aminobiphenyl derived from the Clayson et al. data contrasts sharply with the 33-fold lower potency reported in the more recent and more extensive drinking water study of Schieberstein et al. (10). Use of the Schieberstein et al. data for 4-aminobiphenyl results in a mouse Tds of ratio of 23:1. The analysis by Gold et al., based on the best available rat bioassay for 4-aminobiphenyl by Tanaka et al. (11), suggests that in the rat, 4-aminobiphenyl is 26 times more potent than o-toluidine.

The above comparisons of the ratio of the Tds of 4-aminobiphenyl to that of o-toluidine ignore differences in animal strains and sexes, routes and duration of exposure, numbers of animals, and sites of tumorigenesis. Therefore, it is not entirely clear which represents the “best” estimate of the ratio of carcinogenic potencies. Even if the actual Tds ratio were known with perfect accuracy, the issues of low-dose extrapolation and animal-to-human extrapolation would still complicate any attempt to apply the animal bioassay data to quantitative estimates of human risk. Estimating the range of 4-aminobiphenyl:o-toluidine exposure in the past is also difficult. Information on the level of 4-aminobiphenyl contamination in feedstocks such as aniline is very limited (13), and the levels of 4-aminobiphenyl in present bulk samples may not reflect the extent of 4-aminobiphenyl formation in the past. We continue to seek additional documentation on historical 4-aminobiphenyl levels and are evaluating the feasibility of analyzing blood and urine samples of current workers to confirm that 4-aminobiphenyl levels among workers in the anti-oxidant department are similar to levels in unexposed workers. We nonetheless believe that the weight of available evidence favors o-toluidine as the major etiologic agent in this bladder cancer excess. Based on this study and reviews of human and animal data in the literature, the National Institute for Occupational Safety and Health has concluded that o-toluidine is a potential occupational carcinogen, as defined in the OSHA carcinogen policy (29 CFR 1990) (14).

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(14) NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH: NIOSH Alert: Preventing Bladder Cancer From Exposure to o-Toluidine and Aniline. DHHS Publ No. (NIOSH)90-116, 1990

Investment in Cancer Research Pays Off for Other Diseases

I have read with considerable interest your "News" article "Investment in Cancer Research Pays Off for Other Diseases," and I certainly concur with its conclusion (i.e., "the cross-feeding..."
between cancer and other fields continues to grow") (1).

I noted that the list of cancer treatments named in the table of “Selected Cancer Spin-offs” correctly cites both immuran and allopurinol as being originally designed and tested for anticancer activity, both of which subsequently found application instead in other areas of medicine. In contrast, no mention was made of the fact that AZT, which was first synthesized under the aegis of grants from the National Cancer Institute (CY-5943 and CA-02903), had also been prepared and tested for anticancer activity (2). Like immuran and allopurinol, AZT failed to manifest the requisite properties to warrant further evaluation as an anti-cancer agent but did find application as an antiretroviral agent in the management of AIDS nearly 25 years later. Moreover, ddC (3) and d4T (4), which belong to the same family of dideoxynucleosides to which AZT belongs and which were synthesized in the same era under corresponding grants to the Michigan Cancer Foundation in the search for new anti-cancer agents, are currently being evaluated in clinical trials for the AIDS program. It is important also to note that the dideoxynucleosides found additional, useful application in the procedure developed by Sanger for sequencing DNA.

It is true, of course, that AZT, ddC, and d4T were all synthesized during the period 1964-1966, a few years before the approval of the National Cancer Act. Nonetheless, it lends additional credence to the argument that the investment in cancer research has paid off in “money, treatments, and understanding of basic biology for medicine as a whole.”

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References

Growth of Human Tumor Cells in Athymic Mice

We have read with interest the report by Fridman et al. (1) on the use of Matrigel to support the growth of human tumor xenografts in athymic nude mice. This observation, when confirmed, promises to reduce the difficulties encountered in the development of animal models of selected human cancers. However, the authors' generalization that there is “a paucity of animal models [xenografts] to study the major cancers, including breast, lung, kidney, and colon cancers” is misleading and fails to credit appropriately the NCI’s productive efforts to develop animal models of the major cancers. In fact, there are available at this time from the NCI useful xenograft models comprising no fewer than 18 lung cancer cell lines, 12 colon cancer cell lines, 10 renal cancer cell lines, and eight breast cancer cell lines (2-4). Breast cancer xenografts have indeed proved to be more difficult to develop, and the NCI has intensified its efforts accordingly. Readers of the Journal of the National Cancer Institute should find this clarification helpful.

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Response

We agree with Dr. Harrison and thank him for his helpful comments. We apologize for our poor choice of adjectives. Much progress in cancer research is based on animal models and our method is a further refinement for growing tumors, which should prove useful.

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Erratum: “Isolation of Gene Associated With High Metastatic Potential in Rat Mammary Adenocarcinomas” by S. M. Phillips, A. J. Bendall, and I. A. Ramshaw [J Natl Cancer Inst 82:199-203, 1990 (Issue 3)]. The authors wish to retract the statement that pGM21 shows partial homology to human elongation factor 1 subunit α. Database searches show no significant homology to any known sequence.

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