LETTER

Strengthening the immune system for cancer prevention

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Palmer et al. (1) make the fascinating suggestion that immune system senescence is a better explanation for cancer incidence than the accumulation of random mutations. Specifically, Palmer et al. show that a model based on immune senescence provides a better fit to age-specific cancer incidence than a model based on random mutations. The authors also address the question of whether immune senescence provides a general explanation by showing that the same model can be used for infectious diseases.

Palmer et al. (1) could more explicitly identify how their model explains another key feature of cancer and infectious disease incidence, which would strengthen their argument: that is, the substantially higher rates of cancer in men than in women. In their report, Palmer et al. focus on the role of the thymus in immune senescence and, specifically, naïve T cell production proxied by T cell receptor excision circle DNA, which is higher in women than men. Specifically, identifying and explaining what drives this key difference would provide more insight for translation of the findings to primary care and health policy. Obviously, men could live an unhealthier life than women, making them more vulnerable to random mutations, infections, and falling production of naïve T cells. However, men are more vulnerable to cancer and infections throughout their lives, even at times such as infancy, when a material difference in lifestyle seems unlikely (2, 3). Alternatively, the immune system is known to interact with sex steroids, with thymus function influenced by androgens, such that androgen ablation can reverse thymic atrophy (4). More broadly, given the effects of cancer on lifespan, a difference mediated by sex hormones is also consistent with the well-established evolutionary biology theory that growth—and here specifically reproduction—trades off against longevity (5) potentially in a sex-specific manner (6), given the difference in reproductive potential between men and women (6). As such, sex hormones, as immune modulators, may be modifiable targets of intervention for cancer and infectious disease prevention in public health practice (7).

Palmer et al.'s (1) insightful paper represents a fundamental shift in the focus of cancer prevention from avoiding a variety of mutations to a unifying explanation focusing on strengthening the immune system. The authors draw attention to cancer treatments that increase naïve T cell production. Putting these findings into a broader context within evolutionary biology theory to aid translation, what might also be considered for cancer prevention is repurposing existing treatments that mildly suppress the male reproductive axis. Notably, aspirin appears to have mild effects on testicular function (8), and is increasingly being seen as a possible means of preventing cancer (9) and might now be considered for widespread use, particularly in men. Whether any other preventive interventions with similar properties exist and could be repurposed, such as neurokinin 3 receptor antagonists (10), might also bear consideration.

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