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Vitamin E induces palmitoylation of 67kDa laminin receptor by direct binding .

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Diacylglycerol kinase (DGK) is a lipid kinase to convert DG to phosphatidic acid. Recently, we have reported that α -tocopherol (α Toc) and epigallocatechin gallate (EGCG) activate DGK α via 67kDa laminin receptor (67LR), resulting in improvement of diabetic nephropathy. Interestingly, α Toc directly binds to 67LR at different site for EGCG, suggesting unknown binding site of α Toc in 67LR. Furthermore, 67LR is believed to be concentrated in lipid raft as homo dimer. However, palmitoylation of 67LR hasn't been reported, although many proteins localized in raft are palmitoylated. Therefore, we investigated α Toc binding site of 67LR and palmitoylation of 67LR with its physiological meaning in the activation of DGK α .

We identified the α Toc binding site in 67LR using hydrogen-deuterium exchange mass spectrometry, and found both EGCG and α Toc treatment induced palmitoylation with DGK α translocation (activation). A time course of α Toc-induced palmitoylation was similar with DGK α translocation. A point mutation at Cys of 67LR abolished both 67LR palmitoylation and DGK α activation. These results indicate that palmitoylation of 67LR is necessary for the activation of DGK α by α Toc or EGCG, suggested that, as well as DGK α , 67LR and its palmitoylating enzyme are pharmaceutical targets of diabetic nephropathy.