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Candidate For: Council

Statement of Interest: I graduated from the University of Tokyo, and began my career as an orthopaedic surgeon in 1985. I joined the laboratory of Dr. Lawrence Raisz at the University of Connecticut Medical Center, and there spent my research years from 1991 to 1994 as a postdoctoral research fellow. During the three years, I have achieved works especially on the role of cyclooxygenase-2 in bone metabolism under the supervision of Drs. Raisz and Carol Pilbeam. There I decided my life's work would be on "disease science", i.e. preclinical translational

research leading directly to the treatment of skeletal disorders: osteoporosis, bone fracture, periprosthetic osteolysis, ossification of spinal ligaments, and osteoarthritis. Since then, I have had a career as a "surgeon scientist" in both laboratory and clinical aspects of these disorders, publishing 318 peer-reviewed original articles (total impact factor: 1,537) in prestigious scientific journals such as *Nat Med*, *Nat Mat*, *Nature*, *Science*, *JCI*, *Gene Dev*, *JCB*, *PNAS*, *Dev Cell*, *JBC*, and *JBMR*. Most importantly, some of these reports have already led to clinical use, for example, a recombinant agent for fracture healing and a novel artificial joint with longevity.

I have been an ASBMR member since 1989, kept attending the annual meeting every year, and willingly served in many and varied capacities within the Society, from abstract reviewer to committee member. I served on the Membership Development Committee from 2002 to 2005, and GAP Awards Committee in 2014. I also have received the 2011 Lawrence Raisz Award, as well as the 2009 Kappa Delta Award of AAOS (American Association of Orthopaedic Surgeons), the 2006 Frank Stinchfield Award of the Hip Society, and the 2006 Basic Science Award of OARSI (Osteoarthritis Research Society International).

Furthermore, I have also devoted myself to the education of young researchers as a mentor. In fact, members of my lab group have been awarded the ASBMR Young Investigator Award each of the 19 years since 1998 until now, and three of them the President's Book Award during that period (28 awardees in total).

Throughout my professional life, the ASBMR has been my "home society" where the most exciting science in our field is presented. This has included basic science breakthroughs that have been translated into practice and clinical trials, and finally provided exciting new treatments for skeletal diseases. This is just the "disease science" which I decided to be my life's work when I started my research work.

I am therefore familiar with the history and recent progress of ASBMR, and understand that our society is now at the crossroads. Based on my experiences as above, I view the strategic goals of ASBMR to be the following:

- 1) To further advance research and treatment of skeletal disorders worldwide
- 2) To develop, disseminate and exchange what is known on research and care
- 3) To develop international outreach and foster strategic alliances, thereby increasing ASBMR's visibility
- 4) To maintain financial stability from worldwide including industries in foreign countries

If I am elected as a Council, I will direct my energy particularly toward international members. In fact, I have also had an experience on the Board of Directors of OARSI from 2006 to 2012. As a minority member of the Board, I have been working to popularize the Society by conducting co-sponsored symposiums of OARSI with several representative domestic societies in Japan, Korea, and China. This has led to an increase in Asian members and industry sponsors. Likewise, as a representative and leader of the minority in ASBMR, I would first expand co-sponsored symposiums between ASBMR and domestic societies in countries outside of the United States to develop and foster international alliances. Second, to develop international outreach, I would prepare and distribute newsletters on highlights of the ASBMR annual meeting and on guidelines created by the ASBMR task force, which would be published and widely disseminated worldwide after translation into languages of less represented countries. Third, I would arrange to hold the "Year in Review" session of the ASBMR annual meeting by the native languages in the evening during the meeting term to help young attendees from minor countries to understand the highlight and substance of the meeting. These activities would hopefully lead to increases not only in international members, but also in industry sponsors and subsequent financial support. I believe that these would serve to materially realize the strategic goals of ASBMR.

