Structure of the integrin a2b1 binding collagen peptide., Jonas Emsley,[a*] Graham Knight[b] and Richard Farndale[b], [a]*Department of Biochemistry, University of Leicester, Leicester, UK, and* [b]*Department of Biochemistry, University of Cambridge, Cambridge, UK*. E-mail: je14@le.ac.uk

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We have determined the 1.8Å crystal structure of a triple helical integrin-binding collagen peptide (IBP) with sequence (Gly-Pro-Hyp)2-Gly-Phe-Hyp-Gly-Glu-Arg-(Gly-Pro-Hyp)3 [1]. The central GFOGER hexapeptide is recogised specifically by integrins α2β1, α1β1, α10β1, α11β1. These integrin/collagen interactions are implicated in a number of key physiological processes including cell adhesion, cell growth and differentiation and pathological states such as thrombosis and tumor metastasis. Comparison of the IBP structure with the previously determined structure of an identical collagen peptide in complex with the integrin α2-I domain (IBP^c) [2] allows the first detailed examination of collagen in a bound and an unbound state. The IBP structure shows a direct and a water mediated electrostatic interaction between Glu and Arg sidechains from adjacent strands but no intrastrand interactions. The interactions between IBP Glu and Arg sidechains are disrupted upon integrin binding. A comparison of IBP and IBP^c main chain conformation reveals the flexible nature of the triple helix backbone in the imino poor GFOGER region. The structure reveals this flexibility to be important to the integrin-collagen interaction and provides a possible explanation for the unique orientation of the three GFOGER strands observed in the integrin IBPc complex crystal structure.

[1] J. Emsley, G.C. Knight, R.W. Farndale, M.J. Barnes, (2004) Structure of the integrin α2β1 binding collagen peptide. *J. Mol. Biol* **335**, 1019-1028.
[2] J. Emsley, G.C. Knight, R.W. Farndale, M.J. Barnes, R.C., Liddington. (2000). Structural basis of collagen recognition by integrin α2β1. *Cell* **100**, 47-56.
[3] [Enter a reference here]