

BÜHLER Leo Hans

59 years old (31th August 1961)

Married, three children

Swiss

Faculty of Science and Medicine

Section of Medicine

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EDUCATION

1997 **Specialist in General Surgery**, Federatio Medicorum Helveticorum
1987 **Medical Degree**, University of Geneva, Switzerland
1980 – 1987 **Medical School**, University of Geneva, Switzerland

CURRENT POSITION

2020 **Professor of Surgery, University of Fribourg, Hospital Cantonal Fribourg**

EMPLOYMENT HISTORY

2015 – 2019 **Full Professor**, Head of the Surgical Research Unit, Department of Surgery, University Hospital Geneva Switzerland
2011- 2015 **Associate Professor**, Department of Surgery, University Hospital Geneva
2009 -2011 **Visiting Associate Professor**, Massachusetts General Hospital, Harvard Medical School, Boston
2001 - 2009 **Assistant Professor**, Head of the Surgical Research Unit, Department of Surgery, University Hospital, Geneva
2000 - 2001 **Clinical fellow**, Transplant Unit, Department of Surgery, Massachusetts General Hospital, Harvard Medical School, Boston
1997 - 2000 **Research fellow**, Transplantation and Biology Research Center, Massachusetts General Hospital, Harvard Medical School, Boston
1988 – 1997 **Clinical resident**, Department of Surgery, University Hospital Geneva, Switzerland

APPROVED RESEARCH PROJECTS (LIMITED to 2011-2020)

- **Swiss National Science Foundation**. Nbr 205320_130572/1
"Platelet and liver endothelial cell interactions regulate liver regeneration"
Principal investigator: Pr L. BUHLER. Amount : CHF 292'225 from 01.10.11 to 30.09.14
- **Commission for Technology and Innovation**. Nbr CTI 13804.1 PFFLS-LS
"Optimized Technology and Improved Materials for Cell Microencapsulation"
Principal investigator: Pr L. BUHLER. Amount : CHF 635'183 from 01.10.12 to 31.04.14
- **Ligue genevoise contre le cancer**, ref. 1314 - « New radioisotopes for the treatment of brain and pancreatic cancer »,
Principal investigator: Pr L. BUHLER- Amount : CHF 240'000 from 01.01.2014 to 01.01.2016
- **Swiss National Science Foundation** – n° CR23I2_152974
« Functionalized polymeric hydrogels for cell immobilization »
Co-PI: Pr S. GERBER et Pr L. BUHLER. Amount : Frs 561'285 from 01.05.2014 to 30.04.17
- **Grant Horizon 2020** in collaboration with CERN - Innovative Training Networks (ITN) Call : H2020-MSCA-ITN-2014 - « MEDICIS-produced radioisotope beams for medicine »
Principal investigator Dr T. STORA. Co-investigator: Pr L. BUHLER – Amount : 3,5 Millions d'Euros from 2015 to 2018.
- **Commission for Technology and Innovation**. N° CTI 17309.2.1 PFLS-LS
"Microencapsulated porcine hepatocytes for acute liver disease: development of the cell therapy product"
Principals investigators: Pr L. BUHLER, Pr Dr S. GERBER - Amount : CHF 381'399.00 from 01.01.15 to 30.06.16.

- **Swiss National Science Foundation.** (FNS-ANR international cooperation). 310030E-164250. *New standardized and functionalized microcapsules: Applications to Type 1 Diabetes Cell Therapy*. 01.02.2016 – 31.01.2019. Amount CHF 491'038. Co-investigator: Pr L. BUHLER

SUPERVISION OF JUNIOR RESEARCHERS (LIMITED to 2010-2020)

MD-PhD Thesis, University Geneva, Antonino SGROI, November 2011, « Effects of hepatocyte transplantation and IL1Ra on liver regeneration » was awarded the prize "ETIENNE GORJOUX".

MD-PhD Thesis, University Geneva, Raphaël MEIER, May 2013, « Interleukin-1 receptor antagonist and mesenchymal stem cell transplantation for the treatment of liver fibrosis » was awarded the prize "ARDITTI".

MD-PhD Thesis, University Geneva, Jeremy MEYER, October 2016, « The role of platelet – liver sinusoidal endothelial cell interactions in liver regeneration » was awarded the prize "ARDITTI".

MD Thesis, University Geneva, Antonino SGROI, 2014, « Un inventaire international de la xénotransplantation chez l'homme » was awarded the prize of the best thesis of the Medical Faculty, Geneva University, 2014.

