## ANGIOTENSINOGEN EXPRESSION IN RAT PANCREAS AND ITS SECRETION IN THE PANCREATIC JUICE

E. BERTELLI<sup>1</sup>, M. REGOLI<sup>1</sup>, M. BENDAYAN<sup>2</sup>, L. FONZI<sup>1</sup>

1 Dept. of Anatomical and Biomedical Sciences, University of Siena, Siena, Italy.
2 Dept. of Pathology and Cell Biology, University of Montreal, Montreal, Canada.

Local renin-angiotensin systems (RAS) have been detected in several organs. Recently, the components of a local RAS have been also reported in dog, human and rat pancreas (1, 2). In particular, angiotensin receptors have been observed as located on the luminal plasmatic membrane of pancreatic duct cells (3). The presence of such receptors raises the possibility that angiotensins or angiotensin-related peptides might be generated in the duct lumen. For this reason we decided to verify whether angiotensinogen (AGT), the molecular precursor of angiotensins, is present in the pancreatic juice and which cell type is responsible for its production and secretion.

Pancreatic juice was collected from 5 adult rats carefully avoiding any contamination with blood or bile. Western blot analysis of the samples, using rat plasma proteins as a positive control, carried on with a rat specific anti-AGT polyclonal antiserum, unveiled two major bands of 60 and 64 kDa in all samples. A densitometric analysis was performed to evaluate the relative concentration of AGT in the pancreatic juice compared with its plasmatic concentration. AGT concentration in the pancreatic juice appeared variable with a mean value of 2.67%±1.45% compared with plasmatic concentration.

In order to verify which cell type produced AGT, cryosections of rat pancreas, fixed in cold aceton, were incubated with the same antibody. Surprisingly, AGT-immunoreactivity was not detect in acinar or ductal cells. Rather, a clear and strong reaction was observed in peripheral islet cells. Double staining of the sections with antiglucagon antiboby confirmed that AGT-positive cells were mainly alpha-cells.

Previous studies have shown how the great majority of the pancreatic endocrine entities (islets of Langerhans and smaller clusters of endocrine cells) and the pancreatic ducts are interconnected each other (4, 5). Now, the simultaneous detection of AGT either in the pancreatic juice or in the alpha cells is also consistent with a functional coupling between endocrine pancreas and pancreatic ducts. Taken together these findings suggest that the role played by pancreatic RAS is likely more complex than the mere local regulation of blood flow.

REFERENCES. 1) Leung and Carlsson (2001) J Mol Endocrinol, 26:155-164. 2) Lam and Leung (2002) Eur J Endocrinol 146:567-572. 3) Leung et al (1997) J Endocrinol, 153:269-274. 4) Bertelli et al (1994) 239:371-378. 5) Bertelli et al (2001) Diabetologia, 44:575-584