Molecular basis of VEGFR1 autoinhibition at the plasma membrane

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Spontaneous activation of VEGFRs is a hallmark of diabetes and several cancers. Here, the authors show how in VEGFR1 a juxtamembrane segment connecting the catalytic and ligand-binding domains of the receptor can prevent its spontaneous activation.

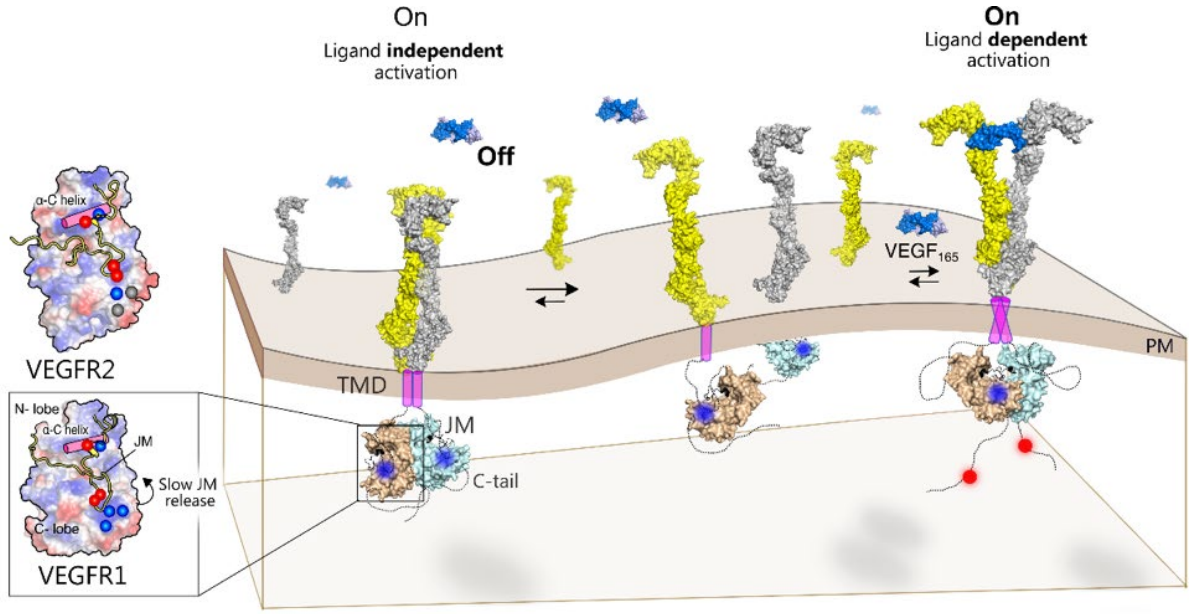

Figure: The ligand binding to the extracellular domain (ECD) induces receptor dimerization and rearrangement of the TM-JM segment. Slow release of JM inhibition in VEGFR1 leads to transient tyrosine phosphorylation at the C-terminal tail. Faster release of JM inhibition in VEGFR2 or VEGFR1 mutants remodels the tyrosine phosphorylation to be sustained. Left: Ligand-independent activation of VEGFR1 is suppressed due to a delicate balance between the slow release of JM inhibition and protein tyrosine phosphatase (PTP) activity.