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**Crystal Structure of Proline-rich Tyrosine Kinase 2.** Kam Y.J. Zhang, Abhinav Kumar, Yoshihisa Suzuki, Ben Powell, Brandi P. Grondona, Heike Krupka, James Tsai, Chao Zhang, Gideon Bollag, Plexxikon Inc., 91 Bolivar Dr., Berkeley, CA 94710.

Integrin-linked signaling is important for regulating cell adhesion and motility. Proline-rich tyrosine kinase 2 (PYK2) is one of the key mediators of integrin-dependent signals. PYK2 mediate cytoskeletal rearrangements as a consequence of integrin ligation. PYK2 is localized to the sites of cell-cell contacts, and becomes activated in response to calcium mobilization. PYK2 activation leads to apoptosis in fibroblasts. PYK2 plays a key role in tumor invasion and metastasis. In order to facilitate the structure-based design of potent and selective PYK2 inhibitors as anti-cancer drugs, we have determined the crystal structure of PYK2 both apo and complexed with AMPPNP at 1.45Å and 1.8Å resolution respectively. These structures have revealed a unique conformation of the activation loop. The binding of AMPPNP has provided insights to the design of small molecule inhibitors.