LETTER

Reply to Lopez-Lazaro: Evidence that digoxin inhibits human cancer

We thank Dr. Lopez-Lazaro for his letter (1) raising the issue of whether our findings in mouse xenograft models (2) can be translated to cancer patients. Extensive differences between mice and humans with regard to the pharmacology of digoxin make extrapolation between species unreliable, and therefore it remains to be determined whether digoxin has anticancer effects at doses that are tolerated in humans. However, Dr. Elizabeth Platz (Department of Epidemiology, The Johns Hopkins Bloomberg School of Public Health) has kindly permitted us to cite her unpublished data: In a longitudinal study of 47,759 health professionals, a significantly decreased relative risk for prostate cancer (PCa) was observed among individuals taking digoxin after adjustment for age ($P = 0.001$), multiple variables (diabetes mellitus, physical activity, body mass index, height, family history, race, pack-years smoked, and dietary factors; $P = 0.004$), or multiple variables plus other medications ($P = 0.008$). Although HIF-1α levels in the PCa cases from this study were not determined, HIF-1α levels are increased in high-grade prostatic intraepithelial neoplasia, which is the precursor of invasive PCa (3) and, among PCa patients, increased HIF-1α levels in the diagnostic biopsy are associated with significantly decreased time to disease progression after radiotherapy or prostatectomy (4). Taken together with our preclinical studies (2), the epidemiological and clinical data cited above suggest the need for trials to determine whether digoxin has therapeutic effects in patients with PCa and possibly other cancers in which increased HIF-1α levels are associated with adverse outcome.

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