

# Biologic Association Annual Summit

## 2020 Report

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Interest and research in biologic approaches for tissue healing are exponentially growing for a variety of musculoskeletal conditions. The recent hype concerning musculoskeletal biological therapies (including viscosupplementation, platelet-rich plasma, and cellular therapies, or “stem cells”) is driven by several factors, including demand by patients promising regenerative evidence supported by substantial basic and translational work, as well as commercial endeavors that complicate the scientific and lay understanding of biological therapy outcomes. While significant improvements have been made in the field, further basic and preclinical research and well-designed randomized clinical trials are needed to better elucidate the optimal indications, processing techniques, delivery, and outcome assessment. Furthermore, biologic treatments may have potential devastating complications when proper methods or techniques are ignored. For these reasons, an association comprising several scientific societies, named the Biologic Association (BA), was created to foster coordinated efforts and speak with a unified voice, advocating for the responsible use of biologics in the musculoskeletal environment in clinical practice, spearheading the development of standards for treatment and outcomes assessment, and reporting on the safety and efficacy of biologic interventions. This article will introduce the BA and its purpose, provide a summary of the 2020 first annual Biologic Association Summit, and outline the future strategic plan for the BA.

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Advancements in musculoskeletal biologic therapies, including viscosupplementation, platelet-rich plasma (PRP), and cellular therapies, or “stem cells,” have exhibited overwhelming growth in the past decade.<sup>2</sup> At first, biologics were envisioned to enhance tissue healing in both acute and chronic conditions by stimulating the recovery processes to restore native or near-native tissue while reducing risks for treatment failure. Recently, symptom management, including reducing pain and

inflammation, has become another important indication for its use.<sup>3,4,7</sup>

The interest in biologic therapies for orthopaedic conditions is multifaceted. Certainly, the potential for improving function and reducing pain with minimally invasive treatments is attractive to both physicians and patients. In addition, the potential to stimulate, regulate, and/or promote the regenerative potential of damaged cells and tissues to their native, functioning state is encouraging. Moreover, many currently available biologic treatments can be offered as a point-of-care procedure either separate from or as an augmentation to surgery. Because of its autologous and minimally manipulated nature, biologic treatments may theoretically be offered at minimal additional risks to the patient, particularly when compared with synthetic and/or allogeneic products.

Overall, the field of biologic treatments for numerous types of musculoskeletal pathology is growing by the day. Importantly, with the exponential increase in research and development, the volume of information and misinformation currently available on biologic therapies can be overwhelming. While peer-reviewed clinical literature on biologic therapies and their efficacy is in its infancy, aggressive marketing and advertising from commercial entities has led to a proliferation of incomplete and inaccurate information that is available to our patients. In some cases, medical clinics staffed by so-called “biologic experts” who lack the fundamental background, training, and/or

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experience are indiscriminately providing treatments to patients on a self-pay basis. Unfortunately, such sources of information in these situations are often fraught with financial bias and the claims made are rarely confirmed by peer review. Furthermore, when administered by inappropriate or poorly trained providers, with improper indications and/or techniques, biologic therapies can result in severe adverse events and complications including, but not limited to, superficial infections, deep infections, pain, and inflammatory responses.

To better understand the rapidly growing field of biologics and to better serve our patients and peers, the Biologic Association (BA) was developed in collaboration with the leadership of several orthopaedic specialty societies. The BA was born in 2018 to address knowledge gaps highlighted by clinical and scientific leaders<sup>1</sup> with a mission to foster and convene a collaboration for shared and coordinated efforts, and ultimately speak with a unified voice in the musculoskeletal biologics environment. More specifically, this organization advocates for the responsible use of biologics in clinical practice, spearheads standards development, and assesses and reports on the safety and efficacy of biologic interventions. The active founding members include the American Orthopaedic Society for Sports Medicine (AOSSM), the International Cartilage Regeneration & Joint Preservation Society (ICRS), the American Arthroscopy Association of North America (AANA), and the Orthoregeneration Network Foundation (ON Foundation).

