

P004 Probing the synergy site in the central cell-binding region of fibronectin by modulating the ⁹F3-¹⁰F3 interface.

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Activation of the $\alpha_5\beta_1$ integrin by fibronectin critically depends on the RGD loop in the 10th F3 module (¹⁰F3), and a synergy site on the 9th F3 module (⁹F3). We created an analogue of the ⁹F3-¹⁰F3 module pair with a disulphide bond spanning the domain interface of the ⁹F3-¹⁰F3.

The synergistic solid-phase binding to $\alpha_5\beta_1$ as well as $\alpha_5\beta_1$ -mediated cell attachment and spreading are switched off and on by formation and breaking of this disulphide bond. Conformation and dynamics of the unperturbed ⁹F3-¹⁰F3 as well as the disulphide bonded analogues in the oxidized and reduced states were studied by recent methods in solution state NMR.

Comparisons of the relative domain orientations as well as local and overall dynamics for the ⁹F3-¹⁰F3 and its analogues suggest that a change in inter-domain orientation is responsible for the differences in biological activity.