Transplantation surgery is a field of medicine that has its foundation in immunology. Immunology is a science that attempts to understand why and how the body recognizes foreign cells, such as virus-infected cells, bacteria, tumor cells, and transplanted organs. This essential function serves to protect the individual (self) from anything foreign (nonself) that would threaten the existence of the individual. In transplantation, we have tried to understand the events that result in a rejection and cause the destruction of the transplanted organ. Today, we know that any transplanted organ, such as the kidney or liver, carries with it proteins and cells from the donor that can travel in the recipient's body to the lymph nodes. Once in the lymph nodes, the donor's proteins and cells meet with the recipient's white cells that are part of the immune system. Here, the donor's proteins and cells trigger a specific type of white cell, known as dendritic cells, to teach the recipient's white cells, known as T cells, to recognize the donor's cells as foreign. Thus, the T cells are transformed into "killer cells." The killer cells travel to the transplanted organ, where they reject and destroy the organ (Figure 1).

Over the past 35 years, several drugs have been developed to control rejection in the immune response. In the 1960s and 1970s, the first generation of immunosuppressive drugs, azathioprine and steroids, were used. These were fairly weak immunosuppressive drugs that required significant immunological manipulations to allow successful outcomes. The mortality rate following kidney transplantation was from 20% to as high as 30%. In liver transplantation, the reported mortality rate averaged 75%. In 1980, cyclosporine was introduced. This new drug was very potent and allowed successful transplantation with minimal immunological manipulations. With the introduction of cyclosporine, the mortality rate declined to 5% to 10% for kidney transplantation and to approximately 20% for liver transplantation. In the 1990s, we have experienced an explosion in the development of new immunosuppressive drugs. The most current drugs on the market are tacrolimus and sirolimus. These are very powerful immunosuppressive drugs that require minimal immunological manipulations and produce even better results. The mortality rate from using these drugs is 2% to 5% for kidney transplantation and 10% or less for liver transplantation. In the future, we will continue to see the development of new drugs that will further reduce mortality rates. However, new drugs will not solve the problem of long-term drug use. Consequently, scientists and clinicians in the transplant community are seeking new ways to perform immunological manipulations.

What are the problems of long-term drug use and why would it be beneficial to eliminate using immunosuppressive drugs to treat transplant patients? The reasons are 2-fold. First, immunosuppressive drugs are very powerful, so there are strong side effects that can occur in major organs such as the kidneys, the liver, and the brain. The drugs also can affect blood pressure, cause diabetes and infections, and increase the risk of cancer. The second reason is economical. Immunosuppressive drug treatment is very expensive. The cost for the
treatment of transplant recipients can be as high as $10,000 a year. Therefore, a more effective, economical treatment is needed to address these issues. This can only come about through establishing research methods that will lead us to a scientific breakthrough.

Recalling the process whereby rejection occurs in the immune system, i.e., when a transplanted organ releases proteins and cells that travel to the lymph node, consider the following: In the future, physicians and surgeons will be able to institute complex treatments that will make the immune system believe that the transplanted organ is its own. This treatment will make it possible for the immune system to believe that the new proteins and cells entering the lymph node are nothing more than those particular substances coming from its own kidney, for example. Consequently, the recipient's white cells (dendritic cells and T cells) will not be able to respond. Thus, killer cells will not form, and rejection will not occur. This process is called tolerance and is often referred to as the "holy grail" in transplantation (Figure 2). To improve our methods of transplantation, it is important that our scientific research be directed toward achieving this process of tolerance.

The strength of Baylor University Medical Center lies in its tremendously strong clinical transplant programs. With the establishment of the new Lieberman Research Building and the Baylor Institute for Immunology Research, we are adding a world-class basic immunology laboratory that will work in concert with the clinical transplant programs. This new laboratory will promote a free exchange of important scientific information between clinicians and scientists. Clinicians will be able to bring their observations and problems to the basic scientists for examination and, in return, the basic scientists will bring their findings to the clinical scientists for final review and consideration for application in the clinical setting. The Baylor Institute for Immunology Research will create a favorable environment for scientists and clinicians to realize the dream of a scientific breakthrough in immunology that we have all been working toward during the last half of this century. This discovery would forever change the field of transplantation.
Figure 1

Figure 2