

CONFORMATION DEPENDENT INTERACTION BETWEEN FIBRONECTIN AND COLLAGEN I IN CELL MEDIATED REMODELING OF ECM

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INTRODUCTION: In order to design engineered scaffolds which mimic the structure and function of host tissues, it is necessary to characterize whether molecular conformation of inherent matrix components regulate design criteria necessary for promotion of tissue reconstruction. We investigate ECM protein conformation changes during cell mediated remodelling of ECM. The conformation of fibronectin (Fn), a prevalent component of the ECM of developing or healing tissues, is known to be highly variable. Although Fn binds and crosslinks numerous ECM components, the impact of its molecular conformation on association with other ECM components in native matrix is unknown.

METHODS: Confocal microscopy and intramolecular fluorescence resonance energy transfer (FRET) are used to study if Fn and collagen fibrils interact in a Fn conformation dependent manner and if Fn fibrillar matrix conformation is affected by presence of collagen. Collagen was imaged using immunohistochemistry with a 3rd color which did not affect FRET. The confocal images were then analyzed to determine whether collagen tended to colocalize with Fn fibrils.

RESULTS: The results showed that collagen I production and Fn-collagen co-localization in 3D matrices begins within one day in culture using fibroblasts. Co-localization was dependent on Fn conformation.

DISCUSSION & CONCLUSIONS: These results suggest that Fn conformation either regulates its association with collagen or is stabilized into a specific conformation thought association with collagen. This investigation is a first step towards understanding how cell force dependent conformation changes of Fn may regulate its integration and assembly into multicomponent ECM.

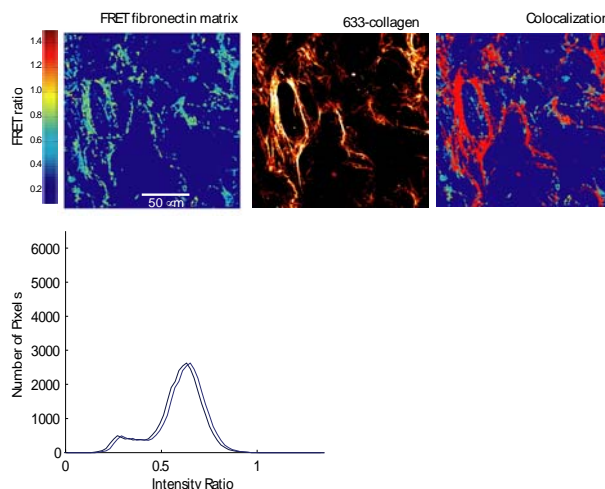


Fig. 1: Collagen I co-localization with Fn is dependent on Fn conformation.

REFERENCES: ¹M.L. Smith, D. Gourdon, W.C. Little, K.E. Kubow, R. A. Eguiluz, S. L. Morris, V. Vogel (2007) *PLoS Biology*, in revision. ²V. Vogel and M. Sheetz (2006) *Nat Rev Mol Cell Biol.* 7(4):265-75. ³Vogel V. (2006). *Annu Rev Biophys Biomol Struct.*35:459-88. ⁴G. Baneyx and V. Vogel (1999) *Proc Natl Acad Sci USA.* 96(22):12518-23.