BIOGRAPHICAL SKETCH

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NAME: Balduini Alessandra

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POSITION TITLE: Associate Professor, University of Pavia

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Pavia, Pavia, Italy	MD (cum laude)	07/1994	Medicine
Université Joseph *Fourier*, *Grenoble*, *France*	Extèrne des Hôpitaux	09/1993	Medicine
University of Indiana, Indianapolis, USA	Post-doc	12/1996	Stem Cell Biology
University of Pavia, Pavia, Italy	Specialization (cum laude)	10/2000	Clinical Biochemistry
IUSS-SAFI, University of Pavia, Pavia, Italy	M.S.	10/2000	Art and Science

A. Personal Statement

I have a broad background in haematology, with specific training and expertise in the research of haematopoietic stem cell biology and clinical aspects of platelet related disorders. Before creating my research group in 2007, I was a staff physician in the laboratory of Clinical Biochemistry, IRCCS San Matteo Foundation, and University of Pavia, Italy. In 2005-2006 I was Visiting Professor at Dana Farber Cancer Institute at Harvard Medical School. Since 2007 I have led a research group that is based in two different academic institutions: the Department of Molecular Medicine - University of Pavia, Italy and the Department of Biomedical Engineering - Tufts University, Boston, USA. The goal is to establish a cross-sectional program that integrates biological with bioengineering approaches to the study of haematopoiesis and bone marrow environment. My research focuses on how the different components of the bone marrow microenvironment regulate platelet production. In 2011 I developed the groundwork for modeling human bone marrow by bioengineering a new 3D model made of porous silk that fully recreates the physiology of the living bone marrow niche environment. This system, completely redesigned in 2015 and 2017, is capable of successfully generating functional platelets ex vivo, offering new opportunities for producing blood components for clinical applications. This superior tissue system also represents a new tool for studying pathologic mechanisms of human platelet production and testing drug efficiency.

B. Positions and Honors

Positions and Employment

2001-2005: Staff Physician, Clinical Biochemistry Laboratory, Policlinico San Matteo Foundation, Pavia, Italy.
2001- 2011: Assistant Professor of Medicine, Department of Biochemistry-University of Pavia, Italy.
2009-2014: Research Assistant Professor, Department of Biomedical Engineering, Tufts University, Boston.
2011-present: Associate Professor, Department of Molecular Medicine, University of Pavia, Italy.
2014-present: Research Associate Professor, Department of Biomedical Engineering, Tufts University, Boston.

Other Experience and Professional Memberships

2005-2006: Visiting Professor, Dana Farber Cancer Institute-Harvard Medical School, Boston, USA
2007-2009: Visiting Scientist, Department of Biomedical Engineering, Tufts University, Boston, USA.
2011: Visiting Professor, Universidad de Buenos Aires, Buenos Aires, Argentina

2007-present: member of the International Society of Thrombosis and Hemostasis (ISTH), the American Society of Hematology (ASH), the Società Italiana di Biochimica (SIB), the European Hematology Association (EHA)

Honors

2005: Award from “Progetto Professionalità” Fondazione Banca Regionale Europea
2011: Award from the International Society of Thrombosis and Haemostasis, Reach the World Education Program
2015: Award from the European Haematology Association-Japanese Society of Hematology
2017: Award from Ministero degli Affari Esteri e Cooperazione Internazionale (MAECI) Progetti di Grande Rilevanza
2019: Elected Chair of the 2021 Gordon Research Conference "Cell Biology of Megakaryocytes and Platelets

Academic activities

1. Professor of Clinical Biochemistry: Medical School (4 CFU), Biotechnology (9 CFU), University of Pavia
2. Professor of Clinical Application for the Biotechnologies: Biotechnology (3 CFU), University of Pavia
3. Professor of Clinical Biochemistry: Specialization in Clinical Biochemistry and Pathology, Internal Medicine, Pulmonology, Microbiology, Surgery, Neurosurgery, Hematology, Endocrinology, Geriatrics, Ophthalmology, University of Pavia (23 CFU)
4. Member of the Board of Doctorate in Bioengineering and Bioinformatics, University of Pavia (2013-2017)
5. Member of the Board of Doctorate in Translational Medicine, University of Pavia (2017-present)
6. In the last 10 years 30 undergraduate students wrote their final thesis and 5 obtained their PhD in my lab
7. In the last 10 years I supported 10 post-doc positions (3 to 6 year each)
7. PhD thesis external reviewer INSERM Paris, University of Strasbourg, University of Toulouse, Cambridge University

International Academic Programs

2012-2013: Whitaker International Program
2013: American Society of Haematology, Visitor Training Program
2014: European Haematology Association-Japanese Society of Hematology Fellowship Exchange Program
2015: EMBO International Student Exchange Program
2016: Japanese Society of Haematology and European Haematology Association program
2017-2019: Progetti di Grande Rilevanza Ministero degli Esteri

C. Contribution to Science

- Author of 87 peer-reviewed publications (PubMed) included 5 Cover Stories in Blood Journal
- Invited speaker at leading international meetings and institutions in the field, including 4 times presenting my work, in oral communication, at the Gordon Research Conference "Cell Biology of Megakaryocytes and Platelets"
- Invited speaker at the American Society of Hematology Annual Meeting December 2019
- Member of the Organizing Committee of the Iternational Society of Thrombosis and Haemostasis Annual Meeting 2020
- Elected Chair of the 2021 Gordon Research Conference "Cell Biology of Megakaryocytes and Platelets"

My career began in 2000 as Staff Physician and Assistant Professor of Medicine in the laboratory of Clinical Biochemistry, IRCCS San Matteo Foundation Hospital, and University of Pavia, Italy. My primary focus at San Matteo Hospital was clinical and diagnostic medicine as a member of the staff of the Clinical Analysis Laboratory.

