

CD103 ANTI-INFLAMMATORY ANTIBODY PROGRAM

THERAPEUTIC CANDIDATE:	mAb to CD103 integrin
CLASS:	murine IgG1 mAb
ACTIVITY:	anti-CD103
CLINICAL INDICATIONS:	chronic inflammation / multiple
STATUS:	partnered with Biogen Idec

CD103 (alpha-E beta-7, HML-1) is a unique integrin that is present on T cells in mucosal tissue. It is considered to have a distinctive role in the activation, homing and retention of T cells that mediate inflammatory diseases affecting the skin and mucosal regions of the intestine, lungs, and genitourinary tract. LigoCyte has partnered with Biogen Idec to develop therapeutics to CD103 for the treatment of chronic inflammatory diseases. Potential indications include respiratory inflammation, inflammatory bowel disease and graft-versus-host disease.

TARGET

Inflammation is an immune response characterized by a sequence of cell binding and activation events, whereby leukocytes migrate to the inflamed site. Leukocyte binding and activation events are governed by a group of molecules known as cell adhesion molecules, or CAMs. Critical members of the CAM family include integrins, cell receptor proteins involved in cell-extracellular matrix and cell-cell interactions. Integrins govern leukocyte homing to inflammatory sites and also have an adhesive role within the tissue, retaining leukocytes that have migrated to inflamed areas. By inhibiting integrins, leukocyte adhesion can be limited and tissue damage associated with chronic inflammation can be reduced.

CD103 is a unique integrin that has a very specific pattern of expression when compared to other integrins. Unlike most integrins, only 2% of lymphocytes that circulate in the blood express CD103. However, more than 95% of intraepithelial lymphocytes (T cells that occupy the epithelial layer just below the surface of tissues) and 50% of T cells in the lamina propria (layer of tissue underlying the epithelium) are CD103 positive, suggesting a distinctive role in mucosal immunology. Furthermore, CD103 is strongly associated with mucosal antigen-presenting dendritic cells and is thought to have a critical role in antigen processing in mucosal tissues. With such a unique pattern of expression, this target holds the promise to limit the side effects associated with current biologic therapies, while offering the improved safety and efficacy now associated with these approved medicines.



CD103 Integrin Binding Domain
*Courtesy of the Laboratory of Functional Immunogenetics,
Babraham Institute*

POTENTIAL INDICATIONS

Respiratory Inflammation

Respiratory inflammation is characterized by the recruitment of large numbers of leukocytes to the lung and is a hallmark of respiratory diseases such as asthma and chronic obstructive pulmonary disease (COPD). In the past few decades, asthma and COPD have become increasingly prevalent, exacting a tremendous toll on patients, providers and society.

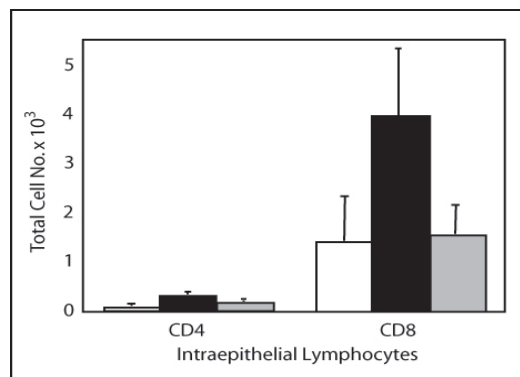
Asthma affects over 7% of the U.S. population, and while usually not life-threatening, it has a major effect on the quality of life. According to the American Lung Association, over 20 million Americans had asthma in 2001, it entailed an economic burden of \$14 billion, and 4,269 people succumbed to the disease. Even more staggering are the COPD statistics, where estimates indicate that 16

million individuals suffer from the disease. In 2001, approximately \$30 billion in medical expenditures and productivity losses were accrued, and as the only leading cause of death that continues to increase, 118,744 people died. Asthma and COPD are defined by an uncontrolled inflammation of the airways. Large numbers of leukocytes are recruited to the lung and their presence causes lung damage that impairs a patient's ability to breath. T cells isolated from the lungs of patients with interstitial lung disease have high levels of expression of CD103 and may play a critical role in the pathogenesis of pulmonary inflammatory diseases.

Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is an idiopathic disease involving an immune reaction of the body to its own intestinal tract, highlighted by a chronic inflammatory response at the mucosal lining. The two major types of IBD are Crohn's disease (CD) and ulcerative colitis (UC). It is estimated that 1,000,000 Americans suffer from IBD, split evenly between CD and UC. Each year, approximately 30,000 new cases of IBD are diagnosed.

Recent research has highlighted the importance of CD103 as a therapeutic target for the treatment of IBD. In studies of CD103-deficient mice, intraepithelial lymphocyte numbers were selectively reduced, while human studies of patients with Crohn's disease showed that the frequency of CD103 positive lymphocytes was significantly higher in colon specimens. In a mouse model of UC, treatment with an antibody against CD103 significantly reduced the mucosal inflammation and improved the course of the disease.



Lymphocyte numbers following the induction of colitis in mice. White = normal, black = colitis, gray = CD103 MAb. (J Immunol. 1999 Apr 15; 162(8): 4975.)

Graft-versus-Host Disease

Graft-versus-host disease (GvHD) is the primary complication of bone marrow transplants and the main factor limiting the wider application of this important therapy. Such transplants are employed to reestablish hematopoietic function in patients with damaged or defective bone marrow, which is commonly associated with cancer immunotherapy (chemotherapy). GvHD occurs when immunologically competent T cells collected from the donor attack the genetically disparate host cells, resulting in significant morbidity and mortality. CD103 expressing T cells have been determined to play a critical role in the destruction of host epithelial cells by the donor cell population. Inhibition of CD103 could potentially limit GvHD and improve the chance for graft success by ameliorating this critical T cell subset.

STATUS

The CD103 program has been partnered with Biogen Idec. The collaboration includes an opportunity for co-development, co-promotion and the sharing of profits resulting from commercialized products.

COMPANY SUMMARY

LigoCyte Pharmaceuticals, Inc., is a biotechnology company focusing on the development of therapeutic antibodies and vaccines. We develop drugs that manipulate the way the immune system recognizes and responds to inflammation and infection to effect the disease process. Our focus is the immunology of mucosal surfaces, which governs gastrointestinal and pulmonary inflammatory diseases and addresses the most common routes of infection. In addition to the CD103 program, LigoCyte's pipeline includes a number of other promising therapeutic antibodies and vaccines.

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