

DIFFERENT ECM SUBSTRATES INDUCE CELL-TYPE SPECIFIC MORPHOLOGY AND/OR DIFFERENTIATION.

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INTRODUCTION: Cell adhesion and migration is dependent on specific interactions between substrates and cell surface expressed receptors that mediate the communication between outside and inside of the cell and induce appropriate reactions towards changing conditions (Humphries, 1990; Hynes 1992; Calderwood et al., 2000; Ivaska and Heino, 2000). Our study shows that providing different ECM-molecules as substrates for a single cell type leads to different morphology and probably also functionality. Providing a single ECM substrate to different cell types also induces different morphology. In this study we compared the effect of surface adsorbed ECM molecules such as matrigel and L1Ig6-modified fibrin on the morphology of human umbilical vein endothelial cells (HUVECs) and on neuronal stem cells (NSCs). Both cell types are known to interact with different ECM-substrates through their integrin receptors expressed on the surface.

METHODS: HUVECs were purchased from PromoCell, Heidelberg, Germany and maintained under low serum conditions (2%) in the absence of additional growth factors. NSCs were obtained.... Both cell types were cultured on the surface of TCPS adsorbed matrigel (Pharmingen) and on covalently L1Ig6-modified fibrin matrices (Hall et al., submitted) at 50000 cells/ml for 24h at 37°C and 5% CO₂. Effects of collagen I and plain fibrin are not shown here. Living cells were fluorescently labelled with fluorescein diacetate (FDA) as described by Hall et al. (submitted) and the morphology of cells was analysed by fluorescence microscopy.

RESULTS AND DISCUSSION: Cell-matrix interactions are responsible for cell-type specific morphology and/or differentiation. Both cell types survive on matrigel and on L1Ig6-modified fibrin as demonstrated by staining of living cells by FDA. However, the morphology of HUVECs and NSC cultured on matrigel and on L1Ig6-modified fibrin was very different. HUVECs on matrigel form tube-like extensions that are interconnected. They have been described as first indications towards the angiogenic differentiation (Pepper et al., 1996). NSCs cultured on matrigel extend neurites. Interactions between NSCs and matrigel

are mediated by integrins and laminin-1, the major component of matrigel. When grown on L1Ig6-modified fibrin, an artificial matrix designed to interact specifically with $\alpha v \beta 3$ -integrins on angiogenic HUVECs, HUVECs show a similar morphology as observed on matrigel. HUVECs extend processes that can be interconnected with each other. The same substrate is not very adhesive for NSCs, since they do not express $\alpha v \beta 3$ -integrins and therefore can not interact with L1Ig6-modified fibrin. The cells stay round and do not attach and spread on the surface.

Our experiments indicate that communication between a cell-type and ECM-molecules is very specific and is mediated by receptors on the cell surface. These include integrins, cell adhesion molecules, cadherins and selectins that are expressed in a cell-type specific manner and, most important, can be addressed specifically to induce a certain reaction of the cell, such as inducing the angiogenic phenotype of HUVECs by triggering $\alpha v \beta 3$ -integrin.

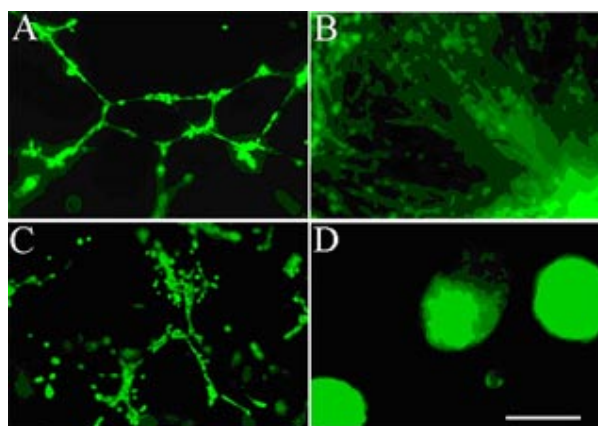


Fig 1: HUVECs were cultured for 24h on matrigel (A) and on L1Ig6-modified fibrin (C), and NSC on matrigel (B) and L1Ig6-modified fibrin (D), respectively. The scale bar represents 200 μ m.

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