

CELL-BASED REGENERATIVE MEDICINE FOR HEART DISEASE

Despite improvements medical and surgical therapy, myocardial infarction or non-ischemic heart disease is often the beginning of a downward spiral leading to congestive heart failure. Other than heart transplantation or implantation of a ventricular assist device (“artificial heart”), current therapies merely help the organism to survive with a heart that is working at a fraction of its original capacity. It is therefore no surprise that cardiac stem cell therapy with its promise to regenerate or rejuvenate the heart has raised many hopes.

Although extensive experimental data support the concept of cardiac cell therapy, neither the ideal source and type of cell nor the critical quantity and mode of application in the clinical setting have been defined so far. In patients with acute myocardial infarction, several cell-based approaches such as intracoronary delivery of mononuclear bone marrow cells or enriched hematopoietic progenitor cell products; systemic cytokine stimulation with release of bone marrow progenitor cells into the systemic circulation; and both intravenous or intracoronary delivery of allogenic mesenchymal stem cells are currently being tested. There are encouraging data for each of these strategies based on small cohorts, but many results regarding recovery of function are conflicting or equivocal. For treatment of patients with chronic heart failure, other approaches such as catheter-based intramyocardial delivery of various cell types but also surgical implantation of bone marrow or blood-derived cells in conjunction with bypass surgery or as surgical stand-alone procedures are being evaluated. Moreover, skeletal muscle-derived myoblasts have been used with various delivery techniques. Again, a number of controlled trials have produced conflicting results, and multicenter studies are currently being conducted. Currently, more advanced forms of cardiac cell therapy are attracting a lot of attention, those include genetic cell engineering, co-implantation of specific extracellular matrix components, preclinical testing of embryonic stem cell-derived cells, as well as imaging techniques for *in situ* cell tracking and imaging of cell function. Prior to clinical routine use, however, numerous technical, medical, and regulatory obstacles will have to be overcome.

Based on their extensive experience with patients suffering from end-stage heart failure, physicians, surgeons, and scientists at the German Heart Institute Berlin (DHZB) have recognized the great potential of cell-based regenerative medicine for heart disease. Together with its local and international partners in academics and industry, DHZB is actively developing novel strategies for cardiac regenerative medicine and pursuing their safety and efficacy evaluation in the clinical setting. Those include clinical pilot trials in patients with end-stage ischemic heart disease as well as patients with non-ischemic heart failure who require implantation of a ventricular assist device. Specific surface marker-defined bone marrow progenitor cells, bone marrow mononuclear cell preparations, and *ex vivo* manipulated marrow cell products are being currently being evaluated.