

# Discovery space

In October 2003 Children's Hospital Boston will unveil its new research facility. Here are just a few examples of the exciting work that will be going on in the building's labs.

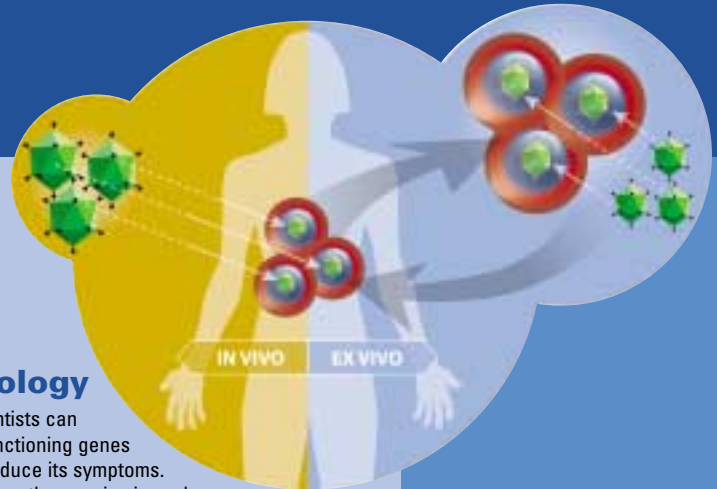


## Hematology/Oncology

Children's researchers in several fields are studying the tiny zebrafish to find answers to human disease because it has a genetic makeup strikingly similar to that of humans. Hematologist-oncologist Leonard Zon, MD, looks to them for help tackling blood diseases like anemia and leukemia, and has found new genes responsible for blood stem cell development. He hopes to manipulate the ability of stem cells to make organs, which would be therapeutically beneficial.

## Molecular biology

Using gene therapy, scientists can replace missing or malfunctioning genes to eliminate disease or reduce its symptoms. There are two kinds of gene therapy: in vivo, where cells are genetically modified in the body; and ex vivo, where cells are removed, a desired gene is added and the cells are returned to the patient. Diseases like Alzheimer's, Parkinson's and cystic fibrosis are the targets of gene therapy, and researchers in Children's Molecular Biology labs are also studying its use in treating cancer and blood diseases.



## Stem cell/ Developmental biology

Embryonic stem (ES) cells have the capacity to develop into many kinds of more mature, specialized cells, which is why so many Children's researchers are studying them. A few examples: one lab is looking at how stem cells differentiate into other blood cell types, as well as which genes are required to form and maintain blood stem cells; another is investigating potential use of muscle stem cells to replace defective muscle in muscular dystrophy; still another is studying the potential for regeneration of heart muscle.

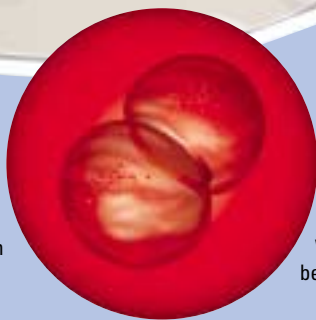
## Endocrinology

Vasopressin is a brain molecule that has at least two roles: to tell the kidneys whether water should stay in the body or be expelled as urine, and to regulate the body's stress response. These mice are standing next to the urine they made over one day: the one on the right lacks its vasopressin gene and produced roughly 20 times more urine than the mouse on the left. Researchers in Children's Endocrinology labs predicted the mouse without the vasopressin gene would show a lower stress response, but found it was higher than the mouse on the left. Their hope is to find molecules that could be made into medicine to dampen the body's response to stress.



## Immunology

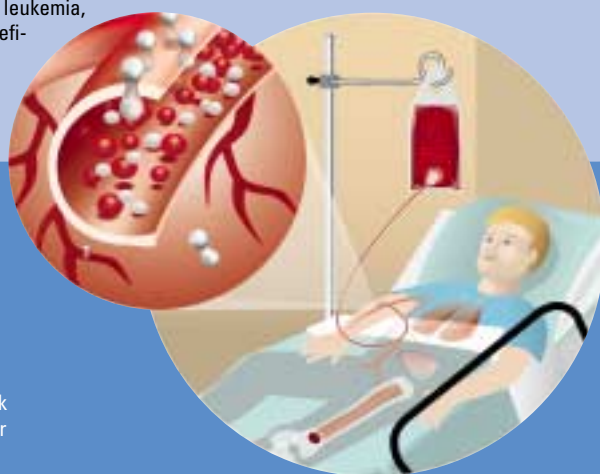
For the body to mount an effective immune response, two types of white blood cells—T and B cells—must interact in an interface called an Immunological Synapse (IS). Cellular actin is critical for the integrity of a productive IS. Children's Immunology researchers are studying the T cell/B cell interaction in relation to an often fatal disorder called Wiskott Aldrich Syndrome (WAS),



characterized by defects in the WAS protein (WASP). They identified a novel protein called WIP that regulates actin and WASP function, and found that the immune response is compromised in mice that lack WIP. They hope study of these mice will lead to better understanding and management of WAS.

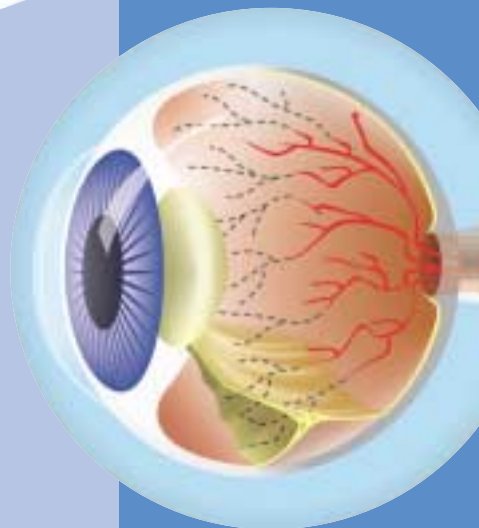
## Transfusion medicine

A variety of blood cells are formed in the bone marrow, and following transfusion of blood into a recipient, individual cells differ in their migration patterns. Because of the blood cells' immune system functions, the Joint Program studies how they leave circulation to go into various tissues, and how they move between compartments within the tissues. An understanding of these mechanisms has direct relevance to hematopoietic stem cell transplantation used for the treatment of leukemia, as well as hereditary disorders like immunodeficiency syndromes and blood disorders.



## Vascular biology

Work by Donald Ingber, MD, PhD, in the Vascular Biology Program has revealed that the internal, filamentous, molecular framework of the cell, or cytoskeleton, plays a central role in control of capillary cell shape, movement and growth during blood vessel development. His discovery that cells use "tensegrity" in their cytoskeleton, the same architecture used in geodesic domes, are changing the view of cell structure and tissue regulation. Ingber's work also has resulted in the development of novel angiogenesis inhibitors for anti-cancer therapy and new approaches to tissue engineering.



## Ophthalmology

Retinopathy of prematurity (ROP) causes blindness in thousands of premature infants every year when blood vessels grow out of control over the retina. Proper blood vessel growth is dependent on growth factors IGF-1 and VEGF. When babies are born prematurely, they stop getting IGF-1 from the mother, and blood vessel growth stops. As the eyes mature the vessels become oxygen starved, VEGF increases and blood vessels grow out of control. Lois Smith, MD, PhD, and her fellow Children's researchers are studying whether giving premature infants extra IGF-1 will stop the abnormal blood vessel growth associated with ROP.