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Developing a systemic monoclonal antibody therapy for the treatment of large burn injuries

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Studies have shown that Flightless (Flii) is elevated in human wounds including burns and reducing the level of Flii is a promising approach for improving wound repair and reducing scar formation. The most effective approach has been to neutralise Flii activity using localized, intradermal application of function blocking monoclonal antibodies. However, large surface area burns are difficult to treat by intradermal injection of therapeutics so the aim of this study was to investigate if systemic injection of a monoclonal antibody against Flii could improve healing in mice following burn injury.

Flii neutralizing antibodies (FnAbs) were labelled with Alxa-Fluor-680 for biodistribution studies and healing effects of systemically administered FnAbs to mice with burn injuries. A partial thickness, 7% (70mm^2) total body surface area scald burn injury was created on the dorsal surface of mice (n=10/group) and 100µL of Alexa-Flour-680-labeled FnAbs were injected into the intraperitoneal cavity (IP) at time of injury. The burns were imaged on days 0, 1, 2, 3, 4 and 7 using IVIS Lumina S5 Imaging System and healing assessed macroscopically, histologically and using immunohistochemistry.

Fluorescent radiance efficiency measurements showed that IP injected Alexa-Fluor-680-FnAbs localized at the site of burn injury from day 1 remaining there for whole 7-day study. The burns treated with FnAbs showed a reduction in macroscopic wound area and increased rate of epithelialization compared to controls. Immunohistochemistry for NIMP-R14 showed a reduction in inflammatory infiltrate while CD31/VEGF staining showed improved angiogenesis post- systemic FnAb treatment. These results suggest that systemically administered FnAbs are active within the burn site and can improve healing outcomes. The clinical application of systemically injected Flii monoclonal antibodies could therefore be a potential approach for promoting healing of large surface area burns immediately after injury.

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