PSORIASIS

# IL-17C IS RESPONSIBLE FOR KERATINOCYTE HYPERPROLIFERATION AND SUSTAINED INFLAMMATION ASSOCIATED WITH PSORIASIS

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Background: IL-17C has been proven to be an essential autocrine cytokine that mediates innate epithelial immune responses We have observed localized clearing of psoriatic plaques extending several centimeters beyond injection sites of an anti-IL-17RA monoclonal antibody. We hypothesize that IL-17C produced by keratinocytes acts on itself and triggers an inflammatory response in neighboring keratinocytes. Localized blockade of IL-17RA on keratinocytes aborts the activity of keratinocyte derived IL-17C, thus, reducing skin inflammation, as it has been observed in murine models.

Observation: A male, age 27, body mass index of 44.6, with a 12-year history of plaque psoriasis was treated with brodalumab, a human monoclonal IgG2 antibody that selectively binds to human IL-17RA and inhibits its interaction with cytokines IL-17A, IL-17F, IL-17C, IL-17A/F heterodimer and IL-25 (also known as IL-17F). Though generalized response was not evident, localized clearing of psoriasis around the injection sites was. Rotating injection sites yielded consistent clearance about the site of injections. Clearance was sustained in previously treated areas.

Key message: The observed clearing cannot be the result of diffusion as several months are required to accomplish the response observed with 14 days of injection. However, proteins are transported to the circulatory system following absorption and transit via the lymphatic system. Localized clearance of plaques psoriasis around an injection site suggests IL-17C acts in a paracrine fashion. Should our hypothesis be correct, localized clearing of plaque psoriasis will not occur or occur only within a very confined diameter with IL-17A antagonism and may require 1L-17RA in order to achieve a sufficient degree of blockade. Additionally, IL-17C blockade alone or in conjunction with IL-17A blockade may provide a novel and effective target for the treatment of plaque psoriasis. Finally, observed localized clearing of psoriasis with IL-17RA blockade may present a novel therapeutic application for the treatment of localized disease.