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Title: Extracellular matrix influences the inflammatory response of primary bronchial epithelial cells

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Body: Rationale: Airway remodelling is a feature in many chronic airway diseases. This is manifested as alterations in the extracellular matrix composition. Our aim was to investigate how different extracellular matrix molecules influenced the production of inflammatory cytokines in epithelial cells. Methods: Primary human bronchial epithelial cells were grown on plates coated with the extracellular matrix proteins collagen-1, collagen-4 and fibronectin. The cells were challenged with a cytomix consisting of TNF-alpha and IL-1-beta (both 10ng / ml) and the cytokine production was examined with proteome profiler antibody arrays (R&D) that detect the production of 40 cytokines simultaneously. Results: Basal and induced production of IL-1-aplha was similar in cells grown on collagen-1 and fibronectin but IL-1-alpha could not be detected in cells grown on collagen-4. Low levels of G-SCF were detected in cells on collagen-1 or fibronectin stimulated with cytomix, but when cell were grown on collagen-4 the levels were dramatically higher. There were no difference in basal and induced production of GRO-alpha and Il-8 on cells grown on collagen-1, collagen-4 or fibronectin. The basal level of Il-6 was dramatically reduced on collagen-4 compared to collagen-1 and fibronectin. However, the cytomix triggered similar levels of IL-6 production regardless of matrix substrate. Conclusions: In this study we show that the extracellular matrix actively contributes to modify cell phenotypes. Cells grown on collagen-4 that represents a “homeostatic matrix” produced a different repertoire of inflammatory mediators than cells grown on “remodeled matrix proteins” collagen-1 and fibronectin.