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Genetic pathways influencing human longevity: From telomere dynamics to caloric restriction mimetics.

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Introduction

Human longevity is a complex trait influenced by a combination of genetic, environmental, and lifestyle factors. While improvements in healthcare and living conditions have extended average life expectancy, the biological underpinnings of exceptional longevity—such as living beyond 100 years—remain an area of intense research. Recent advancements in genomics and molecular biology have shed light on specific genetic pathways that govern aging and longevity, from telomere maintenance to cellular stress responses. These discoveries have opened new avenues for potential interventions, including caloric restriction mimetics, aimed at extending healthy human lifespan [1].

One of the most studied mechanisms in aging is telomere dynamics. Telomeres are repetitive nucleotide sequences at the ends of chromosomes that protect them from degradation. Each time a cell divides, telomeres shorten slightly, eventually leading to cellular senescence or apoptosis when critically short. The enzyme telomerase can elongate telomeres, but its activity is low in most somatic cells. Mutations in genes regulating telomerase, such as TERT and TERC, have been associated with premature aging syndromes and reduced lifespan. Conversely, certain populations of long-lived individuals exhibit longer telomeres and enhanced telomere maintenance [2].

Insulin/IGF-1 signaling (IIS) is another key pathway implicated in aging. This conserved pathway regulates metabolism, growth, and lifespan across multiple species. Studies in model organisms like *C. elegans*, *Drosophila*, and mice have shown that reduced IIS activity leads to extended lifespan. In humans, genetic variants in genes such as FOXO3A, which is a downstream transcription factor of IIS, have been consistently associated with longevity. FOXO3A enhances the expression of genes involved in stress resistance, DNA repair, and apoptosis—all vital for cellular homeostasis during aging [3].

The mTOR (mechanistic target of rapamycin) pathway also plays a central role in regulating longevity. mTOR integrates signals from nutrients, growth factors, and cellular energy status to control protein synthesis and autophagy. Inhibition of mTOR, for example by the drug rapamycin, has been shown to extend lifespan in various species. mTOR inhibitors are currently being explored in clinical trials for their potential to delay aging-related diseases in humans, including neurodegeneration and cancer [4].

Another important pathway is sirtuin signaling. Sirtuins are a family of NAD^+-dependent deacetylases that regulate mitochondrial function, genomic stability, and inflammation. Among them, SIRT1 and SIRT6 have been shown to influence lifespan and resistance to stress. Activation of sirtuins by compounds such as resveratrol, a polyphenol found in red wine, has been proposed as a strategy to mimic the beneficial effects of caloric restriction without actual dietary reduction [5].

Conclusion

In conclusion, the genetic architecture of human longevity is governed by interconnected molecular pathways that regulate metabolism, DNA repair, inflammation, and cellular stress responses.

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Advances in molecular genetics, coupled with systems biology and pharmacological innovations, are bringing us closer to interventions that could not only extend lifespan but, more importantly, promote a longer healthspan. Continued research into these genetic pathways and their modulation will be essential in addressing the global challenges of aging populations.

References

1. Ferreira D, Martins B, Soares M, et al. Gene expression association study in feline mammary carcinomas. PLoS One. 2019;14:e0221776.
2. Gundim LF, Wilson TM, Soares NP, et al. Her-2 expression in feline mammary lesions. Acta Vet Brno. 2019;88:43-47.
3. Hirayama A, Kami K, Sugimoto M, et al. Quantitative metabolome profiling of colon and stomach cancer microenvironment by capillary electrophoresis time-of-flight mass spectrometry. Cancer Res. 2009;69:4918-4925.
4. Chen JL, Fan J, Yan LS, et al. Urine metabolite profiling of human colorectal cancer by capillary electrophoresis mass spectrometry based on MRB. Gastroenterol Res Pract. 2012;2012:125890.
5. Cohen JC, White M, Cruz A. In 2014, can we do better than CA125 in the early detection of ovarian cancer? World J Biol Chem. 2014;5:286-300.

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