

LETTERS TO THE EDITOR

## Pleiotropic effects of bombesin and neurotensin on intestinal mucosa: Not just trefoil peptides

Stelios F Assimakopoulos, Chrisoula D Scopa, Vassiliki N Nikolopoulou, Constantine E Vagianos

Stelios F Assimakopoulos, Department of Internal Medicine, School of Medicine, University of Patras, Patras 26110, Greece  
Chrisoula D Scopa, Department of Pathology, School of Medicine, University of Patras, Patras 26110, Greece  
Vassiliki N Nikolopoulou, Division of Gastroenterology, Department of Internal Medicine, School of Medicine, University of Patras, Patras 26110, Greece  
Constantine E Vagianos, First Surgical Department, "Saint Panteleimon" General Hospital of Nikaia, Piraeus 18454, Greece

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**Correspondence to:** Stelios F Assimakopoulos, MD, PhD, Department of Internal Medicine, School of Medicine, University of Patras, Vironos 18, Patras 26224, Greece. [sassim@upatras.gr](mailto:sassim@upatras.gr)

Telephone: +30-2610-346946 Fax: +30-2610-990775

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### Abstract

Bombesin and neurotensin are neuropeptides which exert a wide spectrum of biological actions on gastrointestinal tissues influencing intestinal growth and adaptation, intestinal motility, blood flow, secretion, nutrient absorption and immune response. Based mainly on their well-established potent enterotrophic effect, numerous experimental studies investigated their potential positive effect on the atrophic or injured intestinal mucosa. These peptides proved to be effective mucosa-healing factors, but the potential molecular and cellular mechanisms for this action remained unresolved. In a recently published study (*World J Gastroenterol* 2008; 14(8): 1222-1230), it was shown that their protective effect on the intestine in experimentally induced inflammatory bowel disease was related to anti-inflammatory, antioxidant and antiapoptotic actions. These results are in close agreement with our previous studies on jaundiced and hepatectomized rats that showed a regulatory effect of bombesin and neurotensin on critical cellular processes such as enterocyte proliferation and death, oxidative stress and redox equilibrium, tight junctions' formation and function, and inflammatory response. The pleiotropic effects of bombesin and neurotensin on diverse types of intestinal injury may justify their consideration for clinical trials.

### TO THE EDITOR

We read with great interest the recently published article (*World J Gastroenterol* 2008; 14(8): 1222-1230) by Dr. Akcan and colleagues<sup>[1]</sup>, on the effect of neuropeptides Bombesin (BBS) and Neurotensin (NTS) on trinitrobenzene sulphonic acid-induced colitis in rats, an experimental model of colonic inflammatory bowel disease. In this nice set of experiments, the authors demonstrated the beneficial effects of both BBS and NTS on the preservation of intestinal macroscopic and microscopic integrity in experimental colitis. Most importantly, it was shown that this positive effect on the intestinal mucosa was related to anti-inflammatory, antioxidant and antiapoptotic actions.

It has been two decades since the issue of the potential beneficial role of BBS and NTS on preservation of intestinal homeostasis arose, based on peptides' well-established potent enterotrophic effect<sup>[2,3]</sup>. Up to now, numerous experimental studies have demonstrated the protective effect of BBS and NTS against diverse types of intestinal injury, such as administration of elemental diets or methotrexate, induction of chemical colitis, burns, radiation therapy, ischemia/reperfusion and small bowel resection<sup>[3-9]</sup>. However, the molecular and cellular mechanisms implicated in their intestinal mucosa-healing effect remained unresolved for a long period. Our recent studies with jaundiced and hepatectomized rats showed

that BBS and NT exert regulatory effects on critical cellular processes of enterocytes such as proliferation and death, oxidative stress, redox equilibrium, tight junctions' formation and function, and inflammatory response<sup>[10-13]</sup>. The results presented in this study by Dr. Akcan *et al* are in close agreement with those previously reported by us and add further support to the hypothesis of a multifactorial mode of action of BBS and NT on the intestinal mucosa, beyond their trophic effect. The pleiotropic (mitogenic, antioxidant, antiapoptotic, anti-inflammatory and tight-junction modulating) effects of BBS and NT on intestinal mucosa and the wide range of intestinal injuries that could be healed or prevented by these peptides render BBS and NTS potential pivotal "gut-regulatory peptides" for many intestinal diseases. Although the authors very precisely state that the results of laboratory experiments are not readily applicable to the clinical situation, we feel that there is already a substantial experimental body of evidence supporting their consideration for clinical trials.

