Journal watch

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Song L, Papaioannou G, Zhao H, Luderer HF, Miller C, Dall'Osso C, Nazarian R, Wagers A & Demay MB. The Vitamin D Receptor Regulates Tissue Resident Macrophage Response to Injury. Endocrinology 2016; en20161474. doi: http://dx.doi.org/10.1210/en.2016-1474

This paper extended prior work by the authors that had determined that increases in macrophage quantity and the formation of granulation tissue following injury required activation of the ligand-dependent activation of the vitamin D receptor. The vitamin D receptor is a nuclear, ligand-dependent transcription factor with a role in regulating the expression of genes (>900) that are associated with varied physiological functions, including response to injury via macrophage function. This study aimed to characterise the activation of macrophages in mice without vitamin D receptors and test interventions to address the impaired macrophage response. Mice with the vitamin D receptor knocked out (VDR-KO) were reared receiving a dietary supplementation to ensure mineral ion haemostasis but were otherwise vitamin D deficient. Punch biopsies were used to give mice full-thickness dorsal wounds. Wound healing was assessed in VDR-KO and compared with mice with normal vitamin D receptor function. The study found significantly higher levels of markers of alternatively activated M2 macrophages arginase-1 and resistin-like molecule alpha in VDR-KO mice. However, the percentage of alternatively activated (M2) macrophages did not significantly differ. Seven days post healing, wounds of VDR-KO mice were characterised by a reduced level of connective tissue compared to the control, suggesting a pathway between the function of the vitamin D receptor, macrophage function, and the maturation of granulation tissue. Through attempts to augment the impaired macrophage function in VDR-KO mice using exogenous cytokines and conjoining control and VDR-KO mice circulations failed to normalise the macrophage response; it did, however, suggest that the initial sources of wound macrophages (within 48 hours) were recruited locally and not from circulation. The paper flags an important role for the vitamin D receptor in wound healing.

Ascione F, Vasaturo A, Caserta S, D'Esposito V, Formisano P & Guido S. Comparison between fibroblast wound healing and cell random migration assays in vitro. Experimental Cell Research 2016; 27, 27. doi: http://dx.doi.org/10.1016/j.yexcr.2016.07.015

This article presents a comparison of two methods to investigate cell migration *in vitro*. The two methods include the (1) wound healing or scratch assay and the (2) cell random motility assay. While the authors describe the mechanisms and uses of both assays, particular focus is given to how the assays enable investigation of single cell level migration. The authors describe the wound healing/scratch assay as traditionally useful for investigating healing effects where cells form close contact and progress in a collective manner with limited information available from this method to understand the movement of cells (that is to say, fibroblasts) that typically migrate as individual cells. In contrast, though a more complex and costly approach, the cell random motility assay enables observation of individual cell motion. In lieu of published quantitative comparisons of these methods, this study contrasted the approaches, additionally applying a tracking method to the wound healing assay to determine the comparability of the information yielded regarding cell migration. Biopsies were obtained from control mice and mice genetically modified to over express the protein PED/PEA-15 (also seen in patients with type 2 diabetes mellitus) for which the migration pattern of fibroblasts has been observed in prior research to vary. The study confirmed that slower wound healing occurred in assays with the over expressed PED/PED-15 protein compared to control. Of note, while cell proliferation (cells migrating in a collective manner) was comparable for the control and PED/PED-15 protein samples, healing as influenced by cell motility was varied. Cell motility estimates were lower in the PED/PED-15 protein sample compared to the control for both approaches to investigating cell migration *in vitro*. The differences in the motility were less pronounced in the wound healing/scratch assay. The authors concluded "substantial agreement" between the two methods of quantifying cell migration, despite the differences in the two techniques.