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Hexokinase 2 is a molecular bridge linking telomerase and autophagy

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Autophagy is systematically regulated by upstream factors and nutrients. Recent studies report that telomerase and hexokinase 2 (HK2) regulate autophagy through mTOR and that telomerase has the capacity to bind to the HK2 promoter. Here, we show that HK2 is a molecular bridge linking telomerase to autophagy. TERT-induced autophagy activation and its further enhancement by glucose deprivation were suppressed by HK2 inhibition in HepG2 cells. The HK2 downstream factor mTOR was responsible for TERT-induced autophagy activation under glucose deprivation, implying that TERT promotes autophagy through a HK2-mTOR pathway. TERC played a similar role as TERT, and simultaneous expression of TERT and TERC synergistically enhanced HK2 expression and autophagy. At the gene level, TERT bound to the HK2 promoter at a specific region harboring the telomerase-responsive sequence TTGGG. Mutagenesis of TERC and the TERT-responsive element on the HK2 promoter revealed that TERC is required for the binding of TERT to the HK2 promoter. We demonstrate the existence of a telomerase-HK2-mTOR-autophagy axis and suggest that inhibition of the interaction between telomerase and the HK2 promoter sensitizes cells to metabolic stress, and this pathway could be targeted for anti-cancer therapies.

Biography

Jae-il Roh has completed his PhD from Yonsei University and continuing his research at the same laboratory. He is working in Prof. Han-Woong Lee's lab and interested in mouse genetics, generation of mouse models, and cancer.

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