

# Small Molecule Inhibitors of Alpha-4-Integrin-Paxillin Interaction

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## BACKGROUND

Inhibition of alpha-4 integrins is effective in alleviating a wide variety of chronic inflammatory diseases (e.g. rheumatoid arthritis, diabetes mellitus type I, multiple sclerosis) by inhibition of the recruitment of leukocytes to sites of inflammation. While blocking the adhesive functions of alpha-4 integrins has been shown to be an effective therapeutic approach in the treatment of autoimmune mediated diseases, it also carries the risk of defects in development, hematopoiesis, and immune surveillance. Interfering with alpha-4 integrin signaling by inhibiting the 4–paxillin interaction decreases 4-mediated cell migration and adhesion to VCAM-1 and MadCAM under shear flow. These *in vitro* effects are accompanied by a selective impairment of leukocyte migration into inflammatory sites when the alpha-4 integrin–paxillin interaction is blocked *in vivo*.

## TECHNOLOGY DESCRIPTION

UC San Diego researchers have identified a non-cytotoxic inhibitor of 4-integrin signaling that selectively impairs integrin alpha 4-mediation but not alpha-L-beta-2-mediation of Jurkat T-cell migration. This inhibitor of high specificity offers a novel strategy for interfering with the functions of these receptors in pathological events (e.g. treatment of immune-mediated diseases) while sparing important physiological functions.

## STATE OF DEVELOPMENT

The specificity of the compound was verified by its lack of effect on the residual α4-mediated cell functions in cells bearing the α4(Y991A) mutation. As a direct test of the utility of this compound, the inventors administered it to mice and found that it impaired the recruitment of leukocytes to a site of inflammation *in vivo*, whereas an isomer that does not inhibit the α4-paxillin interaction had no effect on α4-mediated cell migration, cell spreading, or recruitment of leukocytes to an inflammatory site ([Kummer et al. 2010](#)).

## INTELLECTUAL PROPERTY INFO

Patent pending. Patent application is available for review under confidentiality.

## RELATED MATERIALS

Kummer C, Petrich BG, Rose DM, Ginsberg MH. A Small Molecule that Inhibits the Interaction of Paxillin and Apha 4 Integrin Inhibits Accumulation of Mononuclear Leukocytes at a Site of Inflammation. [J Biol Chem. 2010 Mar 26;285\(13\):9462-9.](#)

## PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	8,987,294	03/24/2015	2007-009

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## OTHER INFORMATION

### CATEGORIZED AS

- **Medical**
- **Disease: Autoimmune and Inflammation**

### RELATED CASES

2007-009-0

