

Inhibition of ERKs/RSK2/I κ B α signaling axis by magnolin suppresses cancer cell invasion and migration

Sun-Mi Yoo, Cheol-Jung Lee, Sueng-Min Kim, Seon-Yeon Cho and Yong-Yeon Cho

The Catholic University of Korea, Korea

Previously, our study demonstrated that I κ B α phosphorylation at Ser32 by RSK2, a kinase regulated their activity by ERK1 and 2, induced NF- κ B transactivation activity through I κ B α destabilization, and magnolin inhibited ERK1 and 2 activities by targeting of the ERK active pocket. However, the role of magnolin in cell migration has not been clearly elucidated. Here, we found that magnolin inhibited NF- κ B transactivation activity by suppression of ERK1/2/RSK2 signaling pathway. We demonstrated that magnolin abrogated increase of EGF-induced COX-2 protein level and wound healing in a dose dependent manner. In human lung cancer cells such as A549 and H1975 which harbor constitutive active Ras and EGFR mutants, respectively, we found that magnolin suppressed wound healing and cell invasion in Boyden chamber assay in a dose dependent manner. Importantly, gene expressions and activities of MMP-2 and -9 were inhibited by magnolin treatment. Notably, E-cadherin levels, an epithelial marker, was elevated by magnolin treatment and N-cadherin, Snail, Vimentin levels, mesenchymal markers, were suppressed by magnolin treatment in a dose dependent manner. In

addition, the knockdown or knockout of RSK2 in A549 lung cancer cells or MEFs revealed that magnolin targeting ERKs/RSK2 signaling suppressed epithelial-mesenchymal transition. These results demonstrated that magnolin is beneficial for the anti-invasion and -migration in cancer metastasis.

Speaker Biography

Sun-Mi Yoo is an Ph. D. course student at the College of Pharmacy, The Catholic University of Korea. Ms Yoo graduated B. S. degree at the Yonsei University (Life science) and entered graduate school of M. S./Ph. D. joint program on major of Pharmaceutical Biochemistry in 2014 supervised by professor Yong-Yeon Cho. Ms. Yoo has studied on the protein-protein interaction and signaling network involved in cell transformation, cancer metastasis and chemoresistance. Ms. Yoo found that ERKs/RSK2 signaling pathway plays a key role in cancer cell metastasis and molecular targeting of ERKs using magnolin, a natural compound abundantly found in magnolia flos, strongly suppressed cancer cell migration and invasion. Moreover, During the M. S./Ph. D. course, she has identified a novel signaling pathway involved in chemoresistance through p90RSKs.

e: apple_ma@naver.com

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