

Inhibition of PDK1 Can Reverse Cell Aging

A study provides insight into the complex mechanism of cellular senescence and presents a potential therapeutic strategy for reducing age-related diseases.

NEW YORK, NEW YORK, UNITED STATES, December 3, 2020 /EINPresswire.com/ -- Recent studies showed that cellular senescence, previously considered an irreversible



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biological phenomenon, may represent a reversible state, but the mechanism for the reversion is not well elucidated. Last month, Research findings by a Korean team provide insight into the complex mechanism of cellular senescence and present a potential therapeutic strategy for reducing age-related diseases associated with the accumulation of senescent cells.

To identify targets the inhibition of which would convert senescent cells into quiescent cells, the researchers constructed a molecular regulatory network model of cellular senescence. From ensemble analysis of network models, they identified 3-phosphoinositide–dependent protein kinase 1 (PDK1) as a promising target for inhibitors to convert the senescent state to the quiescent state. The researchers validated this prediction in experiments with human dermal fibroblasts, which showed that PDK1 inhibition eradicates senescence hallmarks by suppressing both nuclear factor kB and mTOR signaling through the inactivation of a positive feedback loop composed of PDK1, AKT, IKBKB, and PTEN, resulting in restored skin regeneration capacity. The findings were published in the Proceedings of the National Academy of Sciences.

According to experts at <u>VulcanChem</u>, PDPK1 is a master kinase, which is crucial for the activation of AKT/PKB and many other AGC kinases including PKC, S6K, SGK. An important role for PDPK1 is in the signaling pathways activated by several growth factors and hormones including insulin signaling. Inhibitors of PDK1 inhibitors include <u>BX795</u>, <u>BX912</u>, etc.

"Our research opens the door for a new generation that perceives aging as a reversible biological phenomenon," says Professor Kwang-Hyun Cho of the Department of Bio and Brain Engineering at the Korea Advanced Institute of Science and Technology (KAIST), who led the research with colleagues from KAIST and Amorepacific Corporation in Korea. The scientists recommend investigations are next done in organs and organisms to determine the full effect of PDK1 inhibition. Since the gene that codes for PDK1 is overexpressed in some cancers, the scientists

expect that inhibiting it will have both anti-aging and anti-cancer effects.

"The study showed the potential for reverse the aging process, which has been recognized as an irreversible phenomenon in life," Professor Cho said. "This research marked the beginning of a new era that can prevent diseases related to aging and prolong life span."

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