IDENTIFYING THE IMPORTANCE OF PHOSPHORYLATION OF SNAP-25 AT SER187 IN PROTEIN KINASE C-MEDIATED ENHANCEMENT OF EXOCYTOSIS

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ABSTRACT

Protein Kinase C (PKC) activation has been shown to enhance exocytosis in various studies. However, the molecular mechanism for PKC to promote exocytosis is still elusive. A possible target of PKC is SNAP-25 (25 kDa synaptosome-associated protein), which is a key member of the SNARE (soluble *N*-ethylmaleimide-sensitive fusion protein attachment protein receptor) core complex that is essential for exocytosis. Both *in vitro* and *in vivo* experiments demonstrate that activation of PKC results in phosphorylation of SNAP-25 at Ser187. However, the importance of SNAP-25 phosphorylation at Ser187 in PKC-mediated enhancement of exocytosis has not been fully studied. Here, I investigated the importance of SNAP-25 phosphorylation at Ser187 upon activation of PKC by a phorbol ester to stimulate exocytosis in rat insulin-secreting

INS-1 cells. With the transfection of botulinium toxin E (BoNT/E) to disable the endogenous SNAP-25, my results show that SNAP-25 phosphorylation at Ser187 is important for phorbol ester-enhanced exocytosis. However, my results also indicate that SNAP-25 phosphorylation at Ser187 is not the only mechanism involved in phorbol ester-enhanced exocytosis at high $[Ca^{2+}]_i$. This work helps clarify the molecular mechanisms by which phorbol ester and PKC enhance exocytosis. It also contributes to our understanding of the role of SNAP-25 in exocytosis.