I resumed my research career in 2005, developing protocols for culturing megakaryocytes (Mks) from human cord blood and focusing on the study of the mechanisms of haematopoiesis, Mk differentiation and platelet release. In 2005-2006 I was a Visiting Professor at the Dana Farber Cancer Institute, Harvard Medical School, Boston, USA, studying the mechanisms of platelet production in mouse embryonic stem cells. The results of these studies resulted in a breakthrough in the understanding of the regulation of Mk differentiation.

In 2007, I opened my own research lab in the Biotechnology Laboratories of the San Matteo Hospital and Department of Biochemistry-University of Pavia, Italy. With my new research group, I investigated the mechanisms of Mk differentiation and platelet release in physiological and pathological conditions.

1.Chen Z, Naveiras O*, Balduini A*, Mammoto A, Conti MA, Hosoya H, Adelstein R, Ingber D, Daley GQ, Shivdasani R. The May-Hegglin anomaly gene Myh9 is a negative regulator of platelet biogenesis modulated by the Rho-ROCK pathway (2007) **Blood** 110:171-9.
2.Balduini A, Malara A, Pecci A, Badalucco S, Bozzi V, Pallotta I, Noris P, Torti M, Balduini CL. Proplatelet formation in heterozygous Bernard-Soulier syndrome type Bolzano. (2008) **J Thromb Haemost**. 7:478-84.
3.Pecci A, Malara A, Bauducco A, Bozzi V, Torti M, Balduini CL, Balduini A. Megakaryocytes of patients with myh9-related thrombocytopenia present an altered proplatelet formation. (2009) **Thrombosis and Haemost**. 102: 90-6.

Most recently, I proposed that soluble factors contribute to the regulation of Mk behavior in an autocrine manner both in physiology and disease scenarios. In 2014 my research group proved for the first time the importance of calcium as a fundamental regulator of platelet production. The impact of calcium on Mk development was also studied in CALR-mutant Myeloproliferative Neoplasms. Lastly, I took part in the demonstration of the pathogenetic mechanisms of a new form of inherited thrombocytopenia associated to mutations in the ANKRD26 gene.
1.Badalucco S, Di Buduo CA, Campanelli R, Pallotta I, Catarsi P, Rosti V, Kaplan DL, Barosi G, Massa M, Balduini A. Involvement of TGFβ1 in autocrine regulation of proplatelet formation in healthy subjects and patients with primary myelofibrosis. (2013) **Haematologica** 98: 514-7.
2.Di Buduo C, Moccia F, Battiston M, De Marco L, Mazzucato M, Moratti R, Tanzi F, Balduini A. The importance of calcium in the regulation of megakaryocyte function. (2014) **Haematologica** 99: 769-78.
3.Bluteau D*, Balduini A*, Balayn N, Currao M, Nurden P, Deswarte C, Leverger G, Noris P, Perrotta S, Solary E, Vainchenker W, Debili N, Favier R, Raslova H. Thrombocytopenia-associated mutations in the ANKRD26 regulatory region induce MAPK hyperactivation. (2014) **J Clin Invest**. 124: 580-91.
4. Di Buduo CA, Abbonante V, Marty C, Moccia F, Rumi E, Pietra D, Soprano PM, Lim D, Cattaneo D, Iurlo A, Gianelli U, Barosi G, Rosti V, Plo I, Cazzola M, Balduini A. Defective interaction of mutant calreticulin and SOCE in megakaryocytes from patients with myeloproliferative neoplasms. (2020) ***Blood***. Jan 9;135(2):133-144.

