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Eighth Symposium on Biologic Scaffolds for Regenerative Medicine

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Abstract

The Eighth Symposium on Biologic Scaffolds for Regenerative Medicine was held from 24 to 26 April 2014 at the Silverado Resort in Napa, CA, USA. The symposium was well attended by a diverse audience of academic scientists, industry members and physicians from around the world. The conference showcased the strong foundation of both basic and translational research utilizing biologic scaffolds in regenerative medicine applications across nearly all tissue systems and facilitated vibrant discussions among participants. This article provides an overview of the conference by providing a brief synopsis of selected presentations, each focused on a unique research and/or clinical investigation currently underway.

From 24 to 26 April 2014, the Eighth Symposium on Biologic Scaffolds for Regenerative Medicine was held at the Silverado Resort, Napa, CA, USA. Stephen Badylak (Professor in the Departments of Surgery and Bioengineering and Deputy Director of the McGowan Institute for Regenerative Medicine at the University of Pittsburgh, PA, USA) chaired the symposium (Figure 1). This gathering was the eighth event in the symposia series, which began in 1996. The overarching theme of the symposium is to bring together an internationally recognized group of academic scientists, physicians and industry members to discuss the latest preclinical and clinical research findings, both positive and negative, regarding the use of biologic scaffolds for regenerative medicine applications. Research presented during the symposium spans the full spectrum of science – from basic science studies aimed at identifying molecular mechanisms to recent clinical translation activities – all with a unified goal of improving patient care and quality of life.

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Spread across 2 days, the symposium showcased 33 oral presentations, including two keynote addresses, and a poster session that covered a wide array of tissue systems, including cardiovascular, gastrointestinal, urologic, dermatologic, musculoskeletal and the CNS. The symposium was divided into plenary sessions, each focused on a central topic including: whole organ engineering, variables that influence the host remodeling response, fundamental concepts of cell-scaffold interactions, tissue source and processing/manufacturing methods, role of the innate immune response and outcomes of human clinical applications.

Day 1

The conference began with a keynote address by Joseph Vacanti (Massachusetts General Hospital, USA) entitled 'Tissue Engineered Organs: More than One Way to the End Zone' (Figure 2). Dr Vacanti is a pioneer in the field of tissue engineering and over the last several decades his group has focused on creating complete vascular networks that serve as an integral part of complex living implantable tissue engineered devices, such as vital organs [1, 2,3]. During his keynote Dr Vacanti offered an insightful perspective of his past experiences in the field of tissue engineering and an optimistic outlook on the future use of tissue engineered therapies in the clinic.

The first plenary session, chaired by Gordana Vunjak-Novakovic (Columbia University, NY, USA), explored the topic of 'Whole Organ Engineering with Biologic Scaffold Materials'. During this session, Laura Niklason (Yale University, CT, USA) gave an overview of her group's work on 'Scaffolds for Lung and Vascular Regeneration'. Specifically, Dr Niklason discussed their studies aimed at creating an implantable 'off-the-shelf' engineered artery derived from human vascular smooth muscle cell-based extracellular matrix (ECM). These materials have shown excellent function out to 6 months as a 6-mm arteriovenous graft in baboons and early data suggest similar positive outcomes when used for dialysis patients [4,5].

The second plenary session, chaired by Christopher Dearth (University of Pittsburgh), was titled 'Bone, Blood Vessels, and Cardiac Reconstruction'. Of the many great talks during this session, Lisa White's (University of Nottingham, UK) presentation entitled 'Hydrogels from Demineralized and Decellularized Bone Extracellular Matrix for Bone Regeneration' was particularly intriguing. Recent efforts by Dr White's group to produce bDBM and bECM hydrogels have shown that each possess distinct structural, mechanical and biological properties, including osteogenic functionality [6]. These materials offer exciting new potential for use in bone regeneration applications.

The third plenary session, chaired by Buddy Ratner PhD (University of Washington, WA, USA), was focused on 'Variables that Affect Clinical Performance of Biologic Scaffold Materials'. During this session, Thomas Wight's (Benaroya Research Institute, WA, USA) presentation entitled 'Controlling Inflammation in Tissue Engineering: A Role of Proteoglycans' detailed his group's work aimed at understanding how components of the ECM, namely versican and hyaluronan, regulate inflammation. Dr Wight's work has shown that synthesis of versican and hyaluronan is elevated in M1, proinflammatory macrophages

and that blocking the accumulation of versican and hyaluronan in the ECM dramatically reduces myeloid accumulation in preclinical animal models [7, 8]. As such, these molecules offer exciting potential as therapeutic targets for augmenting the immune response to biologic scaffold materials.

