Aging Mechanisms

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Editors

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Longevity, Metabolism, and Brain Aging

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Preface

According to a predictive report on the increase in the elderly population in various countries, Japan and Korea are poised to become the world's top two nations, with constantly high elderly populations approaching 35–40 % in the latter half of this century. The rapidly aging populations in Japan and Korea promote movement toward a "senescent" society. Amazingly, however, if we examine the numbers of people living to over 100 years old, more than 60,000 centenarians currently reside in Japan. In Korea, the centenarian population is approximately 3,300, but it is estimated to grow to almost 40,000 by the year 2050. Japan and Korea are thus growing old so rapidly that we are indeed moving "into the unknown," as described in a special report in *The Economist* several years ago (November 18, 2010). In such nations, research on aging is important not only sociologically but also biologically to understand the background of aging in our population.

During the last several decades, our knowledge concerning aging research has been growing rapidly. However, we are still far from achieving a complete understanding of the whole mechanism of aging: how we, as animals, age and how our lifespan is determined. Many researchers are working in this field in both Japan and Korea, and our scientific societies in relation to biomedical aging in the two countries have been interacting with each other. When one of the editors (N.M.) moved from the National Institute for Longevity Science (Research Institute, National Center for Geriatrics and Gerontology, Nagoya) to Nagasaki in 2006, we met on the small island of Ioujima in Nagasaki to discuss and exchange ideas on the basic science of aging. We called this discussion forum the "Asian Aging Core for Longevity" (AACL), and we have continued this series of AACL meetings for the last 10 years, alternating between Japan and Korea. In the last 5 years, it was supported by the Asian CORE program of the Japan Society for the Promotion of Science (JSPS). The studies described in this book were supported, at least in part, by the fund of the JSPS-Asian CORE program, through an intimate discussion at the AACL meetings.

This book was initially planned to summarize the aging research among all of the members of the AACL. However, owing to space and time limitations, we could not include the work of all the AACL members. The book is composed of a series of

topics in aging research which were explored through the daily dedicated laboratory work of our AACL members and their colleagues. Based on the topics of each manuscript, we, the editors, ordered each chapter such that the stories would facilitate the understanding of the scientific outcomes of our latest research on aging from the basic biology of longevity, metabolism, and brain aging with the goal of developing potential therapeutics for age-related diseases, such as Alzheimer's.

For convenience, we subdivided the chapters into seven parts. Part I provides an overview and re-investigation of various hypotheses of aging. Part II introduces studies of centenarians and cells of progeria patients. Part III discusses the usefulness of induced pluripotent stem (iPS) cells and primary cultured neurons for the study of aging and further explores the potentials of using lower organisms, such as budding yeast and nematodes, for the study of longevity and as a model for neurodegenerative disorders. Part IV introduces several key regulatory factors affecting tissue aging, such as α-Klotho, FOXO transcription factors, neuropeptide Y, uremic toxins, and vitamin K. Part V describes the studies of the physiological nature of brain aging. It includes how aging affects potentials of adult neurogenesis in the hippocampus, signaling molecules for cognitive decline, neuroplasticity in the hippocampus and the cerebellum, and volume analysis of aging brains using a large brain database. Part VI addresses the pathophysiology of the aged brain. Alzheimer's disease (AD) is the most debilitating disease in the elderly. The processing mechanisms of amyloid precursor protein (APP), the accumulation and aggregation of amyloid-β, and its degradation mechanisms are discussed here. A novel approach exploring new biomarkers of AD is also discussed. Finally, Part VII explores issues of antiaging, particularly focusing on therapeutic approaches for neurodegenerative diseases, including AD and polyglutamine diseases.

How do we age, and how is longevity determined? These questions are fundamental issues in biology. Solving the mechanisms of biological aging and the determination of longevity is not easy and may never be completely achieved. However, the studies described in this book are on the cutting edge of the science of biological mechanisms for each aspect of the biology of aging. We hope this book will be useful for researchers and graduate students in the field worldwide.

At this point, we would like to express our sincere thanks to all the authors for their valuable contributions to this volume. We are also grateful to Dr. Sang Chul Park, Dr. Eun Seong Hwang, Dr. Isao Shimokawa, and Dr. Yong-Sun Kim for their cooperation and encouragement during the course of our past meetings of the JSPS-AACL. Finally, we would like to thank Ms. Kanako Ishimaru and Ms. Noriko Tominari for their excellent secretarial assistance throughout the course of all the AACL meetings and also for putting this book together for final publication.

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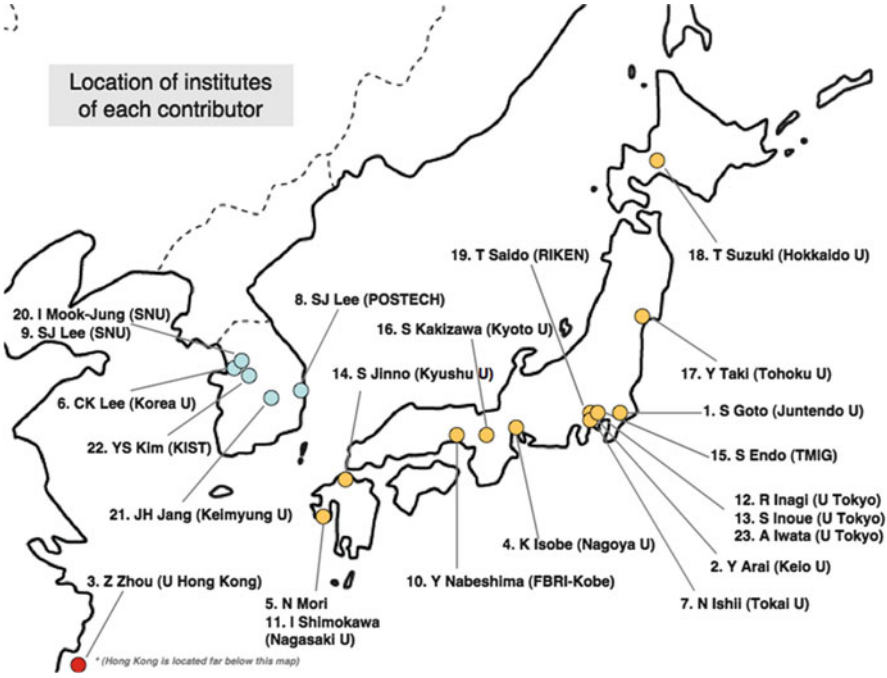
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