I have since focused my work on the mechanisms that regulate type I collagen-Mk interactions in the bone marrow environment with two further publications in Blood Journal on the role of fibronectin in the regulation of Mk function in the bone marrow matrix environment. We then investigated the expression and the function of the new collagen receptor Discoidin Domain Receptor I (DDR1) on human Mks and most recently demonstrated the mechanisms that regulate extracellular matrix component-Mk interactions in the bone marrow environment in in vivo mouse models.
1.Malara A, Gruppi C, Pallotta I, Spedden E, Tenni R, Raspanti M, Kaplan DL, Tira ME, Stai C, Balduini A. Extracellular matrix nano-mechanics determine megakaryocyte function. (2011) **Blood** 118(16): 4449-53
2.Malara A, Gruppi C, Rebuzzini P, Visai L, Perotti C, Moratti R, Balduini C, Tira ME, Balduini A. Megakaryocyte-matrix interaction within bone marrow: new roles for fibronectin and factor XIII-A. (2011) **Blood** 117(8): 2476-83.
3.Abbonante V, Gruppi C, Rubel D, Gross O, Moratti R, Balduini A. Discoidin Domain Receptor 1 is a novel modulator of megakaryocyte-collagen interactions. (2013) **J Biol Chem**. 288: 16738-46.
4.Malara A, Currao M, Gruppi C, Celesti G, Viarengo G, Buracchi C, Laghi L, Kaplan DL, Balduini A. Megakaryocytes Contribute to the Bone Marrow-Matrix Environment by Expressing Fibronectin, Type Iv Collagen and Laminin. (2014) **Stem Cells**. 32: 926-37
5.Abbonante V, Di Buduo CA, Gruppi C, De Maria C, Spedden E, De Acutis A, Staii C, Raspanti M, Vozzi G,Kaplan DL, Moccia F, Ravid K, Balduini A. A new path to platelet production through matrix sensing. (2017) **Haematologica** 102: 1150-1160

This research led to the characterization of Mks in Myeloproliferative Neoplasms. By this approach we identified the role of the fibronectin isoform EIIIA in regulating hemopoiesis in the bone marrow and we patented a new diagnostic tool to detect bone marrow fibrosis with a simple blood test.
1.Abbonante, V., Di Buduo, C.A., Gruppi, C., Malara, A., Gianelli, U., Celesti, G., Anselmo, A., Laghi, L., Vercellino, M., Visai, L., Iurlo, A., Moratti, R., Barosi, G., Rosti, V., and Balduini, A.. Thrombopoietin/TGF-β1 loop regulates megakaryocyte extracellular matrix component synthesis. (2016) **Stem Cells** 34: 1123-1133.
2.Malara A, Gruppi C, Celesti G, Romano B, Laghi L, De Marco L, Muro AF, Balduini A. Alternative splicing of Extra Domain A (EIIIA) of fibronectin plays a tissue-specific role in hematopoietic homeostasis. (2016) **Stem Cells** 34:2263-8.

3.Malara A, Gruppi C, Abbonante V, Cattaneo D, De Marco L, Massa M, Iurlo A, Gianelli U, Balduini CL, Tira ME, Muro AF, Chauhan AK, Rosti V, Barosi G, Balduini A. EDA fibronectin-TLR4 axis sustains megakaryocyte expansion and inflammation in bone marrow fibrosis. (2019) **J Exp Med** 216(3):587-604.

In 2007 I began using silk as biomaterial to develop a 3D bioreactor model to mimic bone marrow and study platelet formation. This model is now patented in USA and Europe.
1.Pallotta I, Lovett M, Kaplan DL, Balduini A. 3D system for the in vitro study of megakaryocytes and functional platelet production using silk-based vascular tubes. (2011) **Tissue Eng Part C Methods** 17:1223-32.
2.Pallotta I, Kluge JA, Moreau J, Calabrese R, Kaplan DL, Balduini A. Enhanced efficacy of platelet gels with silk. (2014) Biomaterials 35: 3678-87.

Most recently, through a complete redesign of the initial bioreactor model, my group bioengineered a new 3D model made of porous silk that fully recreates the physiology of the human bone marrow niche environment. This system is capable of successfully generating functional platelets ex vivo, with endothelial cells co-cultures significantly increasing the numbers of released platelets. By leveraging the biocompatibility, non-thrombogenic features, programmable mechanical properties of silk, this system allows for the binding of cytokines, extracellular matrix components and endothelial-derived proteins. This in turn offers new opportunities for producing blood components ex vivo for clinical applications and provides a superior tissue system for the studying of pathologic mechanisms of human platelet production and testing drug efficiency.
1.Di Buduo CA, Wray LS, Tozzi L, Malara A, Chen Y, Ghezzi CE, Smoot D, Sfara C, Antonelli A, Spedden E, Bruni G, Staii C, De Marco L, Magnani M, Kaplan DL, Balduini A. Programmable 3D silk bone marrow niche for platelet generation ex vivo and modeling of megakaryopoiesis pathologies. (2015) **Blood** 125(14): 2254-64.
2.Di Buduo CA, Pecci A, Kaplan DL, Balduini CL, Balduini A. Ex vivo modeling of Eltrombopag reveals key role in meakaryocyte and platelet formation. (2016) H**aematologica** 101(12): 1479-1488.
3.Di Buduo CA, Soprano PM, Tozzi L, Marconi S, Auricchio F, Kaplan DL, Balduini A. Modular flow chamber for engineering bone marrow architecture and function. (2017) **Biomaterials** 146:60-71

Patents:
1. PCT Patent Application PCT/US2014/057541 filed 9/25/2014 entitled “Silk/Platelet Composition and UseThereof”
2. US Provisional Patent Application 62/034,727 filed 8/7/2014 entitled “Microphysiologic Methods and Compositions”
3. International Patent Application filled 15/1/2018 entitled "Diagnostic and Prognostic Method for Myelofibrosis"

Complete List of Published Work in My Bibliography:
www.ncbi.nlm.nih.gov/pubmed/?term=balduini+a