GROWTH HORMONE CONTROL OF MESSENGER RNA SYNTHESIS

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Hypophysectomy reduces, and treatment with growth hormone (GH) increases, the body weight of the rat (Simpson, Evans and Li, 1949). The hormone acts by stimulating protein biosynthesis by changing the ribosomes so that their ability to assemble activated amino acids into protein is enhanced (Korner, 1958, 1961a, 1962). Several lines of evidence are summarised here which lead to the conclusion that the hormonal control of ribosomal protein-synthetic ability is exercised by means of hormonal control of the rate of synthesis of RNA in general and of messenger RNA (m-RNA) in particular (see Korner, 1963).

Ribosomes, prepared by methods described (Korner, 1961b) from 10,000g deoxycholate supernatant of a liver homogenate from hypophysectomized (hypox.) rats incorporate only half as much amino acid into protein in vitro as those from normal rat liver prepared under identical conditions (Korner, 1961a). Yet polysomes (Wettstein, Staehelin and Noll, 1963), prepared from the same 10,000g deoxycholate supernatant used to prepare the ribosomes showed only small differences in incorporating ability (Table 1).

The yield of polysomes (expressed as a percentage of the total RNP particles and assayed by sucrose gradient centrifugation) was smaller from liver of hypox rats than from normal rat liver and the yield rose if the rats had been treated with GH. This suggests that less m-RNA is present in preparations from hypox rats or that the ribosomes from hypox rats are less able to attach themselves to m-RNA: either of these events

would result in a fall in the yield of polysomes. The polysomes themselves, being a preparation of the active particles from the total particle population, would all be expected to have the same activity per mg RNA.

TABLE 1

Amino acid incorporation into protein of ribosomes and polysomes from normal and hypox rats

		cpm/mg protein/mg particle RNA
Ribosomes from	normal rats	900
	hypox rats	490
Polysomes from	normal rats	1200
	hypox rats	1120

Stimulation of phenylalanine incorporation by addition of poly U to the ribosome system was at least as great with preparations from liver of hypox rats as with preparations from normal ones showing that the ability of ribosomes to add on to m-RNA was not impaired by hypophysectomy.

Actinomycin treatment of rats resulted in a fall in the incorporating ability of the ribosomes (Korner & Munro, 1963), partly because of inhibition of m-RNA synthesis in the treated rats. Treatment of the rats with GH at the same time as administration of actinomycin resulted in less inhibition of incorporation (Table 2). GH stimulated amino acid incorporation into protein *in vitro* even in the presence of actinomycin provided that the doses of actinomycin given were not excessive: in rats given higher doses of the antibiotic, GH was only able to stimulate incorporation to a lesser extent (Table 2).

Hypophysectomy reduced, and treatment with a single dose of 2mg of GH enhanced incorporation of ^{3}H-orotic acid into nuclear and microsomal RNA (Table 3). Talwar *et al* (1962) showed stimulation of labelling of RNA by GH administered to normal rats. The first effect of GH was on the

synthesis of nuclear RNA but if longer pulse times of orotic acid were used, enhanced incorporation was seen in microsomal RNA. Analysis of the RNA by linear sucrose gradient centrifugation showed that all types of RNA increased at the behest of GH including the rapidly labelled 14S-RNA which has the characteristics of m-RNA (Munro & Korner, 1962).

TABLE 2

Incorporation of amino acids into ribosomal protein in actinomycin and GH treated rats

	cpm/mg protein/mg particle RNA
Normal	850
Actinomycin (200μg, 12 hours before death)	320
Actinomycin (200μg + 2mg GH 12 hours before death)	680
Actinomycin (500μg, 12 hours before death)	190
Actinomycin (500μg + 2mg GH 12 hours before death)	280

TABLE 3

^{3}H-orotic acid incorporation into RNA: 45 min pulse.

	cpm/O.D.260	
	Nuclear RNA	Microsomal RNA
Normal rats		
Control	800	1900
+ 2mg GH	1690	2620
+ 200μg actinomycin	385	280
+ GH + actinomycin	562	430
Hypox rats		
Control	440	1060
+ 2mg GH	1580	2020
+ 200μg actinomycin	230	410
+ GH + actinomycin	320	585

Actinomycin treatment of rats inhibits most of the RNA synthesis (cf. Meritz, 1963) but GH could still elicit a stimulation of RNA synthesis provided the conditions used were such that a GH stimulation of amino acid incorporation could be elicited, i.e. moderate doses of actinomycin (Table 3).

It is concluded that GH controls the synthesis of cellular RNA, including m-RNA, and that the GH effects on protein synthesis and body growth can be explained in terms of its action on RNA synthesis and in particular in terms of GH control of the synthesis of m-RNA. Preliminary experiments indicate that insulin acts similarly and it seems possible that other protein anabolic hormones act by controlling m-RNA synthesis (Laio & Williams-Ashman, 1962; Noteboom & Gorki, 1963; Talwar & Segal, 1963; Tata, 1963; Widnell & Tata, 1963; Ui & Meuller, 1963). Full details of these experiments will be published elsewhere.

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