The Organ-specific Growth Inhibition of the Tubule Cells of the Rat's Kidney

Hans Saetren

*Institute for Medical Biochemistry, University of Oslo, Norway**

Earlier experiments¹ indicated that organ-specific growth inhibitors are released from autolyzing kidney and liver cells, respectively. The inhibition of growth appeared as an apparent depression of the mitotic rate of the tubule cells of the kidney 48 h after subtotal nephrectomy, when finely disrupted kidney tissue was spread in the peritoneal cavity. Later on this procedure proved to be equivocal as the peak of the first mitotic wave may be attained several hours earlier than 48 h after the operation. The first mitotic wave to appear after subtotal nephrectomy is by far the largest with a peak between 38 and 48 h after the operation; the peak of the small second wave is attained between 60 and 75 h after the operation. By determining the actual course of the mitotic waves in each kidney dealt with, it was possible to confirm that the first wave was specifically suppressed by autolyzing kidney cells, while the second wave increased in size. Autolyzing liver cells had no effect upon these mitotic waves. The temporary activity of the growth inhibitor(s) could be demonstrated also in the very young rat. The mitotic rate that was due to the normal growth of the kidney tubules, was suppressed for several hours both when finely disrupted kidney tissue was spread in subcutaneous pockets or in the peritoneal cavity. A third way of demonstrating the release of organ-specific growth inhibitor(s) from autolyzing kidney tissue was brought to light by a study of how the removal of perinephrium affected the mitotic rates of the tubules. Application of kidney mass directly to the uncovered kidney surface resulted in a significant decrease in the mitotic rate at this place, as compared to the rates effectuated deeper in the cortex. The mitotic rate of the tubules close to the kidney surface was not changed when this latter was covered by finely disrupted liver tissue.

* Present address: National Institute of Public Health, The Virus Institute, Geitmyrsveien 75, Oslo, Norway.

Because the kidney mass was prepared from the entire kidney, an eventual cellular specificity of the growth inhibition could not be disclosed and the term "organ-specificity" had to be used in the present context.

1. Saetren, H. *Exptl. Cell Research* **11** (1956) 229.

The Cytidine Diphosphate Reductase System

Peter Reichard and
E. Colleen Moore

Dept. of Medical Chemistry, Uppsala University, Uppsala, Sweden

A partially purified enzyme system ("Fraction B") from *Escherichia coli* B catalyzes the formation of deoxyCDP from CDP¹. The reaction shows absolute requirements for ATP, Mg²⁺ and reduced lipoic acid. Fraction B contains at least two protein fractions (B1 and B2).

A similar reaction occurs in preparations from Novikoff hepatoma². An enzyme system showing requirements similar to bacterial Fraction B was prepared from the tumor.

The requirement for reduced lipoic acid was studied with both the bacterial and tumor Fraction B. With bacterial Fraction B reduced lipoic acid could be completely replaced by a heatstable protein (Factor S₂) together with TPNH. Factor S₂ was purified about 6000 fold over an extract from *E. coli*. It behaved as a single component on agar electrophoresis and during ultracentrifugation.

With tumor Fraction B, Factor S₂ and TPNH replaced reduced lipoic acid only in the presence of an additional enzyme fraction (Enzyme C). This was purified about 300 fold from *E. coli*. Bacterial Fraction B was heavily contaminated with Enzyme C.

Enzyme C catalyzed the stoichiometric reduction of Factor S₂ by TPNH:

It is believed that Factor (SH)₂ — and not reduced lipoic acid — is the physiological hydrogen donor for the reduction of CDP. Our