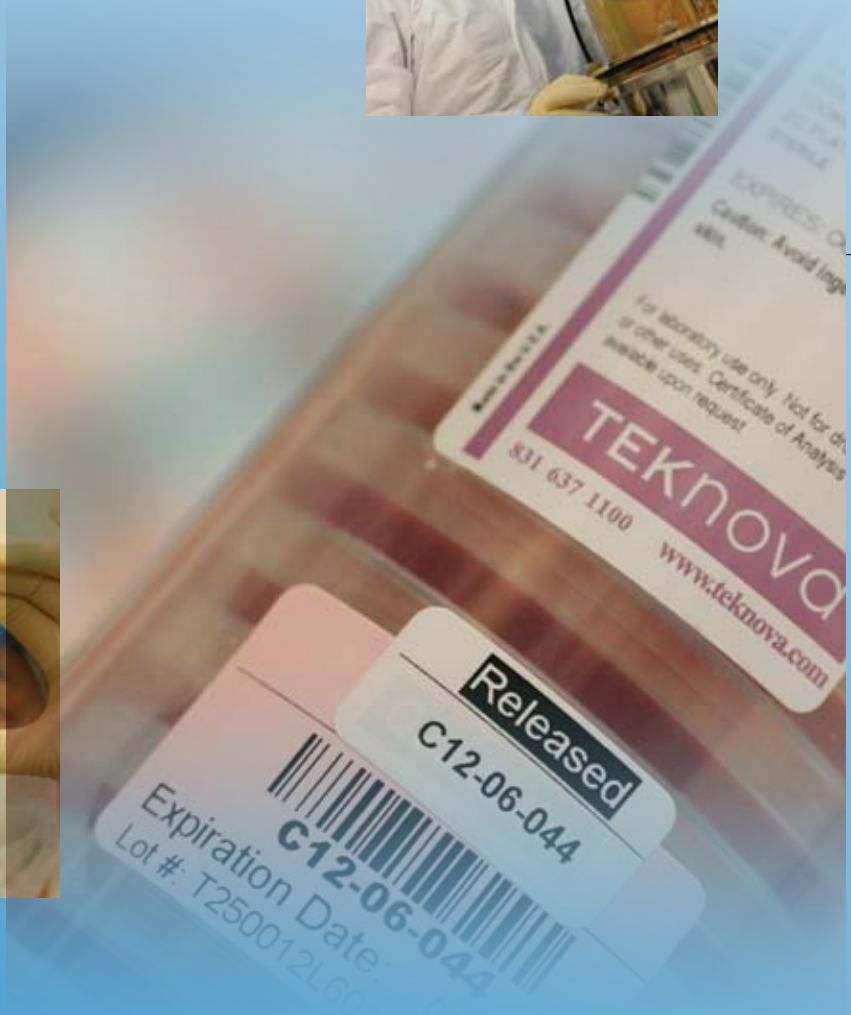
Upper Right:  
Michael C. Jensen, M.D.,  
Associate Chair,  
Division of Cancer Immunotherapeutics  
and Tumor Immunology, City of Hope

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# COLLABORATIONS





City of Hope's National Gene Vector Laboratory rapidly manufactures biological therapeutics so that these new therapies can move into clinical trials without delay.

1997

1998  
 CBG conceived  
 May 1998

Began construction  
 of CBG  
 January 1999

1999

CBG funded  
 July 1998

2000

CBG completed  
 February 2000

City of Hope produces DNA plasmids for all qualified, federally funded laboratories nationwide.

The CBG’s prolific output, scientific expertise and certification as a Good Manufacturing Practices facility led the National Institutes of Health (NIH) to commission it as an NGVL, one of only five such facilities in the U.S. today. Specifically, the laboratory produces clinical-grade DNA plasmid vectors for use in phase I and II clinical protocols. DNA plasmids, also called “naked DNA,” are circular pieces of DNA carrying genes that can be transferred into cells with therapeutic effects.

Plasmids are in demand by researchers because unlike viral vectors, they have the advantage of producing little or no immune response. As the only NIH-supported plasmid manufacturer in the U.S., City of Hope’s NGVL produces DNA plasmids for all qualified, federally funded laboratories nationwide. In addition, the facility also has

produced a lentivirus vector and is a designated back-up site for the production of adenovirus gene therapy vectors.

With its robust manufacturing capacity and ability to quickly produce novel therapeutics at a small scale, the CBG provides a fast track for scientists seeking to move their research from bench to bedside. It also generates valuable collaborations between City of Hope and other institutions. With material from the NGVL, Jennifer Grandics, M.D., at the University of Pittsburgh has made rapid progress in antisense gene therapy that can inhibit cancer of the head and neck. At the University of Wisconsin, Douglas McNeel, M.D., Ph.D., is taking a promising DNA plasmid vaccine that fights prostate cancer into phase II clinical trials. In the search for better, faster cures, City of Hope is giving researchers across the country the genetic tools they need today.

CBG MANUFACTURED PRODUCTS		
MANUFACTURE DATE	PRODUCT NAME	PRODUCT TYPE
12/12/2001	IL-13	Plasmid DNA
1/14/2002	CE7R	Plasmid DNA
7/22/2002	293	Human Cell MCB
8/22/2002	293T	Human Cell MCB
4/17/2003	TM-LCL	Human Cell MCB
4/30/2003	L29.19	Plasmid DNA
5/23/2003	pTVG-hPAP	Plasmid DNA
1/29/2004	EGFRAS	Plasmid DNA
2/25/2004	T84.66 Diabody	Monoclonal Antibody
6/14/2004	Anti-CD19	Plasmid DNA
1/3/2005	pHIV7-shi-TAR-CCR5RZ	Plasmid DNA
1/12/2005	TM-LCL	Human Cell WCB
1/20/2005	pCgp	Plasmid DNA
3/21/2005	pCMV-Rev2	Plasmid DNA
5/12/2005	pCMV-G	Plasmid DNA
6/1/2005	Lentivirus	Viral Vector
6/20/2005	pHIV7-shi-TAR-CCR5RZ	Plasmid DNA
12/14/2005	Gene Modified T-cell	Engineered patient-specific cells
2/15/2006	Anti-CEA hT84.66 M5A/NHS-DOTA	Monoclonal Antibody
3/23/2006	pCB-AT-Zero	Plasmid DNA
4/25/2006	Zenapax	Monoclonal Antibody
5/2006	Lentivirus	Viral Vector
6/2006	pCMV-Rev2	Plasmid DNA
8/2006	Gene Modified T-cell	Engineered patient-specific cells
12/2006	CD19Rop epHIV7	Plasmid DNA

2001

First production December 2000

Designated National Gene Vector Lab September 2001

Designated Southern California Islet Cell Resource Center September 2001

2002

California Food and Drug Branch License March 2002