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Fibroblasts and Myofibroblasts in Peritoneal Pathophysiology

Fibroblasts are the major cell type that synthesise extracellular matrix to provide structure and support to organs and tissues of the body. Following tissue damage, they play a pivotal role in repairing the wound site albeit often with scar formation. Indeed, many pathological conditions result from inappropriate activation of fibroblast populations leading to increased or dysregulated extracellular matrix deposition frequently in association with tissue contraction and loss of function. For instance, injury to the peritoneum often causes thickening of the serosa and formation of adhesions, fibrous bands of tissue that join together normally separated organs. These structures develop as part of the repair response where fibrin-rich strands deposited between damaged closely opposed denuded serosal surfaces become remodelled into permanent fibrous bands. Whilst peritoneal fibroblasts are recognised to be intricately involved in this process, their exact origin, role and fate during adhesion formation are still unclear.

Using a surgery-induced murine adhesion model, we have shown that fibroblast-like cells are present within the developing fibrin-rich adhesion from day 3 post-injury.¹ The source of these fibroblasts is not clear but may involve proliferation and inward migration of a resident population, transdifferentiation of mesothelial cells, dedifferentiation of adipocytes or possibly a circulating progenitor. Within this provisional wound environment, these cells proliferate and deposit extracellular matrix to stabilise the immature adhesion and reinforce its persistence. Indeed, we have shown both *in vitro* and *in vivo* that fibroblasts grown within a fibrin-rich matrix under reduced fibrinolytic conditions are induced to produce collagen.^{2, 3} Two weeks post-injury, alpha-smooth muscle actin-positive cells or myofibroblasts are observed and contraction of the adhesion noted.⁴ Fibroblasts undergo differentiation to myofibroblasts and in some cases to a smooth muscle-like phenotype when subjected to tension. Such forces may be generated within developing adhesions tethered between mobile organs, which may explain the appearance of myofibroblasts. The fate of these cells within established adhesions is not known although a detailed study of human peritoneal adhesions demonstrated that all were vascularised and innervated and that the majority displayed proliferating and collagen-producing cells.^{1,5,6} These findings clearly demonstrate that established adhesions are dynamic regenerating structures rather than static redundant scar tissue. Further understanding of the cellular and molecular mechanisms regulating peritoneal fibroblast behaviour may lead to novel therapies that target adhesion formation and so prevent serious complications such as bowel obstruction and female infertility.

References

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