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DNA synthesis in exocrine and endocrine pancreas after partial hepatectomy in Syrian golden hamsters¹

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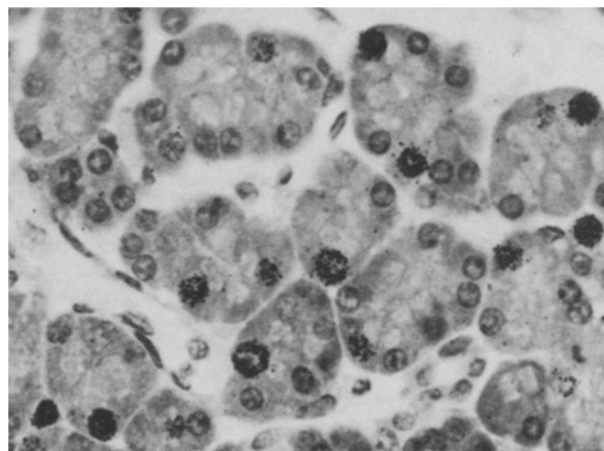
Summary. ³H-thymidine autoradiography showed an enhanced DNA synthesis in acinar and islet cells of pancreas after partial hepatectomy in syrian golden hamsters. A significant nuclear labeling index of acinar cells was observed between 48 and 84 h and reached control levels by 120 h. An increased labeling index of islet cells was also observed, however, this increase was not statistically significant. These results indicate growth factor(s) produced after partial hepatectomy is capable of inducing DNA synthesis in pancreas.

Key words. Partial hepatectomy; DNA synthesis; thymidine; acinar cells.

Surgical removal of a portion of the liver results in compensatory hyperplasia of the remaining portion and reaches original weight within a few days in many species of animals³. During a study analyzing the effect of partial hepatectomy (PH) on pancreatic hepatocytes in hamsters⁴, we have observed hyperplasia of pancreatic acinar cells. This finding was rather surprising because 1) the common notion is that the exocrine pancreas is a 'nondividing tissue'⁵ and 2) pancreatic regeneration could be induced in adult hamsters, rats and guinea pigs only after producing pancreatic necrosis⁶⁻⁹, or after surgical removal of a portion of the pancreas^{10,11}. In the present experiment, we have systematically studied the effect of PH on stimulation of pancreatic DNA synthesis at different intervals. The results of this study demonstrate that PH leads to enhanced DNA synthesis in acinar and islet cells of the pancreas.

Methods. Seventy-five male syrian golden hamsters weighing 50-60 g were purchased from Charles River Breeding Laboratories (Wilmington, Mass.). Hamsters were housed in plastic cages in groups of 3-4/cage on san-i-cel bedding under standard conditions of temperature, humidity and light dark cycle. All the hamsters were maintained on pelleted hamster diet (Tekland Test diets, Madison, Wis.) and had free access to water. In 42 hamsters partial hepatectomy (PH) was done by removal of median and left lobes as described before⁴. To avoid diurnal variation, PH was performed between 07.00 and 11.00 h. Hamsters were sacrificed in groups of 3-4 at 6-h intervals, starting from 24 h after PH up to 72 h, and at 84, 96 and 120 h. Another 24 hamsters were subjected to sham operation and sacrificed in groups of 3-4 at 42, 48, 60, 72, 84, 96 and 120 h. The remaining 4 animals were used as standard controls. All the hamsters were given ³H-thymidine i.p. (SP activity 2 Ci/m mol; Research Product International Corp., Elk Grove Village, Ill.) at a dose of 1 µCi/g b.wt, 2 h before sacrifice. Portions of pancreas and liver were fixed in neutral buffered formalin and processed for light microscopy. Five micron thick paraffin sections were routinely stained with hematoxylin and eosin. To assess DNA synthesis, paraffin sections were coated with Kodak NTB₂

nuclear emulsion (Eastman Kodak Company, Rochester, NY) for autoradiography, as previously described⁸. Labeling index was obtained by counting 1000 nuclei from acinar and islet cells. **Results and discussion.** Regenerative changes in the liver after PH are very similar to those previously published⁴. Pancreas of hepatectomized and sham operated animals were grossly unremarkable. Histologically, no necrosis or inflammation was observed. Labeling indices of acinar and islet cells in hepatectomized, sham operated and control animals are presented in the table. Increased incorporation of labeled thymidine into acinar cell nuclei was first detected at 42 h after PH, and reached a maximum at 54 h (p < 0.001) and persisted at high levels up to 84 h when compared with controls (fig.). A slight increase in label-



³H-thymidine autoradiograph of hamster pancreas, 60 h after partial hepatectomy. Several acinar cell nuclei are labeled. Hematoxylin and eosin stain, × 550.

