BIOGRAPHICAL SKETCH

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NAME: Tomei, Alice A.

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Politecnico di Milano, Milan, Italy	M.S.	04/2004	Materials Engineering
École Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland	Ph.D.	10/2008	Biotechnology & Bioengineering
École Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland	Post-doc	2/2012	Molecular Engineering

A. Personal Statement

I am an Assistant Professor in the department of Biomedical Engineering and the director of the *Islet Immunoengineering Laboratory* (www.tomeilab.com) at the University of Miami Diabetes Research Institute (DRI). My background uniquely combines expertise *in bioengineering and immunology* and I am applying my skills to the development of novel immunoengineering platforms to prevent rejection after islet transplantation and to promote antigen-specific tolerance for a cure of type-1 diabetes (T1D). To that end, my strategy is to design and develop novel technology platforms with strong clinical translation potential that are supported by solid mechanistic studies in preclinical models of T1D that are relevant to the human disease.

My enthusiastic commitment to T1D cure-focused research is matched by a solid track record of academic achievements and translational efforts. I have trained in the best engineering school in Italy, the Politecnico di Milano. Then, I conducted my PhD work at the École Polytechnique Fédérale de Lausanne (EPFL), Switzerland, under the mentorship of Dr. Melody Swartz, world leader in lymphatic and cancer mechanobiology. I conducted my postdoctoral fellowship at EPFL in the laboratory of Dr. Jeffrey Hubbell, world leader in biomaterials and molecular engineering, in collaboration with Dr. Cherie Stabler, well-known scientist in the field of T1D tissue engineering.

Among my research achievements, I developed a novel method for conformal encapsulation of cell clusters, including pancreatic islets, that is based on microfluidics. Several scientific commentaries have regarded this new technology as a breakthrough in the encapsulation field. I have demonstrated that conformal coating is immunoisolating and I plan to conduct the necessary preclinical studies to translate the technology to clinical trials. Further, I started evaluating my innovative encapsulation technology with stem cell-derived insulin-secreting cell products in collaboration with Semma Therapeutics (a spin-off of Dr. Doug Melton's lab at the Harvard Stem Cell Institute). In a parallel track, I demonstrated that local CCL21 secretion mediates antigen-specific immunological tolerance in cancer and in autoimmune diabetes. I am now translating those findings into a clinically applicable biomaterial platform for co-delivery of CCL21 and beta cell antigens for induction of antigen-specific tolerance. This work is in collaboration with Drs. Bayer and Pugliese at the DRI.

In recognition of these accomplishments, in 2012 I was invited to become part of the prestigious JDRF encapsulation consortium, which gathers the world leaders in islet encapsulation and immunomodulation, and promotes collaborations, sharing of data and protocols with the overall goal of advancing the field. I have presented my research work at several international conferences, including an invited oral presentation at the Key Opinion Leaders Meeting on Stem Cell Derived Beta Cells at Harvard Medical School in Boston in October

2016, an oral presentation at the annual meeting of the Immunology of Diabetes Society in San Francisco in January 2017, and an invited oral presentation at the annual meeting of the international society for cellular therapy (ISCT) in the special advancements in cellular therapies and regenerative medicine in digestive diseases workshop in London, in May 2017 and an invited oral presentation at the annual meeting of the American Diabetes Association in San Diego in June 2017. Finally, I was invited to serve as member of the grant review panels for both the JDRF and for the California Institute for Regenerative Medicine (CIRM). These important achievements further highlight my recognition in the field of immunoengineering for T1D.

My multidisciplinary team at the DRI comprises an assistant scientist with expertise in biology and immunology, an assistant scientist with expertise in organic chemistry and biomaterials for nanomedicine, a senior research associate II with expertise in islet encapsulation and preclinical models of T1D, one senior research associate I, with expertise in device design, two graduate students in biomedical engineering, and several biomedical engineering undergraduate students that conduct volunteer research in my laboratory.

