Age Dimension Homeostasis of Physiological Systems, a Slow Dynamics Model in Biology

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Biological systems are controlled by complex arrays of homeostatic mechanisms so that they are maintained within certain permissible fluctuations. In our research, the age axis homeostasis and its regulatory mechanisms were taken as a complex biological model for extensive studies. The age related homeostasis of physiological systems is not constant through out the life span, but it gradually and irreversibly changes along the age axis. This may represent a biological slow dynamic system. The age axis homeostasis is of particular interest because it is not only an essential mechanism of normal physiological systems but also its significant disturbances are closely linked with the pathogenesis of many diseases as well.

Through the systematic analyses of transgenic mice designed for finding age related expression patterns of genes for human blood coagulation factors, we previously discovered the first age related regulatory mechanisms of gene expression, which we called the ASE/AIE type age related regulatory mechanism of gene expression (1,2,3)(Fig. 1). This mechanism involves two genetic elements, ASE (Age-related Stability Elements, G/CAGGAAG) required for age stable gene expression and AIE (Age-related Increase Element, a stretch of dinucleotide repeats) required for age-related increase in gene expression. ASE and AIE function independently, but AIE needs ASE for its full effects in generation of age related increase patterns of gene expression. These two elements found to be able to generate four situations of age related regulatory patterns, (a) absence of both elements for the puberty-onset decrease in gene expression to the background, (b) presence of ASE alone for age stable gene expression, (c) presence of AIE alone for age related less steep decrease in gene expression than the case of no ASE and AIE, ending up with a significant residual level of expression, and (d) presence of both ASE and AIE for age related increase in gene expression. ASE also has a critical role in both temporal (age) and spacial (tissue specific) regulations of gene expression. Furthermore, the first mechanism discovered has the functional universality, thus in principle enabling development of a novel field of technology (Age Dimension Technology) for arbitrary age-related regulation of genes, therefore of proteins.

The discovery of the first age related regulatory mechanism gave the basis for launching a series of search efforts for unidentified other unique age related regulatory mechanisms of gene expression. As a part of our efforts, we carried out global analyses of expression patterns of mouse liver proteins and genes along the age axis. Results obtained from these studies clearly support our hypothesis that many yet unidentified new molecular mechanisms for age related gene expression exist. Many genes, therefore, may be differently and delicately regulated along the age axis by numerous combinations of genetic elements including ASE, AIE and many yet to be identified.

These observations we have made to date suggest that the age axis homeostasis and its regulatory mechanisms may serve as a very interesting biological model for slow dynamics for further study.

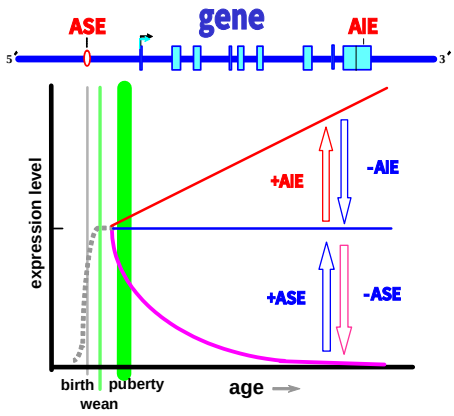

Fig. 1. Schematic presentation of the ASE/AIE type age related molecular regulatory mechanisms of gene expression. Relative positions of ASE and AIE in a gene and their relationships with the specific age related regulatory functions are shown. To make the relationships simple and easy to see, the situation (c), no AIE, is not shown here.

References

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