Re: A Prospective Study of Incident Squamous Cell Carcinoma of the Skin in the Nurses' Health Study

In this excellent paper, Grodstein et al. (1) stated that, to their knowledge, only two studies have been conducted in humans evaluating cigarette smoking as a risk factor for squamous cell carcinoma (SCC). They refer to prior studies by Aubry and MacGibbon (2) and Karagas et al. (3). In 1990, we published a study on risk factors for SCC of the skin in Saskatchewan, Canada, and included an extensive questionnaire on smoking as a possible risk factor (4). No association was noted in our study between smoking and SCC. In our study, the most important risk factors for SCC of the skin in women were agricultural occupation (relative risk [RR] = 1.83) and skin types of 1 or 2 (RR = 1.48) (5).

References


Note

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tumor development. The tumorigenic process can be examined from initiation to promotion to progression and metas-
tasis, as applied to prevention and therapy for the disease. Thus far, the L-
W system has demonstrated that the inci-
cence of metastasizing spontaneous tumors can be reduced from 25.7% to
6.3% by a 30% reduction of daily caloric intake, with the average latent
periods of the tumors extended from 26.6 to 36.7 months, respectively (3).
However, once malignancy developed, dietary restriction was of no therapeutic
benefit. The incidence of large autoch-
thonous testosterone-promoted tumors was changed from 17.5% to 5% by
reduction of dietary fat from 20% to 5%
(4), but such benefit was not demonstra-
able after the development of malign-
cy.

Autochthonous tumorigenesis is the
only acceptable model as a counterpart
to neoplasms in humans. The era of
transplanted tumors as models of human
disease has progressed to studies using
animals with autochthonous tumors.
Transplantation experiments are pre-
ferred because they yield a high volume of results in a relatively short time span;
however, the assessment of those results
does not equate with better under-
standing of the disease. It is time to
move on.

My comments are directed at the sys-
tem, not specifically at the article by
Wang et al. (1).

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References

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lished human prostate LNCaP tumors in nude
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testosterone and high fat diet on the develop-
ment of autochthonous prostate cancer in rats.

Response

In his letter to the editor, Pollard
states that only autochthonous models
have value as tumor models and that
transplantable model systems are only
of historical significance. All models are
imperfect representations of tumors in
humans.

Strong epidemiologic evidence sug-
gests that the worldwide incidence of
microfocal cancers in the prostate is
nearly the same, yet in countries like the
United States, manyfold more prostate
cancers progress to clinically relevant
disease than in Asian Pacific Rim
countries. Thus, it is important to iden-
tify factors that support the growth of
"established" tumors and to determine
whether removal of such "progression" factors might be beneficial in patients
with clinically relevant prostate cancer.

Epidemiologic data strongly suggest
that high levels of fat in the American
diet support tumor progression. Would
reducing dietary fat slow the progres-
sion of prostate cancer in patients and
reduce the recurrence rate expected fol-
lowing therapy for localized disease?
Results using the transplantable human
LNCaP model suggest that a reduction
in dietary fat could be helpful in reduc-
ing the rate of tumor growth (1).

We have also found that a low-fat
diet reduces the growth of orthotopically
transplanted LNCaP cells, which sup-
ports the viability of the LNCaP model
(Corr JC, Fair WR, Heston WD: unpul-
blished results). Most clinically rele-
vant prostate cancers are being detected
and followed by serum prostate-specific
antigen (PSA) measurements. LNCaP is
one of the few models that produces
PSA. We wanted to know whether
modification of dietary fat would inter-
fere with the use of PSA as an inter-
mediary marker of tumor progression
and found that it did not (1). PSA is not
produced by the Lobund-Wistar model
described by Pollard. Indeed, rodent
prostates often differ from human pros-
tates in the type of specific proteins that
are produced.

The identity and pattern of the genetic
abnormalities responsible for the devel-
opment of clinically relevant prostate
cancer in the United States have not
been established. However, it is very
usual to observe the development of
cancer in the seminal vesicles of men.
In the autochthonous tumor in Lobund-
Wistar rats, the development of tumors
of the seminal vesicles are very com-
mon. Thus, one may question whether the
tumor that develops in the Lobund-
Wistar rat is similar to the human dis-
ease.

In an editorial, Jasny (2) states that "It
has been [her] experience that inves-
tigators who deal with model systems
tend to be chauvinistic about their
beasts." Tumor model systems continue
to evolve to better represent the real
thing; nevertheless, each model presently
available has limitations, including
the transplantable LNCaP and autoch-
thonous Lobund–Wistar models. At the
Memorial Sloan-Kettering Cancer Cen-
ter, we hope that we are not chauvinists
and will use all appropriate models to
defeat the real beast.

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