8. Introduction to

"Diacylglycerol Kinase-α phosphorylation by Src on Y_{335} is required for activation, membrane recruitment and HGF induced cell motility"

by

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In our laboratory it was previously demonstrated that HGF-, VEGF- and ALK-induced activation of Dgkα was mediated by Src kinase [19,18,20]. Moreover we showed that Dgkα is required for v-Src-induced MDCK cell scatter, beside the HGF-induced one, mainly contributing to Rac small GTPase activation. In the manuscript submitted to Oncogene, we analyze the molecular determinants of Dgkα which mediate its regulation by Src. We demonstrate that both HGF stimulation and Src transformation induce tyrosine phosphorylation of Dgkα on tyrosine 335, through a mechanism requiring the proline-rich C-terminal sequence of Dgkα. Both proline-rich sequence and phosphorylation of tyrosine 335 of Dgkα are shown to mediate its enzymatic activation, its ability to interact respectively with the SH3 and SH2 domains of Src and its recruitment to the plasma membrane. Finally, phosphorylation of Dgkα on tyrosine 335 is shown to be required for HGF-induced cell migration, while constitutive recruitment of Dgkα at the plasma membrane by myristoylation is sufficient to trigger spontaneous cell motility in absence of HGF.

Thus, we provide significant advances in the understanding of Dgkα regulation, highlighting the domains that in Dgkα are critical for the transduction of migratory signals triggered by tyrosine kinase receptors and oncogenic Src.