Physiologic and Pathologic role of RANKL : beyond the skeletal system

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Receptor activator of nuclear factor- κ B ligand (RANKL), a transmembrane protein of the TNF superfamily cytokine, was originally identified in 1997 as a dendritic cell activator produced by activated T cells, and rediscovered in 1998 as a master regulator of osteoclast differentiation, activation, and survival. Recently, the involvement of RANKL in many physiological and pathological functions other than bone metabolism has been revealed. RANKL provides a paradigm that enables the molecular understanding of the linkage among organization of lymphoid tissues, establishment of the thymic microenvironment, thermoregulation, metabolic regulation, mammary gland development and tumorigenesis.

In addition to the rapid progress in the basic research, what is noteworthy is the speed with which the discovery

of RANKL has progressed to clinical application. The human anti-RANKL antibody, denosumab, was developed in less than 10 years of the finding of RANKL, and was subsequently approved as a therapeutic option for not only osteoporosis but also for bone destruction by metastatic bone tumors and bone erosion in rheumatoid arthritis.

This special issue covers the history of RANKL discovery, the biological and pathological significance of RANKL, the molecular mechanism of action, and the clinical efficacy of denosumab, and provides the future of RANKL research. We believe that the articles in this issue will foster further research efforts leading to better understanding of the mystery of biological systems, as well as better treatment of patients.

Guest Editors, JBMM

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