

Reversal of heart failure during mechanical support of left ventricular function - role of nucleotides and energetics in cardiac cells

Heart failure is a major challenge of human health that leads to severe disability and premature death. There is not enough donors to cure everyone by heart transplantation and artificial hearts are still far from perfection. Scientists and doctors try therefore to find alternative ways to cure failing heart. One option is to use device that will temporary support heart function called left ventricular assist device (LVAD) and in this time to let the own patient heart to heal and take full function again. This procedure is called "Bridge to recovery". There are patients who have been cured with this procedure, but many more that were not. This project will first try to analyse situation with newest research technologies that allow to detect changes in thousands molecules that are present in human tissues. Very small samples taken from part of heart that is routinely removed during procedure of LVAD implantation and during LVAD removal as well as blood samples will be collected in this project. Samples will be then analysed for changes in metabolites, proteins and RNA that controls formation of specific proteins. Results of these analyses will tell where new drugs could be designed to treat heart failure and especially to help to regenerate heart during support with LVAD. Second part of the project will be conducted with experimental animals that develop similar heart dysfunction as humans. Then procedures will be tested to establish whether assumption that increasing mitochondrial formation in heart cells combined with LVAD will cure the disease. As with human samples, detailed analysis will be conducted to gather as much as possible information to understand changes that will be observed in heart function. This will be important also to predict unwanted effects as too much mitochondria may increase formation of destructive free radicals. In great complexity of biological processes only *in vivo* experiments as proposed in this project may answer the question whether benefits will outweighs potential deleterious effects. Experiments proposed in this application will help to understand better changes in processes that occur at level of chemical reaction in human body that cause heart failure and will help to cure this disease. As it is difficult to collect experience and resources in a single research center, several units gather together to conduct this project. These research units already established effective collaboration that resulted in more than 100 of scientific publications. Heart Science Centre at Harefield Hospital was first to clinically apply LVAD as Bridge to Recovery procedure. University of Arizona runs performs big number of LVAD implantation and heart transplantations and is experienced in research on mitochondria. Electrophysiology group at Imperial College is very experienced in work with animals that develop heart failure and Medical University of Gdansk has experience and resources to study metabolites, proteins and RNA in heart and blood and its role in heart disease.