

QUESTIONNAIRE

(*) – mandatory fields

	Details about organisation
* Organisation name	Tbilisi State Medical University
Organisation acronym	TSMU
* Organisation Activity Type (RES - Research, HE - University, SME - Small and Medium Enterprise, IND - Industry, OTH - Other)	HE- University
* Keywords of main research areas	hepatocyte transplantation, islet transplantation, small intestinal submucosa, I type diabetes, adult stem cell transplantation, liver injury
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* Description of organisation and its research achievements for the last five years (~ 5000 signs)
<p>The overall goal of Prof. Kakabadze and Prof. Berishvili concerns development of novel therapies. They have been interested in combining the principles of tissue bioengineering and surgical sciences to create auxiliary organs. These principles are applicable to developing therapies for diseases characterized by organ failure, especially in the context of metabolic deficiencies, tissue injury and genetic disorders, as exemplified by acute or chronic liver failure, coagulation disorders, inherited jaundice, and type-1 diabetes mellitus. These disorders can be treated by transplantation of the whole liver or pancreas, as well as by transplantation of liver cells and pancreatic beta cells. However, transplantation of whole organs is often technically complex, expensive and not available in the developing world. Also, shortages of donor organs limit organ transplantation and cell therapy even in economically advanced communities. To overcome these limitations, Prof. Kakabadze and Prof. Berishvili have been investigating the potential of creating auxiliary organs in additional sites, such that native organs will not be perturbed. This should have significant advantages in diseases requiring transient organ support, such as acute liver failure, where the native liver can regenerate, or production of deficient proteins in monogenic disorders, such as hemophilia, where native organs remain undamaged.</p> <p>Prof. Kakabadze and Prof. Berishvili hypothesized that small intestinal segments denuded of the mucosal lining and with intact blood supply will serve as suitable hosts for transplanted tissue fragments. This hypothesis has undergone initial</p>

testing with transplantation of liver microfragments in rats and mice. These initial studies have been most promising and were recently published in scientific journals of the greatest prestige. The data established that transplanted liver tissue is promptly reorganized in intestinal segments with new vessel formation and expression of a variety of genes needed for angiogenesis and other critical events in tissue survival. Also, transplanted tissues demonstrate suitable metabolic, synthetic and excretory function, including release of liver proteins in genetically deficient animals. This initial work will be of great value for establishing a variety of important principles as indicated by the following issues that must be addressed.

Representative publications:

1: Wu YM, Joseph B, Berishvili E, Kumaran V, Gupta S. Hepatocyte transplantation and drug-induced perturbations in liver cell compartments. *Hepatology*. 2008 Jan;47(1):279-87.

2: Joseph B, Kumaran V, Berishvili E, Bhargava KK, Palestro CJ, Gupta S. Monocrotaline promotes transplanted cell engraftment and advances liver repopulation in rats via liver conditioning. *Hepatology*. 2006 Dec;44(6):1411-20.

3: Joseph B, Berishvili E, Benten D, Kumaran V, Liponava E, Bhargava K, Palestro C, Kakabadze Z, Gupta S. Isolated small intestinal segments support auxiliary livers with maintenance of hepatic functions. *Nat Med*. 2004 Jul;10(7):749-53. Epub 2004 May 30.

4: Kakabadze Z, Berishvili E, Długosz JW. The experimental distention of dissected bile duct for the restoration of its continuity in dogs using a device of own construction. *Rocz Akad Med Białymst*. 2003;48:52-6.

5: Berishvili E, Liponava E, Kochlavashvili N, Kalandarishvili K, Benashvili L, Gupta S, Kakabadze Z. Heterotopic auxiliary liver in an isolated and vascularized segment of the small intestine in rats. *Transplantation*. 2003 Jun 15;75(11):1827-32.

6: Kakabadze Z, Benashvili L, Berishvili E. The intracorporeal autoorganic biofilter of portal blood in portal hypertension surgery. *Hepatogastroenterology*. 2001 May-Jun;48(39):752-6.

	Contact Information
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International co-operation / Participation in EU RTD programmes or other bilateral / multilateral actions
INTAS, TACIS, TEMPUS, COST, EUREKA, other RTD programmes (please specify programme/s, project title/s and year/s)
ISTC- Project G-362 “Donor Organs Alternative” – 2000 -2003

	* Please, use “X” to indicate the scientific area/s of your potential project
CHEMISTRY	
SOCIAL AND HUMAN SCIENCES	
ECONOMIC SCIENCES	
ENGINEERING SCIENCE	
ENVIRONMENT	
AGRICULTURE AND FOOD	
HEALTH	X
MATHEMATICS	
INFORMATION SCIENCE	
PHYSICS	
NANOTECHNOLOGIES	
ENERGY	
TRANSPORT	
SPACE	

* Summary of potential research project envisaged hosting of European researcher for the period of between 1 and 2 years
<p>The juvenile diabetes is an epidemic of increasing proportions that is currently estimated to reach an excess of 220 million cases by 2010. As far as healthcare expenditures, it costs over \$220 Billion/year in the USA alone, or 1 of every 6 dollars spent for healthcare.</p> <p>Islet transplantation is a potential treatment for patients with type 1 diabetes mellitus that can restore normal blood sugar without the need for insulin injections and can improve quality of life. However, the long-term outcome of intraportal clinical islet transplantation is relatively low and 2-3 donor pancreata are needed to reach insulin independence in a patient.</p> <p>We hypothesize that clinical islet transplantation outcome can be significantly improved utilizing extrahepatic sites for islet implantation avoiding detrimental IBMIR that is associated with intraportal islet transplantation.</p>

In previous studies we demonstrated that the vascularized intestinal segments that are ablated from the mucose provide excellent conditions for the survival of implanted liver fragments. We assume that this graft site provides also improved conditions for the implantation of isolated islets of Langerhans.

The general goal of the proposed study is to determine whether the small intestinal segment will be capable of providing a suitable location for supporting survival and function of pancreatic rat islets transplanted into isologous recipients. In addition we will investigate whether isolated pancreatic islets will survive in the animals, whether the expression of angiogenic factors, growth factors and extracellular matrix components will promote tissue survival and/or cell differentiation, and whether incorporation of liver fragments will be helpful in the survival and organization of pancreatic islets by providing synergistic support. Our research is a novel approach that may improve the success rate of clinical islet transplants and the quality of life for an increasing number of type 1 diabetics.

	Please, confirm your agreement on data publication and dissemination
I agree with the publication of the data on the web-site http://www.inco-ecca.net , and dissemination among Mobility National Contact Points of the EU MS and AC (YES / NO)	YES
Date	09/12/08