Volume 227, number 1, 81–82 FEB 05470 January 1988

Comment

Remarks on the article 'Cleavage of the Arg-Ile bond in the polypeptide chain of human pancreatic stone protein' by P. Rouimi, J. Bonicel, M. Rovery and A. De Caro

Catherine Figarella

Groupe de Recherches sur les Glandes Exocrines, 27 boulevard Leï Roure, 13009 Marseille, France

Received 28 October 1987

The authors of the above cited paper [1] remind readers that the 'pancreatic stone protein' was isolated in 1979 from pancreatic stones in patients suffering from chronic calcifying pancreatitis [2]. This protein was purified and characterized and the term of 'pancreatic stone protein' was associated to a phosphoglycoprotein of 14 kDa with an unusual chemical composition containing a high (42%) acidic amino acid content, lacking methionine and presenting an AsX as N-terminal residue [3]. These molecular characteristics similar to those of inhibitors of crystal nucleation and growth found in saliva and in urine apparently explained the putative role of the protein in inhibiting in vivo the $CaCO_3$-crystal growth in pancreatic juice and therefore preventing stone formation [3].

In 1986 the same authors [4] published the partial amino acid sequence of 'pancreatic stone protein' but this protein was clearly different from that previously characterized. It was no more a phosphoglycoprotein but a protein apparently devoid of sugars and presenting an amino acid composition completely different from the first pancreatic stone protein. This new amino acid composition closely corresponded to that of a degradation product of the same molecular mass that we had isolated from human pancreatic juice in 1984 and called protein X [5]. Moreover the first 15 N-terminal residues of this novel stone protein were identical to those we published for protein X (except for 3 missing amino acids in our sequence), and to those reported in 1985 for a protein isolated from human pancreas by Gross et al. [6]. In the same paper [5] we showed that the 14 kDa protein was generated by proteolysis of a family of 19 kDa precursors which could be isolated from human pancreatic juice when the purification experiments were performed in the presence of additional proteinase inhibitors. We realized the proteolytic conversion of the precursors into protein X by using chymotrypsin which demonstrated that the 14 kDa protein was not secreted as such by human pancreas as claimed later by Giorgi et al. [7].

No reference to our previous data was mentioned in the paper of Rouimi et al. [1] who confirmed that the 14 kDa protein was generated by proteolysis (tryptic instead of chymotryptic) from precursors of higher molecular mass. These precursors remain to be identified, they are apparently not structurally related to trypsinogen 1 despite the immunological relationship found with denatured zymogen [5,8].

The now clear evidence that the 14 kDa protein found in pancreatic stones [1] and activated pancreatic juice [5] was not a native secretory protein

Correspondence address: C. Figarella, Groupe de Recherches sur les Glandes Exocrines, 27 boulevard Leï Roure, 13009 Marseille, France

Published by Elsevier Science Publishers B.V. (Biomedical Division)
00145793/88/$3.50

but a proteolysis product having a strong tendency to precipitate at pH 8.0 [6], gave support to our previous hypothesis of a pathogenic role for the premature zymogen activation of over-stimulated acinar cells in pancreatitis [9,10].

REFERENCES

[1] Rouimi, P., Bonicel, J., Rovery, M. and De Caro, A. (1987) FEBS Lett. 216, 195–199.
[2] De Caro, A., Lohse, J. and Sarles, H. (1979) Biochem. Biophys. Res. Commun. 87, 1176–1182.
[3] De Caro, A., Multigner, L., Lafont, H., Lombardo, D. and Sarles, H. (1984) Biochem. J. 222, 669–677.
[4] Montalto, G., Bonicel, J., Multigner, L., Rovery, M., Sarles, H. and De Caro, A. (1986) Biochem. J. 238, 227–232.
[5] Guy-Crotte, O., Amouric, M. and Figarella, C. (1984) Biochem. Biophys. Res. Commun. 125, 516–523.
[6] Gross, J., Carlson, R.I., Brauer, A.W., Margolies, M.N., Warshaw, A.L. and Wands, J.R. (1985) J. Clin. Invest. 76, 2115–2126.
[7] Giorgi, D., Bernard, J.P., De Caro, A., Multigner, L., Lapointe, R., Sarles, H. and Dagorn, J.C. (1985) Gastroenterology 89, 381–386.
[8] Figarella, C., Amouric, M. and Guy-Crotte, O. (1984) Biochem. Biophys. Res. Commun. 118, 154–161.
[9] Figarella, C. (1980) Gastroenterol. Clin. Biol. 4, 631–635.
[10] Steer, M.L., Meldolesi, J. and Figarella, C. (1984) Dig. Dis. Sci. 29, 934–938.

Volume 227, number 1, 82–84 FEB 05471 January 1988

Answers to Dr. Figarella's comment

P. Rouimi, J. Bonicel and M. Rovery and A. De Caro+

Centre de Biochimie et de Biologie Moléculaire, CNRS, 31, Chemin Joseph-Aiguier, BP 71, 13402 Marseille Cedex 9 and *+Groupe de Biochimie Fondamentale, Unité de Recherches de Pathologie Digestive, U 31, INSERM, 46 Blvd. de la Gaye, 13258 Marseille Cedex 9, France*

Received 25 November 1987

1. P. ROUIMI, J. BONICEL AND M. ROVERY'S ANSWER

First we would like to specify that our research group in the Centre de Biochimie et de Biologie Moléculaire, CNRS, Marseille, had nothing to do with the misunderstandings by several members of the same team which led to its breaking up in 1981.

In 1985, Professor H. Sarles and Dr A. De Caro asked us to collaborate in the determination of the primary structure of the human pancreatic stone protein prepared from calculi (PSP) as well as of its immunoreactive forms from the pancreatic juice (PSP S1–5). Our research group is indeed equipped for protein sequencing and trained in structural determination methods. Having worked for several years on pancreas proteolytic enzyme precursors, their activation, their proteolyses, the proposed research was of great interest to us and fitted into the frame of our research field. Together with Dr A. De Caro we endeavoured a thorough study of the various PSP forms.

In the first report [1] written in collaboration, our contribution dealt with amino acid compositions and N-terminal sequence determinations of the 40 and 65 first amino acids of PSP and PSP S1, respectively. At that time we mentioned the report of Dr Figarella's group [2] since the 15 first amino

Correspondence address: P. Rouimi, Centre Biochemie et de Biologie Moléculaire, CNRS, 31, Chemin Joseph-Aiguier, BP 71, 13402 Marseille Cedex 9, France; or A. De Caro, Groupe de Biochemie Fondamentale, Unité de Recherches de Pathologie Digestive, U 31, INSERM, 46 Blvd. de la Gaye, 13258 Marseille Cedex 9, France

Published by Elsevier Science Publishers B.V. (Biomedical Division)
00145793/88/$3.50