at 37°C. More than 95% of the acid-precipitable radioactivity incorporated from UTP and approx. 15% of that incorporated from *S*-adenosyl-L-methionine was present in the hot-trichloroacetic acid-soluble fraction. When nuclei (1mg of DNA) were incubated for 5min at 37°C with labelled *S*-adenosyl-L-methionine and all four nucleoside triphosphates the hot-trichloroacetic acid-soluble fraction contained 53pmol of methyl group, but only 36pmol of methyl group when the nucleoside triphosphates were omitted or when actinomycin D was added to the incubation. With all four nucleoside triphosphates present 900pmol of UMP was incorporated in 5min. If the nucleoside triphosphate-dependent methylation (17pmol of methyl group) represented incorporation into newly synthesized RNA, then 17×30 pmol, or 57% of the UMP incorporation, should represent synthesis of ribosomal precursor RNA.

Starvation leads to an inhibition of ribosome synthesis in rat liver (Hirsch & Hiatt, 1966). When the total methylase activity of the nuclei was measured in the presence of *S*-adenosyl-L-[Me-¹⁴C]-methionine and added yeast RNA, no change was found after 24h starvation. However, the nucleoside triphosphate-dependent methylation by these nuclei was decreased by 47% to 9pmol of methyl group, and it was calculated that of the total UMP incorporation (610pmol) only 45% represented the synthesis of ribosomal precursor RNA.

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Control of Histone Modification within Chromatin by Adenine Nucleotides and Steroid Hormones

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Chromatin from Krebs 2 ascites-tumour cells can catalyse the transfer of methyl groups from *S*-adenosyl-L-methionine to its histone and DNA. Certain lysine residues of the histone are modified resulting in the formation of *N*^ε-mono-, -di-, and -trimethyl-L-lysine residues, and kinetics suggest that DNA methylation actually occurs as a result of transfer of methyl groups from these residues (Burdon & Garven, 1969; Burdon, 1971). The histone-methylating enzyme(s) can be solubilized from the intact chromatin and have been shown to

have a unique requirement for histone (Burdon & Garven, 1969, 1971). Studies with the soluble preparation, as well as with the intact chromatin, now reveal AMP, even at low concentrations (50nM), to be a specific stimulator of this modification reaction.

Examination of other histone-modifying enzymes, both in the intact chromatin of Krebs 2 cells and in soluble preparations from chromatin, have indicated that phosphorylation of histone by a histone kinase-like enzyme (Langan, 1968) is inhibited specifically by low concentrations of AMP. Cyclic AMP (adenosine cyclic 3':5'-monophosphate), contrary to expectation, proved to have no convincing stimulatory effect. Nevertheless cyclic AMP stimulated the histone kinase in soluble preparations obtained by high-speed centrifugation of homogenates of Krebs 2 cells, as has been found to be the case for soluble preparations from acetone-dried powders of rat liver (Langan, 1968). Although histone acetylase activity (Galliwitz, 1970) was readily detectable in both the chromatin of Krebs 2 cells and in the soluble preparation from it, the activities were not influenced by either cyclic AMP or AMP.

Attempts were made to determine whether chromatin from Krebs 2 cells itself had any special potential to regulate *in situ* the concentrations of AMP (or cyclic AMP) and hence the methylation and phosphorylation of histone moieties. These revealed the presence of both adenylate cyclase and cyclic AMP phosphodiesterase activities. Moreover, of these chromatin enzymes the latter was found to be inhibited by low concentrations of hormones such as testosterone, oestradiol-17 β and progesterone.

Preliminary studies, in which intact chromatin is either 'methylated' or 'phosphorylated' as a result of prior incubation with *S*-adenosyl-L-methionine or ATP, have indicated that these respective treatments can influence, either negatively or positively, the amount of RNA made subsequently by the endogenous RNA polymerase of that chromatin.

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