B. Positions and Honors

Positions and Employment

2008-2010	Postdoctoral Fellow, École Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland, in the laboratory of Prof. Jeffrey Hubbell
2010-2012	Assistant Scientist, Diabetes Research Institute, University of Miami, Miller's School of Medicine, FL, in the laboratories of Prof. Cherie Stabler and Dr. Luca Inverardi and in collaboration with the laboratory of Prof. Jeffrey Hubbell at the EPFL
2012-Present	Research Assistant Professor in the DeWitt Daughtry Family Department of Surgery, Division of Cellular Transplantation, and the Diabetes Research Institute at the University of Miami Miller School of Medicine, FL
2015-Current	Assistant Professor in the Department of Biomedical Engineering and the Diabetes Research Institute at the University of Miami, FL

Professional Activities

Grant Review Committees:

2013-Present	Italian Ministry of Health (MOH) FY15 grants
2014-Present	Czech Health Research Council FY15 grants
2015-Present	JDRF Developing and Testing Retrievable Devices and Scaffolds for Beta Cell Replacement Therapies
2016-Present	California Institute for Regenerative Medicine's (CIRM) Discovery & Inception Research Program
2017-Present	JDRF Novel Bioengineered Materials And Device Concepts To Facilitate Development Of Encapsulation Systems

Editorial Responsibilities:

2013-Present	Editorial Board Member, CellR4 Repair, Replacement, Regeneration, and Reprogramming
2013-Present	Invited Reviewer, CellR4
2013-Present	Invited Reviewer, Cell Transplantation
2013-Present	Invited Reviewer, Clinical and Developmental Immunology
2014-Present	Invited Reviewer, American Journal of Transplantation
2014-Present	Invited Reviewer, Journal of Stem Cell Research and Transplantation
2015-Present	Invited Reviewer, Immunopharmacology And Immunotoxicology
2015-Present	Invited Reviewer, International Journal of Nanomedicine
2015-Present	Invited Reviewer, Transplantation
2015-Present	Invited Reviewer, Biotechnology & Bioengineering
2015-Present	Invited Reviewer, International Journal of Artificial Organs (IJAO)
2015-Present	Invited Reviewer, Canadian Journal of Diabetes
2017-Present	Invited Reviewer, Jove
2017-Present	Invited Reviewer, ACS Biomaterials Science & Engineering
2017-Present	Invited Reviewer, Transplant International
2017-Present	Invited Reviewer, ACS Nano
2017-Present	Invited Reviewer, Science Advances
2017-Present	Invited Reviewer, Taylor and Francis Books

Honors & Awards

- CTSI Fellowship to take the **Eureka certification in Translational Medicine 2017**
- Recipient of the University of Miami College of Engineering 2016 **Eliahu I. Jury Early Career Research Award** for obtaining major research grants
- Recipient of the 2016 **JDRF CDA** (career development award)
- Recipient of the 2016 **Provost's Research Award**
- Recipient of the 2015 **Marc S. Goodman Prize** to an Outstanding Young Scientist
- Member of the JDRF Encapsulation Consortium since 2012
- **Fellowship** to participate to the 2013 Advanced Course in Basic & Clinical Immunology organized by FOCIS (two fellows were selected among all applicants from the University of Miami)
- Finalist (4 out of >1000) of **Student Award**, Annual Meeting of the European Society of Biomechanics (ESB), 2006, Munich, Germany
- Best **Poster Award** (12 out of >1000), Annual meeting of the Biomedical Engineering Society (BMES), 2005, Baltimore, USA
- Awarded 5-year fellowship (based on average grades > 28.5/30) and 100/100 final grade at the M.S. of the Politecnico di Milano (top engineering school in Italy)
- Awarded 60/60 final grade at Leonardo da Vinci High School (top scientific high schools in Milan, Italy)