TEACHING ACTIVITIES (LIMITED to 2010-2020)

Regular teaching for bachelor and master degrees, seminars of visceral surgery, transplant immunology, at the Medical Faculty of the Geneva University, Faculty of Fribourg University

Supervision of master projects 1-4 per year

MEMBERSHIPS IN PANEL, BOARDS

Editor in chief of the medical journal "Xenotransplantation" (current impact factor 3,9) since 2012

President of the International Xenotransplantation Association (2017- 2019)

President of the Research Section of the Swiss Surgical Society, since 2015

Member of the Editorial board of the medical journal "Transplant International" since 2004

Member of the Editorial Board of the medical journal "Transplantation" since 2003

ORGANIZATION OF CONFERENCES (LIMITED to 2010-2020)

Scientific Program Chair, congress of the International Society for Organ Donation and Procurement, Geneva, September 2017

PRIZES, AWARDS, FELLOWSHIPS

Award for the 5th International Xenotransplantation Association, Nagoya, Japon, 1999

L. Buhler, A nonmyeloablative regimen with CD40L blockade leads to humoral/cellular hyporesponsiveness to pig hematopoietic cells in baboons.

XXIV Massachusetts General Hospital Research symposium : Poster of distinction, Boston, USA, 2000

L. Buhler. CD40L blockade requires host macrophages to induce humoral unresponsiveness to pig hematopoietic cells in baboons.

Young Investigator Award at the first joint annual meeting of the American Society of Transplant Surgeons and American Society of Transplantation, Chicago, USA, 2000

L. Buhler. Engraftment of pig peripheral blood progenitor cells in baboons conditioned with a non-myeloablative regimen and CD40L blockade.

Prix de recherche de la Société Suisse de Chirurgie, Davos, 2004

G. Mai, Th. Nguyen, Ph. Morel, D. Trono, L. Buhler.

Treatment of fulminant liver failure by transplantation of microencapsulated primary or immortalized xenogeneic hepatocytes.

Prix de recherche de la Société Suisse de Chirurgie, Lausanne, 2007

R. Baertschiger, D. Bosco, Ph. Morel, A. Kaelin, A. Sgroi, V. Serre-Beinier, L. Buhler, C. Gonelle-Gispert. Potential of hepatocyte differentiation for human mesenchymal stem cells is age dependent.

Prix de recherche de la Société Suisse de Chirurgie, Bern, 2014

E. Montanari, R. Meier, R. Mahou, F. Borcard, A. Bollinger, Ch. Wandrey, C. Gonelle-Gispert, L. Buhler.

Alginate-PEG biomaterial for cell microencapsulation and xenotransplantation.

Leo Buhler – MAJOR RECENT SCIENTIFIC ACHIEVEMENTS

Hepatocyte encapsulation and transplantation

The treatment for acute and chronic liver failure is still limited and the only current strategy is the whole liver transplantation. Due to the shortage of human organ donors, a significant number of potential recipients die without receiving a transplant. Alternative solutions to whole organ have not yet reached large clinical application and my research group has focused over the last 15 years on xenogeneic hepatocyte isolation, encapsulation and transplantation. We first developed the techniques of rodent and porcine hepatocyte isolation and encapsulation. We analysed the anabolic and catabolic functions of encapsulated hepatocytes in vitro and then tested the effect of such cells in small animal models of acute liver failure. We showed that xenogeneic encapsulated hepatocytes transplanted in large quantities into the peritoneum of mice with acute liver failure could rescue the failing metabolism and significantly increased the survival. In collaboration with the research group of the Transplant Unit at the Massachusetts General Hospital, Harvard Medical School (Pr James Markmann), we translated this application to the pig-to-nonhuman primate model and transplanted encapsulated porcine hepatocytes to baboons with acute liver failure. We could show that also in the large animal model, encapsulated liver cells improve survival of recipients. Our recent work in collaboration with Pr Sandrine Gerber has focused on the improvement of the microcapsules and the co-transplantation of stroma cells with the hepatocytes in order to improve cell function and survival. The plan is to initiate a clinical trial of encapsulated porcine hepatocytes to rescue patients with acute liver failure. We have contacted Swiss Medic in 2013 and have designed a road map to initiate such trial and have also launched the start-up “Cell-Caps” in order to collect private funding for the creation of a clean pig breeding facility.

Mesenchymal Stroma Cells interactions with hepatocytes and pancreatic islets

Enzymatic cell isolation induces major modifications of the local cell environment with loss of cell viability and function. In order to improve these outcomes, my group has investigated over the last 10 years the effect of bone marrow Mesenchymal Stroma Cells on liver and pancreatic cells (MSC). We showed that co-encapsulation and transplantation of isolated MSC with hepatocytes or islet cells improved their viability and function. This positive effect was dependent on cell-to-cell contact for MSC-pancreatic islets with involvement of the adhesion molecule N-cadherin.

Liver regeneration

The process of liver regeneration is complex and several aspects are still not understood. Taking advantage of the techniques available in my research group to isolate various liver cell populations, we initiated over the last 5 years in collaboration with a research group at Harvard Medical School (Pr Simon Robson) studies analysing the effects of the different liver cell populations on the regenerative process. We could show in vitro that activated platelets interact with liver sinusoidal endothelial cells and stimulate these to secrete IL6, which will activate the liver stellate cells to secrete hepatocyte growth factor, inducing the hepatocyte replication cycle.