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Sulforaphane inhibits upregulation of the eIF4F translation initiation complex in human colorectal cancer via the PI3K/AKT/mTOR/4E-BP1 signaling pathway

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The eIF4F translation initiation complex plays an important role in tumorigenesis. The interaction of eIF4E:eIF4G is the crucial component of the eIF4F complex. In this study, we found that eIF4E:eIF4G interactions were upregulated in human primary (n=10; matched controls: healthy colon tissue from the same patients) and liver metastatic CRC (n=10) tissues using in situ proximity ligation assay (PLA) method (P = 0.0020; P = 0.6694, respectively). Unexpectedly, eIF4E:4E-BP1 interactions, the competitive inhibitor of eIF4E:eIF4G interactions, were increased simultaneously (P = 0.0137; P = 0.1044, respectively). Furthermore, immunofluorescence (IF) of the same tissue samples showed that there was no significant difference in the single expressions of eIF4E, eIF4G, and 4E-BP1 (P = 0.5781, P = 0.4688, P = 0.2188; P = 0.1733, P = 0.2200, P = 0.9412, in primary and liver metastatic CRC tissues respectively). In vitro, sulforaphane (SFN), an anti-tumor reagent extracted from broccoli, was proved be able to inhibit formation of eIF4F complex in primary (HCT116, HT29, and SW480) and metastatic (SW620) CRC cell lines, and this inhibition was affected by different PIK3CA and K-RAS genetic mutations in various cell lines. The inhibition of eIF4F formation was resulted from SFN-induced dephosphorylation of 4E-BP1 via the PI3K/AKT/mTOR/4E-BP1 signaling pathway. Taken together, these results demonstrate that the eIF4F complex is upregulated in human CRC tissue and is a potential new therapeutic target. Additionally, SFN is probably effective in the treatment for CRC patients.