

Poster presentation

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The self-sustained regulation of PKM ζ activity during the maintenance of L-LTP

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What could be the mechanism of enduring synaptic efficacies despite the fast turnover of proteins at synapses? The de-novo synthesis of plasticity related proteins may partially provide the answer. However, the newly synthesized proteins must be activated before they are functional which requires a persistent signal of second messenger. In contrast, to conventional kinases the PKM ζ is an autonomous and constitutively active kinase, which does not require a second messenger for its sustained activity. Previous experimental results have shown that inhibiting PKM ζ activity can effectively reverse the established L-LTP (3–5 hr in slices and 22 hrs in vivo) [1-3]. Here, we explore a question of what could be the mechanism to

regulate the PKM ζ activity during the maintenance of L-LTP. We propose a self-sustained regulation of PKM ζ activity through another autonomously active kinase PDK1. Here, our specific instantiation of an activity regulation loop is the PKM ζ -PDK1 molecular pair. The PDK1 regulates the PKM ζ activity and its stability through a phosphorylation cycle [4]. We show that the PKM ζ -PDK1 loop acts as a bistable switch. Our results imply that L-LTP induction should produce an increase in the total amount of PKM ζ at active synapses, and this increase in PKM ζ is maintained through activity regulation in the enduring

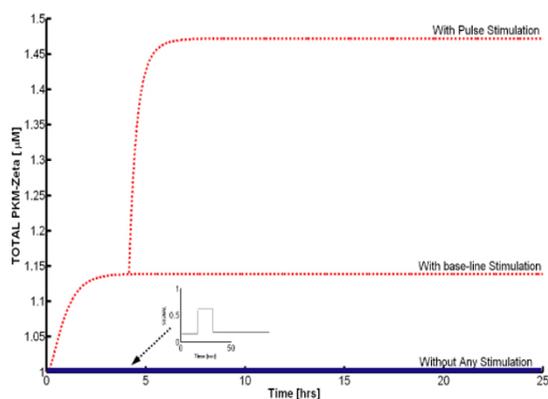


Figure 1
Bistability characteristics of the PKM ζ -PDK I molecular pair.

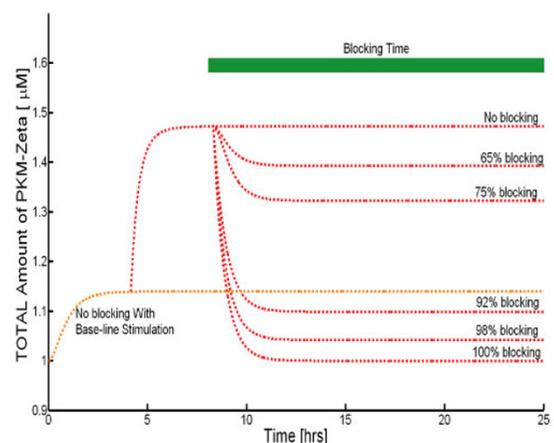


Figure 2
Blocking the PKM ζ activity during maintenance of L-LTP.

phase of L-LTP (Fig 1). Our results also show that blocking the PKM ζ activity in a dose dependent manner can effectively abolish the increase in total amount of PKM ζ , (Fig 2) which is in consistent with previous experimental findings [1,2].

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