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Effects of the RGD loop and C-terminus of rhodostomin on regulating integrin αIIbβ3 recognition.

Yao-Tsung Chang, Jia-Hau Shiu, Chun-Hao Huang, Yi-Chun Chen, Chiu-Yueh Chen, Yung-Sheng Chang, Woei-Jer Chuang*

Department of Biochemistry and Molecular Biology, National Cheng Kung University College of Medicine

wjcnmr@mail.ncku.edu.tw

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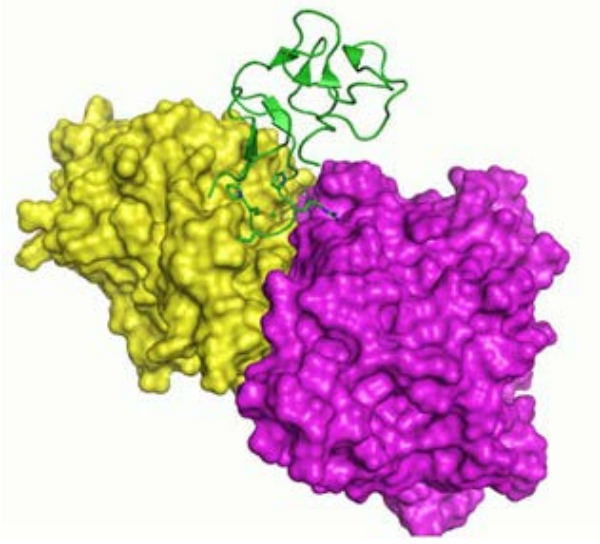
Integrins are αβ heterodimeric receptors that are expressed on virtual all cells with adhesive capacity. They are involved in many common diseases including neoplasia, tumor metastasis, immune dysfunction, ischemia-reperfusion injury, viral infections, osteoporosis, and coagulopathies. Disintegrins are a family of integrin inhibitors found in snake venoms that are potent integrin inhibitors. Our studies have shown that alternations in RGD loop and the C-terminal region of these disintegrins affect their binding specificities and affinities. Rhodostomin (Rho) is a snake venom protein isolated from *Calloselasma rhodostoma*. Rho is a disintegrin that inhibits platelet aggregation by blocking the binding of fibrinogen to the integrin $\alpha_{IIb}\beta_3$ of platelets. In our study, we have successfully expressed Rho in *P. pastoris* and showed that Rho possesses the same function and structure as native protein. We also used NMR spectroscopy to determine 3D structure of rhodostomin and designed a potent and selective anti-platelet agent.



3D structure of the disintegrin/integrin complex