ognition sites of disintegrin would be very useful for drug design directed against specific integrin-related diseases. These achievements can be reached by a research team encompassing protein structure, genetic engineering, recombinatory chemistry, pharmacology/toxicology, and clinical trials. Some disintegrins appear to be rather selective in recognizing specific integrins, and their selectivity can be further enhanced by producing recombinant mutants or synthetic derivatives with optimal substitutions. Studies of disintegrins have the potential to contribute both academically and clinically to therapeutic applications in the fields of thrombosis, cell adhesion, cell migration, angiogenesis, and other integrin-related diseases. A lot of work regarding the structure-function relationships of the venom metalloproteinase (especially the large hemorrhagins) remains to be done in order to understand how they interfere with hemostasis on a molecular basis. For example, how the disintegrin-like domain interacts with the integrins, $\alpha_2\beta_1$, $\alpha_{IIb}\beta_3$, and $\alpha v\beta_3$, or with vWF, collagen, laminin, and other ECMs. These studies will help us understand the molecular mechanism of ligand-receptor and cell-cell interactions in normal physiological processes. The possible functions of ADAMs are still awaiting exploration, especially cell-cell fusion, cell-matrix interaction, degradation of ECMs, and bidirectional signal transduction. The discovery of disintegrins and their related venom metalloproteinase (hemorrhagin) and ADAM molecules reminds us that once upon a time there was a smart snake that aroused Adam and Eve's curiosity about the acquisition of knowledge, an event whose consequences we are still living with. The snake has taught us a lot about integrins, and I believe there is still more mystery in cell biology hidden in snake venoms that remains to be explored.

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REFERENCES

1. Ouyang, C., Teng, C.M., Huang, T.F. Characterization of snake venom components acting on blood coagulation and platelet function. *Toxicon*. 1992; **30**:945-966.
2. Teng, C.M., Huang, T.F. Snake venom consituents that affect platelet function. *Platelets* 1991; **2**:77-87.
3. Fujimura, Y., Kawasaki, T., Titani, K. Snake venom proteins modulating the interaction between von Wilebrand factor and platelet glycoprotein Ib. *Thromb. Haemostas*. 1996; **76**:633-639.
4. Bjarmason, J.B., Fox, J.W. Hemorrhagic metalloproteinases from snake venoms. *Pharmacol. Ther.* 1994; **62**:325-372.
5. Wolfsberg, T.G., White, J.M. ADAMs in fertilization and development. *Dev. Biol.* 1996; **180**:389-401.
6. Hynes, R.O. Intergrins: a family of cell surface receptors. *Cell*. 1987; **48**:549-554.
7. Hynes, R.O. Integrins: versatility, modulation and signaling in cell adhesion. *Cell*. 1992; **69**:11-25.
8. Ginsberg, M.H., Loftus, J.C., Plow, E.F. Cytoadhesion, integrins and platelet adhesion. *Thromb. Haemost*. 1988; **59**:1-6.
9. Staatz, W.D., Rajpara, S.M., Wayner, E.A. et al. The membrane glycoprotein Ia/Iia (VLA-2) complex mediates the Mg^{2+}-dependent adhesion of platelets to collagen. *J. Cell. Biol.* 1989; **108**:1917-1924.
10. Kehrel, B., Wierwille, S., Clemetson, K.J., Anders, O., Steiner, M., Knight, C.G., *et al.* Glycoprokin VI is a major collagen receptor for platelet activation: It recognizes the platelet-activating quarternary structure of collagen, whereas CD36, glycoprotein IIb/IIIa, and von Willebrand factor do not. *Blood*. 1998; **91**:491-499.
11. Stein B., Fuster, V., Halperin, J.L., Chesebro, J.H. Antithrombotic therapy in cardiac disease: an emerging approach based on pathogenesis and risk. *Circulation*. 1989; **80**:1501-1513.
12. Coller, B.S. Platelets and thrombolytic therapy. *N. Engl. J. Med*. 1990; **322**:33-42.
13. George, J.N., Caen, J.P., Nurden, A.T. Glanzmann's thrombasthenia: the spectrum of clinical disease. *Blood*. 1990; **75**:1383-1395.
14. Nieuwenhuis, H.K., Akkerman, J.W.N., Houdijk, W.P.M., Sixma, J.J. Human blood platelets showing no response to collagen fail to express surface glycoprotein