What were the key objectives of this study?
The events in wound healing are carefully orchestrated. The concept that we investigated was that a transcription factor would coordinate the regulation of events that are needed in order for wound healing to occur properly. Based on our previous work, we focused on the transcription factor FOXO1. Transcription factors are important in wound healing because they control the expression of other genes, which are needed for healing to occur.

What were some of the important techniques used in the study?
The most important aspect of the study from a technical standpoint was the deletion of FOXO1 in a single type of cell in vivo. These studies used a genetically modified mouse in which the FOXO1 transcription factor was deleted only in keratinocytes, an epithelial cell type that lines mucosal and skin surfaces. All of the other cell types were normal, allowing us to focus on the impact of deleting FOXO1 only in keratinocytes.

What results were most surprising or of particular clinical relevance?
When FOXO1 was deleted in keratinocytes normal wound healing was significantly delayed. We found that this was largely due to FOXO1 regulation of two very important aspects of wound healing. The first was that FOXO1 was needed for keratinocytes to migrate. The second was that FOXO1 protected the cells during wound healing from oxidative stress. When FOXO1 was deleted, keratinocytes did not migrate as well and suffered damage from oxidative stress.

What conclusions or other applications could the findings lead to?
The simple answer would be that increasing FOXO1 should help wound healing based on our result that FOXO1 is needed for normal healing to occur. However, it is more complicated than this since high levels of FOXO1 are just as detrimental as not having enough FOXO1.

FOXO1 PROMOTES WOUND HEALING THROUGH THE UP-REGULATION OF TGF-β1 AND PREVENTION OF OXIDATIVE STRESS
Journal of Cell Biology (10.8 Impact Factor)
Ponugoti, B., Xu, F., Zhang, C., Tian, C., Pacios, S., Graves, D.T.

What were the key objectives of this study?
Osteonecrosis of the jaw (ONJ) is a condition involving the necrosis of the jaw bone that is associated with certain anti-resorptive drugs to treat cancer or prevent bone loss in osteoporosis. The objective of this study is to explore the potential role of interleukin 17 (IL-17)-mediated regulation of macrophage function, specifically the subtype M1/M2 macrophage, in the pathogenesis of bisphosphonate-related osteonecrosis of the jaw (BRONJ).

What were some of the important techniques used in the study?
The study concludes that IL-17-mediated M1/M2 macrophage alteration induced by zoledronate may be beneficial for cancer therapy, but might have contributed to an increased susceptibility to BRONJ development.

What conclusions or other applications could the findings lead to?
The study concludes that increased Th17 cells and IL-17 cytokine levels correlate with an increase in M1/M2 macrophages ratio at the non-healing extraction sockets of both BRONJ patients and murine models; adoptive transfer of ex vivo expanded M2 macrophages could reverse systemic increase of IL-17 and ONJ severity, and blocking IL-17 activity significantly decreased M1/M2 ratio and concomitantly suppressed BRONJ condition in mice. These findings have provided compelling evidence that IL-17-mediated M1/M2 macrophage alteration plays a critical role in the pathophysiology of BRONJ, a promising breakthrough for identifying novel biomarkers and therapeutic targets for this debilitating and painful disease.
What were the key objectives of this study?
Diabetes mellitus (DM) involves metabolic changes that can impair bone repair, including a prolonged inflammatory response. A salicylic acid-based poly(anhydride-ester) (SA-PAE) provides controlled and sustained release of salicylic acid (SA) that locally resolves inflammation. This study investigates the effect of polymer-controlled SA release on bone regeneration in diabetic rats where enhanced inflammation is expected.

What were some of the important techniques used in the study?
This study is the first time that an SA-PAE has been applied to diabetic animals for bone regeneration purposes. The difficult part in this project was the surgical procedure and postoperative management. Because of the diabetic animals, the grafting procedure needed to be minimally invasive and postoperative monitoring has a significant impact on wound healing process.

What results were most surprising or of particular clinical relevance?
We found that treatment with SA-PAE enhances bone regeneration in diabetic rats. Plus, it can accelerate bone regeneration in normoglycemic (non-diabetic) animals. It could be possible for this polymer to combine with a bone graft in order to achieve more predictable bone formation for oral and maxillofacial reconstruction purposes.

What conclusions or other applications could the findings lead to?
The advantages of localized, controlled, and sustained SA release, our polymer system enables the incorporation of other bioactives (such as insulin) to further improve bone regeneration.