In addition to the founding members of the BA, members of several other national and international musculoskeletal specialty societies are also represented in this group. The organization intends to be inclusive of all clinicians and researchers with an interest in promoting improved understanding of the safe, ethical, and efficacious use of biologic treatments across a variety of musculoskeletal conditions. The BA has experienced tremendous growth in membership, committee development, drafting of bylaws, website development, submission of manuscripts for peer review, and the creation of our first annual Biologic Association Summit since its inception 2 years ago. This first Summit of the BA was held on February 5-7, 2020, in Carlsbad, California. The faculty was comprised of world-renowned experts in the field of biologics, each of whom are members of the BA, and several of whom are or have been presidents of a variety of specialty societies. A comprehensive program was presented, with a key goal of developing new approaches and fostering collaboration among its members. The final program (and future programs) can be viewed in detail at <https://www.thebiologicassociation.com/Biologics/Conference.aspx>. The attendees of this first-ever BA Summit included multidisciplinary stakeholders in this space, including a diverse group of scientists, clinicians, industry representatives, and regulators.

The following sections of the manuscript will introduce the BA and its purpose, provide a summary of the 2020 first annual Biologic Association Summit, and outline the future strategic plan for the BA, including overall association goals, research priorities, strategies for peer review and self-regulation, and strategies for development of consensus statements. Notably, the BA is not a regulatory body,

nor does the BA make policy for any of the involved societies represented; rather, the BA serves as a platform to communicate up-to-date standards with biologic treatments for musculoskeletal conditions.

## SUMMARY OF 2020 BIOLOGIC ASSOCIATION SUMMIT

The 2020 Biologic Association Summit agenda included 1.5 days of lectures and didactic sessions provided by world-renowned experts in all areas of orthobiologics. The opening session of the summit was entitled, “Biologics: What is Currently Available?” and provided cutting-edge lectures on PRP, bone marrow concentrate, adipose cellular therapy, amniotic cellular therapy, long- and short-acting cortisone injections, and viscosupplementation. The goal of this session was to provide a framework for the current state of biologic therapies in the United States and to disseminate knowledge on these critical therapies from leading experts. Following a question-and-answer session, the next session focused on the important topic of “Regulatory Process and Ethical Implications” and included lectures on regulatory processes, implications of using products “off-label,” nomenclature challenges, complications associated with rogue stem cell clinics, and an overview of cellular expansion and culture. This critical session provided vital information on how to use and research biologics safely and to begin to reach consensus on the confusing nomenclature related to biologics. Even among experts, the definition of a “stromal cell” or “stem cell” is controversial. The content provided in this session helped develop consistent concepts and terminology and set the stage for establishing consensus with respect to current and future biologic technologies. While outside the scope of this review, future publications will discuss consensus statements generated with validated research methods.

The next session of the BA Summit expanded upon the framework provided by the first 2 sessions and discussed real-world clinical applications of biologics, including the use of biologics for tendinopathies, osteoarthritis and acute tendon injuries, either alone or as augmentation to surgical repairs and reconstructions, such as anterior cruciate ligament reconstruction and rotator cuff repair. From here, the afternoon continued with a session on the use of biologics in the office setting with respect to office management and logistics, and it provided the attendees with real-life context as to how practitioners are currently utilizing biologics on a daily basis. The final session of the first day of the Summit focused on the status of the BA as a means to transparently introduce the organization to the attendees and discuss its purpose and future strategies, mission, vision, and goals.

## FUTURE GOALS AND HOW TO ACCOMPLISH THEM

Overall, the BA seeks to develop a musculoskeletal collaboration for shared and coordinated efforts to (1) establish a unified voice of recognized and expert musculoskeletal practitioners in the orthobiologics space to advocate for the

TABLE 1  
Summary of the Subcommittees and Goals of the Biologic Association (BA)

