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OVERVIEW

# Cell Proliferation Measurements as Intermediate Endpoints

Many studies have now shown that a wide variety of naturally occurring compounds can inhibit the development of tumors in animal models. Although studies of this type have been carried out for several decades, few have attempted to test the efficacy of chemopreventive interventions in human populations. Studies in humans have generally looked for the occurrence of cancer as an endpoint, and have required large numbers of human subjects to be studied for many years.

Since new compounds with chemopreventive efficacy in rodent models are now becoming available for study in human subjects, an increased ability to test their efficacy would be potentially useful. To facilitate carrying out clinical investigations it has been suggested that intermediate biomarkers of cell proliferation, differentiation and related metabolic functions be studied in human subjects by measuring the effect that chemopreventive regimens have in normalizing the biomarkers in small groups of human subjects over short durations. This might enable testing potentially useful regimens in human subjects more rapidly for possible efficacy. Interventions successful in normalizing the intermediate endpoints could then be advanced to larger human studies for longer durations, testing efficacy against the occurrence of benign and malignant neoplasms.

Previous studies in both rodents and humans have suggested that cell proliferation measurements in the gastrointestinal tract might serve as intermediate endpoints in chemoprevention trials. In this session recent work on this topic will be reviewed. A variety of measurements related to cell proliferation will be described, as well as the necessity for comparison, standardization and validation of these new biomarkers of cell proliferation. The aim of this session is to provide a comprehensive and critical review of the subject, and to review its potential application to the field of chemoprevention.

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