## REFERENCES

- 1 **Akcan A**, Muhtaroglu S, Akgun H, Akyildiz H, Kucuk C, Sozuer E, Yurci A, Yilmaz N. Ameliorative effects of bombesin and neurotensin on trinitrobenzene sulphonic acid-induced colitis, oxidative damage and apoptosis in rats. *World J Gastroenterol* 2008; **14**: 1222-1230
- 2 **Wood JG**, Hoang HD, Bussjaeger LJ, Solomon TE. Neurotensin stimulates growth of small intestine in rats. *Am J Physiol* 1988; **255**: G813-G817
- 3 **Evers BM**, Izukura M, Townsend CM Jr, Uchida T, Thompson JC. Differential effects of gut hormones on pancreatic and intestinal growth during administration of an elemental diet. *Ann Surg* 1990; **211**: 630-636; discussion 636-638
- 4 **Chu KU**, Evers BM, Ishizuka J, Townsend CM Jr, Thompson JC. Role of bombesin on gut mucosal growth. *Ann Surg* 1995; **222**: 94-100
- 5 **Gulluoglu BM**, Kurtel H, Gulluoglu MG, Aktan AO, Yegen BC, Dizdaroglu F, Yalin R. Bombesin ameliorates colonic damage in experimental colitis. *Dig Dis Sci* 1999; **44**: 1531-1538
- 6 **Alican I**, Unluer EE, Yegen C, Yegen BC. Bombesin improves burn-induced intestinal injury in the rat. *Peptides* 2000; **21**: 1265-1269
- 7 **Vagianos C**, Karatzas T, Scopa CD, Panagopoulos C, Tsoni I, Spiliopoulou I, Kalfarentzos F. Neurotensin reduces microbial translocation and improves intestinal mucosa integrity after abdominal radiation. *Eur Surg Res* 1992; **24**: 77-83
- 8 **Ryan CK**, Miller JH, Seydel AS, de Mesy Jensen K, Sax HC. Epidermal growth factor and neurotensin induce microvillus hypertrophy following massive enterectomy. *J Gastrointest Surg* 1997; **1**: 467-473
- 9 **Heuser M**, Pfaar O, Gralla O, Grone HJ, Nustede R, Post S. Impact of gastrin-releasing peptide on intestinal microcirculation after ischemia-reperfusion in rats. *Digestion* 2000; **61**: 172-180
- 10 **Assimakopoulos SF**, Scopa CD, Charonis A, Spiliopoulou I, Georgiou C, Nikolopoulou V, Vagianos CE. Experimental obstructive jaundice disrupts intestinal mucosal barrier by altering occludin expression: beneficial effect of bombesin and neurotensin. *J Am Coll Surg* 2004; **198**: 748-757
- 11 **Assimakopoulos SF**, Scopa CD, Zervoudakis G, Mylonas PG, Georgiou C, Nikolopoulou V, Vagianos CE. Bombesin and neurotensin reduce endotoxemia, intestinal oxidative stress, and apoptosis in experimental obstructive jaundice. *Ann Surg* 2005; **241**: 159-167
- 12 **Assimakopoulos SF**, Alexandris IH, Scopa CD, Mylonas PG, Thomopoulos KC, Georgiou CD, Nikolopoulou VN, Vagianos CE. Effect of bombesin and neurotensin on gut barrier function in partially hepatectomized rats. *World J Gastroenterol* 2005; **11**: 6757-6764
- 13 **Assimakopoulos SF**, Vagianos CE, Charonis AS, Alexandris IH, Spiliopoulou I, Thomopoulos KC, Nikolopoulou VN, Scopa CD. Experimental obstructive jaundice alters claudin-4 expression in intestinal mucosa: effect of bombesin and neurotensin. *World J Gastroenterol* 2006; **12**: 3410-3415

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