

Systemically administered wound-homing peptide accelerates wound healing

Tero A.H. Järvinen^{1,2} and Erkki Ruoslahti²

¹Medical School, University of Tampere, Finland

²University of California, USA

We have previously described two wound-homing peptides (Järvinen and Ruoslahti, *Am. J. Pathol.* 2007) have used one of them (CARSKNKDC; dubbed CAR) to a wound-targeted anti-scarring agent, CAR-decorin (Järvinen and Ruoslahti, *PNAS* 2010). The CAR peptide without decorin had no effect in these experiments. We have now discovered that CAR, when given in doses 100 times higher than the amount of CAR delivered in the CAR-decorin experiments has an inherent wound healing-promoting activity. CAR penetrates into cells and tissues and is capable of inducing the transport of non-conjugated compounds from the blood into extravascular wound tissue in a manner similar to the recently identified CendR peptides (Sugahara et al., *Science* 2010). Cell migration is a rate-limiting step in wound closure. It has been shown that naturally occurring plasma->serum->plasma transition controls wound closure, and that the serum generated by blood clotting drives the cell migration effecting wound closure. A wound is exposed to serum only for a short period of time, which could be limiting the regenerative potential. We hypothesized that CAR might be capable improving the availability to a wound of factors that promote healing. We gave mice with skin wounds twice a day intravenous injections of 60 µg of CAR peptide over 10 days. Three independent treatment experiments (n=24/group) in a mouse skin wound model have been conducted and show that wounds close ($P > 0.001$ for days 5 - 10) (Fig. 1) and re-epithelialize ($P > 0.001$ at day 5, 7 and 10) significantly faster in CAR-treated mice than in control groups. The mice remained healthy, and no obvious side effects were seen. A possible mechanism is that CAR helps deliver additional regenerative factors into the wounds. The CAR peptide may provide an entirely new way of enhancing wound healing, and perhaps tissue regeneration in general, that is systemic, yet target-specific, and non-toxic.

Key Words: Homing peptide, systemic therapy, re-epithelialization, anti-scarring, cell penetrating peptide.

Tero.AH.Jarvinen@uta.fi