

Molecular basis of nuclear receptors and their downstream targets in aging

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【 Outline of survey 】

As human lifespan is extending and the number of elderly people is rapidly increasing in Japan and western countries nowadays, prevention of pathological aging and aging-associated diseases as well as promotion of healthy aging is a most requisite for public health. In this project, we focus on actions of nuclear receptors in aging process. Nuclear receptors are primary receivers of various living signals such as steroid hormones, thyroid hormone, retinoic acids, cholesterol and fatty acids, and those receptors are thought to be essential factors that determine senescence of tissues and organs as well as a whole body. The functions of nuclear receptors are closely associated with the aging and pathogenesis of age-related diseases of multiple organs including bone, blood vessels, brain, and reproductive organs. We consider that the knowledge of various functions and molecular mechanisms of nuclear receptors in aging is an essential issue to prevent age-related diseases. The aims of this project are 1) to elucidate functions of nuclear receptors, their mutual interactions, and their cofactors and downstream targets, 2) to explore novel molecular mechanisms of nuclear receptors and to define physiological relevance of nuclear receptors in cell growth, cell differentiation, and anti-aging reactions. The final goal is to apply the research results of this project into clinical medicine including diagnosis, treatment and regulation of age-related pathological conditions.

【 Expected results 】

The overall goal of this project is to reveal aging process and pathogenesis of aging-associated diseases through functional study of nuclear receptors and to prevent pathological aging by clinically applying anti-aging actions of nuclear receptors. This project will be performed on the basis of both clinical and experimental medicine. We aim to elucidate new molecular mechanisms of nuclear receptors and to identify novel molecular targets of nuclear receptors in pathological aging. We also expect to clarify mechanisms of aging process and to prevent aging-associated diseases, as well as to develop novel diagnostic and therapeutic technology and to establish the basis of drug discovery.

【 References by the principal researcher 】

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- 2) Inoue S, Kondo S, Muramatsu M: Identification of target genes for a transcription factor by genomic binding site (GBS) cloning (1999) *Transcription Factors - A Practical Approach*, 2nd Edition (Edited by Latchman, D. S.) Oxford University Press, New York, (pp 165-178)

【 Term of project 】 FY 2004 - 2008

【 Budget allocation 】 88,600,000 yen

【 Homepage address 】 none