Labeling indices of acinar and islet cells at various intervals, starting from 24 h after partial hepatectomy (No. of labeled nuclei/1000 cells)

		Time interval											
		24	30	36	42	48	54	60	66	72	84	96	120
Acinar cells	PH	0.2 ± 0.2 ¹	0.2 ± 0.2	0.7 ± 0.5	9 ± 4	32 ± 6 ^b	71 ± 3 ^b	50 ± 17 ^c	43 ± 9 ^a	68 ± 17 ^c	70 ± 18 ^d	37 ± 16	4 ± 2
	Sham				4 ± 1	21 ± 1		18 ± 6		6 ± 3	2 ± 1	8 ± 3	4 ± 2
Islet cells	PH	11 ± 6 ¹	29 ± 2	35 ± 7	34 ± 17	19 ± 9	10 ± 7	21 ± 5	10 ± 3	11 ± 2	6 ± 2	6 ± 1	6 ± 0
	Sham				8 ± 1	3 ± 1		7 ± 1		7 ± 1	10 ± 1	9 ± 3	4 ± 2

¹ mean ± SE. (In PH group, 4 animals are sacrificed at 24, 30, 36, 42, 66, 72 and 96 h and at each remaining interval 3 animals are sacrificed. In sham group, 4 animals are sacrificed at 42, 60, 96 and 120 h and 3 animals at each remaining period.) ^a p < 0.02, ^b p < 0.001, ^c p < 0.05, ^d p < 0.01. Labeling indices in acinar and islet cells of control hamsters were 2 ± 1 and 13 ± 3 respectively. The labeling index in PH and sham operated groups are compared with the control animals. The labeling index in acinar cells of PH group is significantly greater at 48, 54, 60, 66, 72 and 84 h and in sham group at 48 h, whereas the increase in labeling index of islet cells in PH and sham groups is not significant.

ing indices of islet cells was also noted from 30–60 h, and this increase was not statistically significant. Cells of duct system also showed a minimal increase in labeling indices. However, the labeling indices of the duct cells varied tremendously from one segment of the duct to the other (i.e. interlobular, intralobular and intercalated ducts). To obtain meaningful statistical data on the indices of the duct system, we plan to examine a large number of animals and will be reported in a separate communication. Interestingly, in sham operated animals, acinar cells showed a significant increase in the number of labeled nuclei at 48 h (p < 0.01) over the control values. No increased DNA synthesis was seen in islet cells of sham operated animals.

The regenerative response in PH animals is qualitatively similar to that observed in hamsters after ethionine induced degeneration and necrosis⁶. However, the magnitude of response was lower in PH animals. In pancreatic regeneration induced after ethionine treatment, the maximum labeling index was 226 ± 25/1000 cells as compared to 71 ± 3 after PH.

From PH rats, serum factors capable of stimulating hepatocyte growth have been isolated by various investigators^{12–14}. These growth factors, in addition to stimulating liver growth, are also capable of inducing pancreatic DNA synthesis as shown here². This response is not surprising, since both liver and pancreas are derived from gut endoderm embryologically. In this regard, it is pertinent to note that hepatocytes can be induced in the pancreas of hamsters and rats after carcinogen administration and dietary modulation^{15–17}. Similarly, pancreatic acinar tissue was induced in livers of rats treated with polychlorinated biphenyls¹⁸.

The results of this study clearly demonstrate that the growth stimulatory effect of serum factor(s) released after PH is not organ specific and can stimulate both liver and pancreas. However, the effect of this serum factor on other organs remains to be examined.

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High molecular transport proteins for JH-III in insect hemolymph

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Summary. Using two independent techniques, ultracentrifugation in a KBr-gradient, and native pore polyacrylamide gel electrophoresis in combination with [³H]-epoxyfarnesyl diazoacetate photoaffinity labeling, we showed that in the hemolymph of *Periplaneta americana*, and probably also in *Leptinotarsa decemlineata* JH-III binds to the lipophorin, whereas in *Locusta migratoria* JH-III binds to a different protein.

Key words. Juvenile hormone binding protein; lipophorin; juvenile hormone I; juvenile hormone III.

In the hemolymph, juvenile hormone (JH) occurs in association with specific binding proteins (JHBP). The first JHBP to be isolated and characterized was that of *Manduca sexta*. It appeared to be a single chain polypeptide of 28,000 mol. wt, capable of binding one molecule of JH (K_d = 4.4 × 10⁻⁷ M). Its affinity for JH-I was higher than that for JH-III and it displayed

stereoselectivity¹. However, JH-I only occurs in *Lepidoptera*, and in most other orders of insects JH-III is the principal hormone². In a number of species containing only JH-III, a JHBP with a higher affinity for JH-III (K_d < 10⁻⁷ M) than for JH-I was found^{3–5}. This BP appeared to have a high molecular weight (~500,000) and it was also shown to be stereoselective^{4,6}. An