C. Contribution to Science

1. Islet transplantation is a promising approach for replacing beta cells and re-establishing glucose homeostasis in patients with T1D. Currently, islets are transplanted intraportally and chronic immunosuppression is required to prevent allorejection and recurrence of autoimmunity. Poor islet revascularization after transplantation is one of the major impediments to islet engraftment and long-term function. To augment islet vascularization several approaches have been undertaken. Building on my postdoctoral work in Dr. Hubbell's lab, I have undertaken a novel approach to augment islet vascularization after transplantation that relies on transplanting islets in engineered fibrin scaffolds that allow for extended release of pro-angiogenic factors and for their synergistic signaling with extracellular matrix-binding domains after transplantation[a]. The advantages of such approach include minimization of growth factor quantities (cost effective) and potential risks (increase safety) and the possibility to transplant islets in confined and well-vascularized spaces (like the omental pouch in humans). Further, our approach can be utilized for engineering the transplantation site of microencapsulated islets, which are at high risk of hypoxia and central necrosis after transplantation. More recently, we demonstrated that this approach for transplantation of microencapsulated islets in confined and vascularized sites improves engraftment and long-term survival of fully MHC-mismatched islet allografts in mice and is also applicable to transplantation of primate islets in diabetic NOD-scid mice[b].

   a. Najjar M., Manzoli V., Villa C., Martino M.M., Molano R.D., Torrente Y., Pileggi A., Inverardi L., Ricordi C., Hubbell J.A., **Tomei A.A.**, Fibrin Gels Engineered with Pro-Angiogenic Growth Factors Promote Engraftment of Pancreatic Islets in Extrahepatic Sites in Mice', ***Biotechnology and Bioengineering*** 112 (9) 2015 *Highlighted*

   b. Chiara Villa, Vita Manzoli, Maria Abreu, Connor A. Verheyen, Michael Seskin, Mejdi Najjar, R. Damaris Molano, Yvan Torrente, Camillo Ricordi, **Alice A. Tomei**, 'Composition and Transplant Site of Alginate-Polyethylene Glycol Microcapsules Affect the Outcome of the Encapsulated Islet Graft in Mice', ***Transplantation*** 2016 Aug 12. [Epub ahead of print]

2. Long-term efficacy of islets encapsulated in traditional capsules (≈500-1500 μm diameter) has not been proven in patients after transplantation in the intraperitoneal (IP) space. Most likely, this is because large capsules limit nutrient transport leading to loss of functionality and, ultimately, death of the islet graft. I have brought innovation to this field using a novel method that addresses the above shortcoming. My platform allows generating thin (as low as 10 μm) and conformal coatings (CC) through a microfluidic approach[a-c]. CC prepared with our new technology increases nutrient transport to the encapsulated islets by reducing the diffusion distance 10-fold because the size of CC capsules is adapted to each islet – coating thickness is constant around differently sized islets. Furthermore, by reducing the total graft volume around 200-fold, CC also allows transplantation in vascularized sites further maximizing nutrient transport compared to the traditionally used IP site, hence, further increasing islet functionality and viability. Finally, we recently demonstrated that our CC platform technology allows long-term diabetes reversal after transplantation of

fully MHC-mismatched CC islet allografts in confined and vascularized sites without immunosuppression[d]. As such, our novel encapsulation technology platform addresses all the issues that have been associated with failure of islet encapsulation in patients. Accordingly, we expect our unique CC technology to allow long-term function of islet transplantation without the need for immunosuppression while also reducing the number of islets needed to reverse T1D. In support of this approach, our novel computational models predict that, contrary to traditional microcapsules, CC grafts at vascularized sites will prevent hypoxia and so central necrosis, and will allow physiological GSIR.