Subcommittee	Goal/Mission
Advocacy	To facilitate a means to allow for development in the field of biologics across local, regional, national, and international boundaries to best serve our patients and peers To promote patient education and awareness as well as facilitate patient and practitioner reporting of false claims and adverse events To develop a forum for the anonymous reporting of rogue “stem cell clinics”
Education and Best Practices	To produce best practices summaries and consensus statements, resulting in peer-reviewed publication and presentations
Registry and Biorepository	To establish and maintain a biologics registry for outcomes and complications and develop a biospecimen and tissue repository for future research purposes
Standards	To establish standards and ensure all material presented by the BA meets those designated standards in a transparent, unbiased, and ethical manner
Finances and Membership	To increase membership across all orthopaedic and musculoskeletal societies, both operative and nonoperative To ensure business matters of the BA are carried out in a responsible, ethical, and transparent fashion
Website Oversight	To improve website accessibility, design, and content, while ensuring that only rigorous, peer-reviewed, evidence-based material is available via our site
Scientific and Education Meetings	To maintain a high-quality annual BA Summit to deliver the most up-to-date information on current and future biologic interventions, plan future breakout meetings specific to biologic topics including specific interventions (ie, cellular therapies), and plan future lab-/skills-based courses To provide regular webinar/virtual educational content focused on the clinical application of orthobiologics to educate colleagues in real time To provide regular webinar/virtual educational content focused on ongoing research related to orthobiologics to educate colleagues in real time on areas of current and future investigation To provide support to the other subcommittees as well as society/individual members from a scientific and research perspective

safe and ethical use of orthobiologics in clinical practice; (2) lead efforts to develop standardized definitions, terminologies, and reporting requirements; (3) monitor and participate in the assessment and reporting of the safety and efficacy of orthobiologic interventions; and (4) advocate for patient education, awareness, and protection. Over the past 2 years, the BA has pursued this mission by developing a grassroots effort into an international, collaborative organization focused on providing the best possible care for patients and education for peers. Despite being a new organization, the cumulative experience of the leadership and membership of the BA speaks to its ability to set and accomplish goals.

One of the first goals of the BA was to develop organizational bylaws and membership requirements. This first step transformed our group into an accountable, transparent organization with a strong governance structure. This was followed by the establishment of subcommittees (via BA leadership) focusing on separate, mission-critical goals (Table 1). The subcommittees include the Advocacy Subcommittee, the Education and Best Practices Subcommittee, the Registry and Biorepository Subcommittee, the Standards Subcommittee, the Finances and New Membership Committee, the Website Oversight Committee, and the Scientific and Education Meetings Subcommittee. These subcommittees have proved vital in the early success of the BA. A summary of these subcommittees is provided in Table 1, with more in-depth information in the following section.

The Advocacy Committee is critical in helping to maintain a unified voice to advocate for the safe, ethical, and efficacious use of orthobiologics in clinical practice and for

patient education and awareness. By prioritizing safe and ethical patient care, this committee seeks to put patients first at all times, regardless of outside influences and agendas. Action items of this subcommittee include improving transparency and accuracy of physician, practice, and biologics-focused websites and advertisements. The advocacy committee also seeks to work with other organizations, including state advocacy programs and the US Food and Drug Administration, as well as social media platforms, to better educate colleagues, patients, and the public on important biologics topics.

The Education and Best Practices Subcommittee aims to produce consensus statements and critical analysis reviews based on the best available peer-reviewed literature to help guide clinical and surgical decision making regarding the use of biologic therapeutics. This group has developed several peer-reviewed scientific articles with additional manuscripts in development.<sup>5,6</sup> Through this subcommittee, we hope to provide a unified voice to guide the ethical use of biologics and provide a rigorous, peer-reviewed library of clinical literature that has been vetted by experts. In addition, given the speed at which the biologics field is advancing, the subcommittee hopes to keep pace with the introduction of novel biologic technologies and techniques by providing a fast, up-to-date, and rigorous peer review, ensuring a safe and ethical platform for disseminating knowledge and innovation.

The Registry and Biorepository Subcommittee has perhaps one of the most important tasks within the BA: to establish a worldwide registry for the use of biologics. This registry will start small with the intention to be a reference

