Lysine acetyltransferase (KAT) p300 play pivotal role in the diverse physiological processes of higher eukaryotes. As a transcriptional coactivator it interacts with large array of transcription factors. However, its acetyltransferase catalytic activity is regulated by both post-translational modifications and interacting partners. We have discovered a novel regulator of p300 autoacetylation, a phenomenon which is critical in physiological and pathological conditions ranging from neurological disorders to several cancers. p300 is evolutionarily conserved in vertebrates. Recently, we have discovered functional p300 in Zebrafish and found that the genetic disorder due to the lack of p300 KAT activity revealed even in fish, which opens the window for disease model and therapeutic means in the context of this master enzyme. The modulation of the p300 KAT activity thus has tremendous potential to be explored for therapeutic interventions. Our recent findings on these phenomenons will be presented.