a. **Alice A. Tomei** and Jeffrey A. Hubbell, "Conformal Coating of Cells For Immunoisolation". International Application No. PCT/US12/35696 filed with the United States Patent and Trademark Office on October 29, 2013 and with the European Patent Office on November 29, 2013
b. **Tomei AA**, Villa C., Ricordi C, Development of an encapsulated stem cell-based therapy for diabetes', ***Expert Opin Biol Ther.*** 2015 Jul 9:1-16. [Epub ahead of print]
c. **Tomei AA**[*], Vita Manzoli, Christopher Fraker, Jaime A. Giraldo, Diana Velluto, Mejdi Najjar, Antonello Pileggi, Ruth D. Molano, Camillo Ricordi, Cherie L. Stabler, Jeffrey A. Hubbell, 'Conformal Coating of Islets of Langerhans: Device Design and Materials Optimization', ***PNAS*** 111 (29): 10514-9 (2014)***.*** *Cover-art awarded)*
d. **Tomei AA**, invited oral presentation at the Key Opinion Leaders Meeting on Stem Cell Derived Beta Cells, Harvard Medical School in Boston, USA, September 18-20, 2016
e. Manzoli, V., Colter, D. C., Dhanaraj, S., Fornoni, A., Ricordi, C., Pileggi, A., **Tomei, A. A.** (2017). Engineering Human Renal Epithelial Cells for Transplantation in Regenerative Medicine. *Physics and Medical Science*.

3. Understanding the mechanisms that regulate tumor metastasis and survival will help developing better cancer therapies. Further, understanding the mechanisms underlying the induction of tolerance towards tumor antigens in cancer may be exploited for developing novel therapeutics for induction of antigen-specific tolerance in autoimmune diseases. During my doctoral work at the EPFL in the lab of Dr. Swartz I demonstrated and published that CCL21 autologous secretion by melanoma cells induces autologous chemotaxis (through CCR7 expression by the tumor cells)[a] that promotes metastasis and formation of a lymph node-like environment[b]. More importantly, we showed that autologous CCL21 secretion by tumor cells is necessary to promote immune escape and cancer survival in immunocompetent mice. This work has resulted also in a patent application for the induction of immunological tolerance through CCL21 and CCL19 delivery for immunotherapy[c]. I am currently evaluating whether targeted CCL21 release can induce beta cell antigen-specific tolerance in transgenic NOD mice and using CCL21-tethered biomaterials.

   a. [*]Shields J.D., [*]Kourtis I., **Tomei A.A**., Roberts J., Swartz M.A., "Induction of lymphoid-like stroma and immune escape by tumors that express the chemokine CCL21", ***Science*** **328** (5979) 749-52 (2010)
   b. Shields J.D., Fleury M.E., Yong C., **Tomei A.A.,** Randolph G.J., Swartz M.A. "Autologous Chemotaxis as a Mechanism of Tumor Cell Homing to Lymphatics via Interstitial Flow and Autocrine CCR7 Signaling", ***Cancer Cell*** **6**, 526-38 (2007)
   c. **Alice A. Tomei**, Jacqueline Shields, Iraklis Kourtis, Jeffrey Hubbell, Melody Swartz, "CCR7 Ligand Delivery and Co-delivery in Immunotherapy". Application number: 13/025,009 Publication number: US 2011/0206759 A1 Filing date: Feb 10, 2011

4. A tissue-engineered model of lymph nodes allows understanding the pathogenesis of diseases like cancer metastasis with the goal of developing better cancer treatments. During my doctoral work at the EPFL in the lab of Dr. Swartz, I have designed and published a physiological model of the lymph node by three-dimensional culture of lymph node stromal cells (LSCs) in scaffolds that preserve the phenotype of LSCs, including secretion of the CCL21 chemokine[a]. Lymph node resident stromal cells have been identified as critical mediators of peripheral tolerance towards self-antigens. Therefore, a tissue-engineered model of the lymph node that recapitulates the physiological phenotype and structural organization of stromal cells may be utilized for promoting tolerance towards allogeneic cells after cell transplantation and/or for counteracting autoimmunity, which is one of the goals of my current work. Though unpublished yet, my current work on inducing antigen-specific tolerance in autoimmune diabetes has been presented at several prestigious international conferences including two recent oral presentations[a,b].

