

EARLY-LIFE EPIGENETIC PROGRAMMING OF AGING TRAJECTORY

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Accumulating evidence suggests that risk for age-associated pathological conditions can be programmed early in life. Epigenetic regulation of gene expression is likely a key molecular mechanism linking early-life environmental factors to the genome with consequences for life-course health status. Epigenome is most sensitive to environmental cues during early development. In humans, the period of high environmental sensitivity and plasticity of epigenome extends from preconception through weaning. Growth hormone/insulin-like growth factor (GH/IGF) axis is likely a key driver of these processes. An important longevity-determining factor, IGF-1, is likely of particular significance. Based on our own findings and those of others, it can be hypothesized that different aging trajectories can be realized depending on developmentally programmed life-course dynamics of IGF-1. In this hypothetical scenario, intrauterine growth restriction-induced deficit of IGF-1 causes "diabetic" aging trajectory associated with various metabolic disorders in elderly, while fetal macrosomia-induced excessive levels of IGF-1 lead to "cancerous" aging trajectory. If so, then both low (<2.5 kg) and high (>4.5 kg) birth weights are predictors of unhealthy aging, while the normal birth weight is a predictor of healthy aging and maximum longevity potential. In conclusion, by obtaining new knowledge on the early origins of aging-related chronic disorders and on the role of IGF-1 in these processes, it would be possible to develop new approaches to predict which individuals are at risk for particular diseases. Further development of such methodical tools would allow for detection of potentially unfavourable processes long before the clinical manifestation of disease. The use of specific epigenome-targeted nutritional and/or pharmacological interventions seems especially promising due to potential reversibility of developmentally-induced epigenetic disturbances. The further introduction of such therapeutic strategies in clinical practice would hold great promise to prevent and treat chronic disorders and to human health span extension.

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