Galeterone and its analogs inhibit Mnk-eIF4E axis, synergize with gemcitabine, impede pancreatic cancer cell migration, invasion and proliferation and inhibit tumor growth in mice.
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Survival rate for pancreatic cancer (pancreatic ductal adenocarcinoma, PDAC) is poor, with about 80% of patients succumbing to their disease within 5 years of diagnosis. In the absence of effective systemic treatment, the development of novel therapeutic approaches is urgently needed. Currently, new small-molecule inhibitors of the mammalian target of rapamycin (mTOR) pathway are being explored for the treatment of PDAC. The objectives of this study were to examine the effects of gal/analogs on the eukaryotic translation initiation factor 4E (eIF4E) axis and to investigate the potential therapeutic utility of gal/analogs in combination with gemcitabine. 

Gal inhibited the growth of the human PDAC cell line Panc-1 in vitro and in vivo, whereas its analogs exerted growth inhibitory effects on PDAC cells in vitro. The results of cell migration and invasion assays suggested that gal/analogs impeded PDAC cell migration and invasion. Notably, the combination of gal/analogs with gemcitabine showed a marked synergistic effect in the inhibition of PDAC cell migration, invasion and proliferation. Furthermore, gal/analogs inhibited the growth of PDAC tumors in vivo. The effects of gal/analogs on PDAC cell migration, invasion and proliferation were associated with the inhibition of Mnk-eIF4E axis in vitro and in vivo. In summary, these promising findings strongly support further development of gal/analogs as novel therapeutics for PDAC.