‘General Surgery Applications’ of biologic scaffold materials was discussed during the fourth plenary session, chaired by Martin Birchall (University College London, UK). An interesting talk entitled ‘Reconstruction of the Temporomandibular Joint (TMJ) Disc using an ECM Device’ was given by Dr Bryan Brown (University of Pittsburgh). Dr Brown presented data that demonstrated that an ECM scaffold material is capable of serving as an inductive template for reconstruction of the TMJ disc in a canine model [9]. Specifically, the implanted ECM material was observed to progressively remodel after implantation, and the newly formed tissues resembled the native TMJ disc in both gross and histologic morphology, as well as in biochemical content and biomechanical properties. The results from the present study are noteworthy because this ECM device fills a clinical need for which there are currently no effective treatments and may represent a simple and effective ‘off-the-shelf’ solution for reconstruction of the TMJ disc.

Day 2

Alberto Mantovani (University of Milan, Italy) delivered the second keynote address entitled ‘Macrophage Polarization in Tissue Remodeling and Repair’. Macrophages, in response to environmental signals, can occupy various polarized phenotypes along a continuum with proinflammatory, M1 and anti-inflammatory, M2 activation states at each extreme. M1 macrophages are generally associated with classic inflammation and tissue damage whereas M2 macrophages are known to be important for tissue remodeling and repair. Dr Mantovani's group has been instrumental in defining the molecular basis of the continuum of macrophage polarization, including identification of signaling molecules, transcription factors and epigenetic modifications, and their role in tissue remodeling and repair [10,11].

The fifth plenary session, entitled ‘Role of the Innate Immune Response in Constructive Remodeling and Regeneration’, was chaired by Bryan Brown (University of Pittsburgh). Peter Slivka's (University of Pittsburgh) presentation entitled ‘Characterizing the Innate Immune Response to Biologic Scaffolds: A Macrophage Study’ was of particular interest in light of Dr Mantovani's keynote lecture and several recent studies have shown that the interaction of macrophages with biologic scaffolds is one of the key components in the tissue remodeling and wound healing outcome. Specifically, biologic scaffolds promote a bias towards a regulatory, M2 macrophage phenotype and away from a proinflammatory M1 phenotype [12–15]. However, to date, little is known about the molecular mechanisms that mediate this biologic scaffold-induced M2 phenotype. Dr Slivka presented recent work conducted by his group that has begun to characterize several molecular markers and signaling cascades associated with the development of the biologic scaffold-mediated macrophage phenotype. This work is important to the field because it not only enhances the understanding of the molecules and mechanisms involved in biologic scaffold-mediated

constructive remodeling but also begins to classify molecular targets to use as metrics for the development of next-generation biologic scaffolds.

The clinical application of biologic scaffolds in regenerative medicine applications was the topic of the last three plenary sessions of the symposium. Of particular note, Alejandro Nieponice's (Hospital Universitario Fundación Favaloro, Buenos Aires, Argentina) presentation entitled 'Regenerative Medicine and Esophageal Surgery' provided powerful examples of the beneficial clinical use of biologic scaffold materials. Dr Nieponice presented work, both in the pre-clinical and clinical setting, which demonstrated that biologic scaffolds prevent stricture and promote a constructive remodeling response following implantation after esophageal mucosal resection [16,17]. Additionally, Pamela Moalli's (University of Pittsburgh) presentation entitled 'Exposing the Science of Synthetic Prolapse Meshes: A Foundation for the Development of Regenerative Materials' underscored the importance of understanding the biology behind the use of mesh materials for the treatment of pelvic organ prolapse. Using a non-human primate model, Dr Moalli's group found that commercially available mesh materials had a negative impact on the structural and mechanical properties of the vagina [18, 19]. Interestingly, recent work from Dr Moalli's group has shown that use of a synthetic mesh in combination with a biologic scaffold material prevents the negative outcomes associated with the use of synthetic materials alone. As such, this combinatorial approach to treatment of pelvic organ prolapse could offer a significant improvement to the current standard of care and improve the quality of life for affected patients.

Summary & future perspective

Overall, this excellent symposium brought together an internationally recognized panel of interdisciplinary experts to discuss the key topics and the latest research findings in the use of biologic scaffolds in regenerative medicine. The selected presentations highlighted herein underscore the important basic and translational research that is currently taking place in the field and sets the stage for many new research and clinical opportunities that will be investigated in the years to come.

The next (9th) Symposium on Biologic Scaffolds for Regenerative Medicine is planned for 28–30 April 2016 at Silverado Resort, Napa, CA, USA. It is sure to be another great symposium and a must attend for anyone interested in the use of biologic scaffold materials for regenerative medicine applications.

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Figure 1. Dr Stephen F Badylak welcomes the audience to the Eighth Symposium on Biologic Scaffolds for Regenerative Medicine



Figure 2. Dr Joseph P Vacanti speaking to the audience during his keynote address entitled 'Tissue Engineered Organs: More than One Way to the End Zone'