



PAR-2 activation induces inflammation of mouse colon

Nicolas Cenac, Bruno Guiard, Rafael Garcia Villar, Jean Fioramonti, Lionel Bueno

► To cite this version:

Nicolas Cenac, Bruno Guiard, Rafael Garcia Villar, Jean Fioramonti, Lionel Bueno. PAR-2 activation induces inflammation of mouse colon. 5th World Congress on Inflammation, Sep 2001, Edinburgh, Ecosse, United Kingdom. Inflammation Research, 2001, Inflammation Research. hal-01600849

HAL Id: hal-01600849

<https://hal.science/hal-01600849>

Submitted on 4 Jun 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - ShareAlike 4.0 International License

5th World Congress on Inflammation

22 – 26 September 2001

**Edinburgh International Conference Centre
Scotland**

The Abstracts



Congress Steering Committee:

Rod Flower (Congress President), David Howat, Ian Chapman, David Bradshaw,
Graham Wallace, Cathy Phipps, Kevin Bottomley, Nigel Boughton-Smith, Sue Brain,
Kenny Pollock, Ian Adcock, Cliff Whelan

Abstract Sheet

Inflammation 2001

Please fill in and return to the Inflammation 2001 Secretariat by post (on 3.5"diskette) or by e-mail.
Address: Inflammation 2001, Triangle House, Broomhill Road, London, SW18 4HX.
E-mail: Edinburgh@inflammation-IAIS.org

Type only
inside
ruled area
as follows:

Title

Authors

Address

Text

PAR-2 Activation Induces Inflammation of Mouse Colon
N. Cenac, B. Guiard, R. Garcia-Villar, J. Fioramonti, L. Bueno
INRA, Neuro-Gastroenterology & Nutrition Unit, TOULOUSE, France
Proteinase-activated receptors-2 (PAR-2) are expressed throughout the gut. The peptide SLIGRL, the sequence of the tethered ligand, mimics the agonist protease. We investigate whether in vivo activation of colonic PAR-2 lead to colon inflammation in mice. *Methods.* Five groups of 8 male Swiss mice (26-31 g) were infused intracolonicly with 50 µl of the following : SLIGRL (3 groups: 10, 40, 100 µg/mouse respectively); reverse inactive peptide LSLGRL (1 group: 100 µg/mouse); NaCl 0.9% (1 group). Colon was collected 4 h after injections for histology (microscopic damage score; DMS), myeloperoxidase (MPO) assay and cytokine IL1β, IL10, IL4 and TNFα mRNA quantification by competitive RT-PCR. *Results.* All three groups treated with SLIGRL presented a significant increase of DMS (p<0.01) indicating inflammation of the colonic mucosa. MPO activity was dose-dependently increased in groups given SLIGRL (p<0,01). In mice treated with SLIGRL compared with controls, a significant increase (p<0.01) in mRNAs for IL10, IL1β and TNFα was measured, whereas mRNA for IL4 did not change. *Conclusion.* Activation of colonic PAR-2 by a selective activating-peptide induced dose-dependent inflammation of the colon in mice. Our study supports the hypothesis of an immune regulatory role for peripheral PAR-2, especially in the digestive tract.

Please tick this box if you wish to enter the IAIS young investigators Award



Title to be considered for:

oral communication



poster



either



Preferred workshop(s)

Proteinase Activated Receptors (PARs)

keywords (Please provide 3)

PAR-2, Inflammation, Colon

Name

Nicolas CENAC

Address/postcode

INRA
Neuro-Gastroenterology & Nutrition Unit
180 chemin de Tournefeuille, BP.3
F-31931 TOULOUSE cedex 9
France

Fax number

+33 561 28 5145

Tel number

+33 561 28 5151

e-mail

ncenac@toulouse.inra.fr

Inflammation Research

The International Association
of Inflammation Societies

The European Histamine
Research Society

Birkhäuser

07/07

PAR-2 ACTIVATION INDUCES INFLAMMATION OF MOUSE COLON

N. Cenac, B. Guiard, R. Garcia-Villar, J. Fioramonti, L. Bueno
INRA, Neuro-Gastroenterology & Nutrition Unit, TOULOUSE, France
Proteinase-activated receptors-2 (PAR-2) are expressed throughout the gut. The peptide SLIGRL, the sequence of the tethered ligand, mimics the agonist protease. We investigate whether in vivo activation of colonic PAR-2 lead to colon inflammation in mice. **Methods.** Five groups of 8 male Swiss mice (26-31 g) were infused intracolonicly with 50 µl of the following : SLIGRL (3 groups: 10, 40, 100 µg/mouse respectively); reverse inactive peptide LSLGRL (1 group: 100 µg/mouse); NaCl 0.9% (1 group). Colon was collected 4 h after injections for histology (microscopic damage score; DMS), myeloperoxidase (MPO) assay and cytokine IL1β, IL10, IL4 and TNFα mRNA quantification by competitive RT-PCR. **Results.** All three groups treated with SLIGRL presented a significant increase of DMS ($p<0.01$) indicating inflammation of the colonic mucosa. MPO activity was dose-dependently increased in groups given SLIGRL ($p<0.01$). In mice treated with SLIGRL compared with controls, a significant increase ($p<0.01$) in mRNAs for IL10, IL1β and TNFα was measured, whereas mRNA for IL4 did not change. **Conclusion.** Activation of colonic PAR-2 by a selective activating-peptide induced dose-dependent inflammation of the colon in mice. Our study supports the hypothesis of an immune regulatory role for peripheral PAR-2, especially in the digestive tract.

07/08

COX-2 DERIVED PROSTAGLANDIN D₂ CONTRIBUTES TO PROLONGED COLONIC EPITHELIAL DYSFUNCTION AFTER A BOUT OF COLITIS

Warrier N., Wallace J.L.

Mucosal Inflammation Research Group, University of Calgary, AB, Canada

Intestinal epithelial secretion is an important component of mucosal defence. A prolonged colonic secretory dysfunction has been reported following a bout of colitis, contributing to a marked increase in bacterial translocation. As we have observed a significant elevation of COX-2-derived PGD₂ synthesis for many weeks after resolution of colitis in the rat, we tested the hypothesis that this may contribute to the prolonged secretory dysfunction. **Methods:** Rats were given trinitrobenzenesulfonic acid intracolonicly to induce colitis. Six weeks later, when the inflammation had resolved, segments of distal colon were mounted in Ussing chambers for measurement of epithelial secretion in response to electrical field stimulation (EFS) or isobutylmethylxanthine (IBMX). **Results:** Secretion in response to both stimuli were significantly depressed in the post-colitis rats (by 74% and 69%, respectively). Pre-exposure of the tissue to celecoxib (10 µM), a COX-2 inhibitor, reversed this hypo-responsiveness. The colitis-associated epithelial hypo-responsiveness was mimicked by treatment of controls with PGD₂. Mucosal PGD₂ synthesis in the post-colitis rats was derived primarily from COX-2 (inhibited by celecoxib). These data suggest that a prolonged increase in COX-2 expression after a bout of colitis may contribute to the secretory dysfunction.