Education/ Training/ Positions: MD, Faculty of Medicine, University of Tokyo, 1985; PhD, Faculty of Medicine, University of Tokyo, 1996; Assistant Professor (1996-1998), Lecturer (1998-2004), Associate Professor (2004-2009), Professor (2009-2013) at the Department of Orthopaedic Surgery, Faculty of Medicine, University of Tokyo; Chief, Spine Center, Japan Community Health Care Organization, 2013-present.

Honors/Awards: Young Investigator Award of Japanese Society for Bone and Mineral Research, 1991; Young Investigator Award of Japanese Orthopaedic Association, 1995; AOA (American Orthopaedic Association) International Traveling Fellow, 1997; Tokyo University Doctor Society Medical Award, 1997; Most Outstanding Paper Award of Japanese Orthopaedic Association, 1997; Alcare Award of Japan Orthopaedics and Traumatology Foundation, 1998; ASBMR Young Investigator Award, 1998; ASBMR Travel Award, 1998; Academic Award of Japanese Society for Bone and Mineral Research, 2001; Academic Award of Japanese College of Rheumatology, 2002; Academic Award of Osteoporosis Society Japan; 2003; Clinical Award of Japanese College of Rheumatology, 2004; Outstanding Paper Award of Japanese Society for Bone and Mineral Research, 2005; OARSI Basic Science Award, 2006; The Frank Stinchfield Award of the Hip Society, 2006; APLAR (Asia Pacific League of Associations for Rheumatology) Distinguished Basic Investigator Award, 2008; AAOS Kappa Delta Award, 2009; ASBMR Lawrence Raisz Award, 2011

Editorial Duties/ Peer Review Panels: Editorial Board of *the Journal of Orthopaedic Science* (2005-present); Editorial Board of *the Journal of Bone and Mineral Metabolism* (2005-present); Associate Editor of *Osteoarthritis and Cartilage* (2008-present); Associate Editor of *BMC Musculoskeletal Disorders* (2010-present); Editor of *OARSI Primer* (2011-present)

Professional Societies: ASBMR, Membership Development Committee (2002-2005); Japanese Society for Bone and Mineral Metabolism, Council (2003-present); OARSI, the Board at Large (2006-2012); OARSI, Membership Committee (2006-2012); OARSI, Treatment Guideline Committee (2011-2015); Japanese Society of Cartilage Metabolism, the Board at Large (2013-present); ASBMR, GAP Awards Committee (2014); International Early Knee Osteoarthritis Workshop Scientific Advisory Board (2016); Orthopaedic Research Society (ORS), Program Committee (2017-)

Current Research: My interest has expanded to several skeletal disorders based on my daily clinical work as an orthopaedic surgeon. 1) My initial studies focused on the role of cytokines / growth factors on bone metabolism. After disclosing the bone anabolic action of fibroblast growth factor-2 (FGF-2) in various animal models, I performed a randomized, double-blind, placebo-controlled clinical trial, and succeeded in showing that the application of the rhFGF-2 hydrogel accelerated healing of fresh fractures. This agent will be clinically used for fractures and surgical osteotomies in the near future. 2) I have also been involved in the molecular mechanism underlying bone anabolic action of insulin / IGF-I via the IRS1 & 2 / Akt signals during progression of osteoporosis and fracture healing. In addition, I have been investigating involvement of glucose and lipid metabolisms in bone metabolism. 3) Furthermore, by combining experiences from surgical practice and from basic research on bone resorption, I have developed a novel artificial joint with surface grafting by a biocompatible polymer which notably prevented periprosthetic osteolysis. The artificial joint is now used clinically worldwide. 4) I also established the biggest scale of population-based cohorts in the world, called ROAD (research against osteoarthritis/osteoporosis disability) in 2005, and have performed variable epidemiologic and genomic studies. 5) Recently, I am also pursuing translational research on cartilage biology for the treatment of osteoarthritis, and have identified several candidates that could be therapeutic targets for the disease. Among them, hypoxia-inducible factor 2 $\alpha$  (HIF2A), was shown to be the strongest candidate by integration of cell and molecular biology, mouse genetics, and human genomic approaches using the ROAD.

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