tool for the collection of worldwide data with the goal of global expansion. This registry will go through the institutional review board approval process and will ultimately include deidentified information on patient demographics (age, sex, pathology, concomitant pathologies, prior treatments, activity level, etc), treatments (type, frequency, volume, location, indication, etc), validated patient-reported outcomes (PRO) measures, and complications/adverse events. The goal will be to have >75% follow-up across all clinical sites, and to include specific information on actual procedures (what is injected, how it is processed, the system used, etc) as well as standardized PROs. The clinical data will be linked to a repository of biospecimens. Given the heterogeneity in different biologic formulations, there is a critical need to correlate the clinical and imaging outcomes with the composition and biologic activity of the particular treatment. We will develop a system to procure, process, and bank a sample of the specific biologic formulation in a biorepository for later measurement of the cellular, proteomic, and transcriptomic content and biologic activity. These measurements can be later correlated with the clinical and imaging outcomes to identify the specific factors related to successful treatment outcomes. This information will be combined with data on patient demographics, co-morbidities, radiographic studies, and PRO measures to gain a comprehensive understanding of the effect of biologic therapies in musculoskeletal medicine. Another goal of this committee is to develop a repository of surgical tissue specimens and joint fluid aspirates in order to better define the underlying pathology of various conditions, which will help to identify the biologic targets for treatment with biologic interventions.

The Standards Subcommittee will work in conjunction with the other subcommittees and will ensure that all scientific papers, data, statements, and reports generated from the BA meet a minimum standard of care. It will also seek to develop standardization in the definition of biologic therapies and outcomes metrics reporting, in an effort to define a minimum standard of reporting for peer-reviewed publication. Finally, this subcommittee will be responsible for creating standards for orthobiologic provider training and defining scope of practice.

The Finances and New Membership Committee will ensure a standardized and transparent process for vetting new potential members to the BA while ensuring that the organization can operate within an appropriate annual budget. As the BA intends to be inclusive, a specific set of organizational and operational guidelines will be maintained and updated by this subcommittee to ensure a fair and transparent process for appropriate membership expansion.

The Website Oversight Committee has created a robust website with peer-reviewed content and materials (<https://www.thebiologicassociation.com/>). The ultimate goal of the website is to allow for the sharing of peer-reviewed data and dissemination of information on all topics related to biologics.

Finally, the Scientific and Education Meetings Subcommittee has the responsibility of ensuring the delivery of relevant, accurate, efficacious, and ethical content to attendees during our educational conferences and proceedings, including the 2020 Biologic Association Summit.

## RESEARCH AGENDA FOR THE BIOLOGIC ASSOCIATION

One of the most important priorities of the BA is to bring together clinician-scientists, basic scientists, and clinical researchers from centers within the BA membership that are conducting high-quality research focused on orthobiologics. At each annual BA Summit, we aim to highlight research findings from these research teams, allowing for discussion (and collaboration) on current and future research projects. In addition to the annual summit, we aim to hold regular meetings (in-person and/or virtual) with smaller groups to discuss research findings in real time, and provide opportunities for collaboration, including the potential for multi-institutional prospective studies. Over the next several years, some of our top research priorities include investigating the following factors as they relate to the research, development, and production of biologics:

1. Determine the efficacy of biologics treatment.
2. Identify which patient-specific factors (ie, age, comorbidities, etc), as well as preparation-specific factors (ie, timing of treatment, delivery method, number of treatments, etc), are associated with response (or lack of response) to treatment.
3. Establish pragmatic and reliable standards on preparation of biologic therapies.
4. Identify factors that affect the composition and biologic activity of biologics (ie, details related to processing and preparation), and identify key components of biologics (ie, specific growth factors and/or tissue-specific components) that may be amenable to biologics development.
5. Identify target tissues that would be most responsive to biologic therapy.
6. Identification of specific, validated outcomes measures and timing for clinical improvement.
7. Cost-effectiveness analyses of different biologic interventions, including office-based and operating room-based procedures.

## SUMMARY

The BA has grown from merely a conceptual framework to an organization that has successfully implemented its mission to foster a collaborative group of thought leaders to present a unified voice in the musculoskeletal biologics environment, advocating for the responsible use of biologics in clinical practice, fostering patient awareness and education, spearheading standards development, and assessing and reporting on the safety and efficacy of biologic interventions. Pillars fundamental to the early success of this group include a focus on collaboration, inclusion, transparency, and integrity. The inaugural BA Summit, in collaboration with our founding members (ICRS, AOSSM, AANA, and ON Foundation), aims to set a standard to provide rigorous, evidence-based information for clinicians, scientists, and patients interested in biologics. We hope this will

foster and encourage future collaborations and innovations in the field of musculoskeletal biologics.

#### MEMBERS OF THE BIOLOGIC ASSOCIATION AT THE TIME OF THE 2020 BA ANNUAL SUMMIT

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