Available online at www.sciencedirect.com

SCIENCE DIRECT®

Cellular Signalling 17 (2005) 167–175

CELLULAR SIGNALLING

www.elsevier.com/locate/cellsig

CD38 cleavage in fMLP- and IL-8-induced chemotaxis is dependent on p38 MAP kinase but independent of p44/42 MAP kinase

Tsuyoshi Fujita[a,b], Khalid H. Zawawi[a], Hidemi Kurihara[b], Thomas E. Van Dyke[a,*]

[a]*Department of Periodontology and Oral Biology, Goldman School of Dental Medicine, Boston University, 100 East Newton Street, G-107, Boston, MA 02118, USA*

[b]*Division of Frontier Medical Science, Department of Periodontal Medicine, Graduate School of Biomedical Science, Hiroshima University, 1-2-3, Kasumi, Minami-ku, Hiroshima 734-8553, Japan*

Received 2 April 2004; received in revised form 22 June 2004; accepted 30 June 2004
Available online 20 August 2004

Abstract

In this study, we examined the mechanism by which CD38 cleavage is regulated through the mitogen-activated protein (MAP) kinases after stimulation by fMLP and interleukin-8 (IL-8) in neutrophils. Both fMLP and IL-8 increased chemotaxis and decreased CD38 protein in neutrophils, but did not change CD38 mRNA levels. Both fMLP and IL-8 increased CD38 in supernatants, which was inhibitable with PMSF. fMLP stimulation resulted in phosphorylation of p38 MAP kinase and p42/44 MAP kinase (ERK). SB20358, a p38 MAP kinase inhibitor, down-regulated neutrophil chemotaxis. Conversely, PD98059, an ERK inhibitor, did not influence chemotaxis to either agonist. The addition of SB20358 blocked the decrease of CD38 on neutrophils and the increase in supernatants induced by fMLP or IL-8, whereas PD98059 did not. These findings suggest that CD38-mediated chemotaxis to fMLP or IL-8 is characterized by proteolytic cleavage of CD38 and signaling through p38 MAP kinase. Activation of the protease for cleavage appears to be a postreceptor event that is dependent on p38 MAP kinase signaling.

Keywords: CD38; Chemotaxis; Neutrophil; p38 MAP kinase; ERK; fMLP; IL-8