   a. **Tomei A.A.**, Siegert S., Britschgi M.R., Luther S.A., Swartz, M. A. "Fluid Flow Regulates Stromal Cell Organization and CCL21 Expression in a Tissue-engineered Lymph Node Microenvironment", ***Journal of Immunology*** **183**, 4273-83 (2009)

b. **Tomei A.A.**, 'CCL21 Expression in Beta Cells Induces Lymph Node Mimicry in the Pancreas and Prevents Autoimmune Diabetes', oral presentation at **Keystone Stromal Cells in Immunity 2016 and** at the **IDS 2017 Meeting** in San Francisco

5. A tissue-engineered model of the bronchial wall allows understanding the pathogenesis of diseases like asthma and develop better therapeutics. During my doctoral work at EPFL in Dr. Swartz's lab, I designed and published a physiological model of the bronchial wall by co-culture of human bronchial epithelial cells and human lung fibroblasts hydrogels[a]. We demonstrated that in our model, bronchial epithelial cells could reach unprecedented levels of differentiation *in vitro* and display mucociliary function[b]. Further, we demonstrated that by mimicking bronchoconstriction through application of mechanical compression to the co-culture systems, we could model asthmatic bronchoconstriction and understand the role of viral infection in asthmatic vs. healthy subjects[b].
   a. [*]Choe, M. M., [*]**Tomei A.A**., Swartz, M. A. "Physiological 3D Tissue Model of the Airway Wall and Mucosa", ***Nature Protocols*** **1**, 357-362 (2006)
   b. **Tomei A.A.**, Choe, M. M., Swartz, M. A. "Effects of Dynamic Compression on Lentiviral Transduction in an In Vitro Airway Wall Model", ***AJP Lung*** **1**, L79-86 (2008)

http://www.ncbi.nlm.nih.gov/sites/myncbi/alice.tomei.1/bibliography/48515548/public/?sort=date&direction=ascending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

- **5-CDA-2016-171-S-B Tomei (PI),** Funding Period: 5/1/2016 - 04/30/21
  Juvenile Diabetes Research Foundation Role: PI
  Career Development Award
  Resolution of the impediments of immunoisolation technologies
- **Semma SRA M1601026 - Tomei (PI)** Funding Period: 05/15/16 – 05/15/18
  Semma Therapeutics SRA Role: PI
  Conformal Coating Encapsulation of SC-beta cell products
- **JDRF 2-SRA-2016-316-S-B Tomei (PI)** Funding Period: 09/01/16 – 08/31/18
  Juvenile Diabetes Research Foundation Role: PI
  Engineering a novel therapeutic hydrogel with CCL21 and beta cell autoantigens to induce antigen-specific tolerance
- **DK109929/Tomei (PI)** Funding Period: 07/01/16 –06/30/17
  NIH NIDDK Role: PI
  Conformal islet encapsulation for transplantation at vascularized sites to allow physiological insulin secretion
- **JDRF 3-SRA-2017-347-M-B** Ricordi (PI) Funding Period: 08/01/16 –07/31/19
  Juvenile Diabetes Research Foundation Role: PI of Project 3
  Development of an Extrahepatic Site for Islet Transplant without Continuous Immunosuppression (3 Project Center Grant)
- 2016 Provost's Research Award (Tomei) Funding Period: 06/01/16 – 05/31/17
  University of Miami Role: PI
  Exploiting encapsulation to induce islet antigen-specific tolerance through lymphoid stromal cells

Completed Research Support

- 2014-15 Iacocca Award (Tomei) Funding Period: 08/01/14 – 07/31/15
  The Iacocca Family Foundation Role: PI
  Unraveling the role of CCL21 and lymphoid stromal cells in preventing autoimmune diabetes
- JDRF 17-2012-361 (Ricordi) Funding Period: 06/01/12 – 05/31/15
  Juvenile Diabetes Research Foundation Role: PI of Project 3 (Conformal Coating)
  Development of an Extrahepatic Site for Beta Cell Replacement without Continuous, Systemic Immunosuppression (4 Project Center Grant)