Cell cycle and metabolism related candidate human synthetic lethal network

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Synthetic lethal strategy can be used as a power full method in the development of anticancer drug for the fighting against cancer. It is evident from various published literatures that identification of synthetic lethal gene pairs and targeting one of them can be an effective approach in developing targeted anti-cancer drug where the cancer cells carry a mutation in the other pair of the synthetic lethal duo. The strategy is successfully applied in BRCA1 mutant breast cancer by targeting PARP due to the synthetic lethal relationship between these two genes. Identification of synthetic lethal pairs requires genome wide screening and therefore in human is a difficult task. For yeast, nematode, and fly synthetic lethal screening have been reported using in vitro mutagenesis. However, in human, such experimentally validated reports are limited. Although comparative genomics and phylogenetic relationship based predicted synthetic lethal relationship are available. Here, novel bioinformatics approaches were used, based on our strategy, David, ToppGene, and Ospery analysis, we found cell cycle related genes MDM2: MDM4 that are reported to be synthetic lethal in Human, are binding to each other. We have identified cell cycle and metabolism related candidate human synthetic lethal network using yeast proteome. Our analysis is also verified using reported synthetic lethal interactions in human and shows the applied method is enough powerful to screen new synthetic lethal relationships in human. Many key nodes of our identified network are involved in cancer. Therefore, this new synthetic lethal network should be further explored for development of anticancer strategy. These candidate synthetic lethal genes required future experimental validation. Most of the identified candidate synthetic lethal genes are involved in tumorigenesis process and therefore selective targeting of a partner of a pair may provide effective anti-cancer therapy.