

This Week's Citation Classic

Karlson P. New concepts on the mode of action of hormones.

Perspect. Biol. Med. **6**:203-14, 1963.

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The paper presents the concept that hormones control gene activity. This was based on an experiment, i.e., puff induction in giant chromosomes by the insect hormone ecdysone. In biochemical terms, stimulation of transcription and translation, i.e., enzyme induction, was postulated as primary mechanism of action of hormones. [The SCJ® indicates that this paper has been cited over 140 times since 1963.]

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"The paper is essentially a theoretical interpretation of a series of experiments carried out in 1959 together with Ulrich Clever on the control of puffing patterns in salivary gland chromosomes in *Chironomus tentans*. Clever had been studying puffing patterns in giant chromosomes; I was interested in the biochemical and physiological effects of the moulting hormone ecdysone, an insect steroid hormone.

"In the course of a discussion, it became clear that the change of puffing pattern observed by Clever which occurred shortly before pupation might be the action of the moulting hormone. To test this idea, I worked for a week in Clever's laboratory in October 1959. Two months later the essential result

became clear: ecdysone induces puffs in giant chromosomes. The experimental results were published in the summer of 1960.¹

"During our discussions, we were well aware of the implication of our experimental results. Ecdysone seemed to be a timing device for the control of gene activity, turning on certain genes. This was quite a new concept on the mechanism of hormone action; earlier investigators had always looked for a direct influence of steroids on the activity of certain enzymes.

"My review, laying emphasis on the induction of enzyme synthesis by hormones, appeared at about the same time as the well-known paper by Jacob and Monod on the nature of enzyme induction in *E. coli*, i.e., the repressor concept.² Both theories fit together quite easily. That might have been one of the reasons why my review article became so widely known and is so often cited.

"It may be pointed out that my 'Citation Classic' had a forerunner.³ But this review was written in German and published in a medical journal; therefore, it did not reach the international scientific audience.

"The new ideas presented above resulted in a new line of research for our laboratory (possibly also for other laboratories): We dropped many of the research projects in which we were engaged previously, and I interested most of my co-workers to follow up, in various biochemical systems, the mode of action of hormones. We selected steroid hormones, mainly corticosteroids, for our investigations since it was already known that corticosteroids induce enzyme synthesis. This was fortunate; it is now-a-days generally accepted that this mechanism of action is restricted to steroid hormones."

1. **Clever U & Karlson P.** Induktion von Puffveränderungen in den Speicheldriisenchromosomen von *Chironomus tentans* durch Ecdyson. *Exp. Cell. Res.* **20**:623-6, 1960.
2. **Jacob F & Monod J.** Genetic regulatory mechanisms in the synthesis of proteins. *J. Mol. Biol.* **3**:318-56, 1961.
3. **Karlson P.** Biochemische Wirkungsweise der Hormone. *Deut. Med. Wochenschr.* **86**:668-74. 1961.