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Sulforaphane inhibits formation of eIF4F complex in human pancreatic cancer via mTOR/4E-BP1 signaling pathway: a strategy for chemoprevention?

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1. In situ PLA revealed a significantly higher eIF4E-eIF4G interaction in pancreatic ducts of human CP while it was lower in PC if compared with samples from healthy patients (HD), which suggests that eIF4F complex plays a vital role in the conversion from CP to PC.
2. Further eIF4E-4EBP1 interactions on human CP and PC tissues showed no difference, compared with those on the HD pancreatic ducts. Such a phenomenon might probably be interpreted by the amplification of 4E-BP1 coding gene.
3. SFN suppressed interactions of eIF4E-eIF4G and promotes interactions of eIF4E-4EBP1 in human PC cells. Most interestingly SFN suppressed the formation of eIF4F complex through downregulation of p-4EBP1 and inhibition of PI3K/Akt/mTOR signaling pathway.
4. The eIF4F complex consisting of eIF4E, eIF4G and eIF4A plays an important role for tumorigenesis. The interaction of eIF4E and eIF4G is mainly regulated by 4E-BP1, since 4E-BPs and eIF4G share the same binding site on eIF4E. MTOR affects protein

synthesis and neoplasia by phosphorylation of 4E-BP1 directly at Thr37/46. Data presented here clearly show that SFN [20μM/L] inhibits the proliferation of human PC cells, including Capan-1, MIA-PaCa2 and Panca-1. SFN suppresses the formation of eIF4F complex through downregulation of p-4EBP1 and inhibition of PI3K/Akt/mTOR signaling pathway. SFN is rich in broccoli and its sprouts. Therefore, SFN is a potential candidate for both chemoprevention and chemotherapy against PC, which might cease or delay the conversion from CP to PC.