

Bullough W S. Mitotic and functional homeostasis: a speculative review. *Cancer Res.* **25**: 1683-727,1965.

This review put forward a new concept of the control of tissue growth by mitotic inhibitors, called chalones. Slowly this concept has become generally accepted, and it has also proved to have a significant bearing on the understanding of cancer. [The *SCI*[®] indicates that this paper was cited 249 times in the period 1965-1976.]

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"In retrospect the surprising popularity of this review may have had several causes. For one thing it was particularly comprehensive, which is always valuable, although someone, who much later confessed to being one of the referees, complained that great stamina was needed to read it. The comparable stamina needed to write it derived from the excitement of our previous discovery that cell division is controlled by tissue-specific mitotic inhibitors, christened 'chalones,' and not as was previously believed by mitotic stimulants. The main interest of the review thus arose from its complete re-interpretation of the available evidence on tissue growth in both normal and pathological conditions.

"This new angle of approach also made the review controversial, which may have added to its attraction. The old beliefs were so deeply entrenched that skepticism of the new ones was widespread; even *Cancer Research* was nervous and covered itself by

adding the words 'a speculative review' to my original title! It has indeed been enlightening to experience for oneself how resistant scientists in general are to new ideas, and it has taken more than 10 years for the chalone concept to become generally accepted.

"Another obvious feature of the ideas expressed in the review was the light they might shed on the problem of cancer. For me part of the excitement of those days lay in the question: can tumour cells also be inhibited by the chalone of their tissue of origin? The unlikely answer soon proved to be 'yes,' which caused the following poetic outburst:

We have found in murine urine
And in hominal urinal
A substance chalonal. Euphonal!
A tissue controller, and droller,
An answer to cancer!

However, it must now be added that urine is not to be recommended as a practical chalone source.

"The evidence linking chalones to cancer has gradually become overwhelming, and this too may have ensured a continuing interest in the original review. However, my attempt at a follow-up review of this evidence has proved too much for the nerves of *Cancer Research*, who this time have declined to publish it. Again one meets the 'new-idea syndrome,' which is particularly regrettable in a subject that is so short of original ideas. Fortunately, recent successful clinical experiments directed by my colleague Dr. T. Rytömaa, who has used a chalone against myeloid leukemia, may bring the ideas put forward in the 1965 review to a conclusion perhaps as significant in its own way as was the first use of hormones against hormone-deficiency diseases."