


A Solo Dance or a Tango?

Yulin Wan, Shanshan An, Yanchao Zhou, Man Tang and Qiuyun Liu 

State Key Laboratory of Biocontrol, Biomedical Center, Guangdong Provincial Key Laboratory of Improved Variety Reproduction in Aquatic Economic Animals, School of Life Sciences, Sun Yat-sen University, Guangzhou, China.

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ABSTRACT: Previous studies have identified genetic factors and Epstein-Barr virus underlying nasopharyngeal carcinoma. A hypothesis postulated that the local buildup of HCl, mediated by hydrogen bond donors and acceptors and basic amino acids, causes cancer. Nasopharyngeal carcinoma incidences are high in the humid southern coastal China, Southeast Asia, and Mediterranean regions, but not in the noncoastal and nonhumid southern Yunnan Province, China, and nonhumid Central China. The nearly saturated humidity in the *Huinan* period in Guangdong can trigger the expression of proteins with extensive hydrogen bonding to protons, augmenting the formation of HCl that is mutagenic. Given that the Epstein-Barr virus carries high content of hydrogen bond donors and acceptors, the moist environment in the nasal cavity may enable the virus to colonize the site, compounding pertinent investigations as both virus and high humidity are likely to trigger carcinogenesis. Therefore, the phenomena of exceptionally high humidity in regions with high nasopharyngeal cancer rates warrant further investigations.

KEYWORDS: Nasopharyngeal carcinoma, Epstein-Barr virus, hydrogen bond, proton, humidity, risk factor

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CORRESPONDING AUTHOR: Qiuyun Liu, State Key Laboratory of Biocontrol, Biomedical Center, Guangdong Provincial Key Laboratory of Improved Variety Reproduction in Aquatic Economic Animals, School of Life Sciences, Sun Yat-sen University, Guangzhou 510275, China. Email: lsslyq@mail.sysu.edu.cn

Despite decades of intensive research, the causes of carcinogenesis have not been fully elucidated. Xu et al¹ discovered 3 variants strongly associated with nasopharyngeal carcinoma. The study is provocative and comprehensive. However, cautions should be taken before the benchtop work translates to cancer prevention practice.

Cantonese, the hardest hit subpopulation by nasopharyngeal cancer, carry high risks even after they migrate to other parts of the world,^{2,3} despite that the low-risk Epstein-Barr virus (EBV) subtypes are circulated in those regions. The aforementioned observation suggests that some genetic components are critical for this type of malignancy. A hypothesis attributes cancer onset to the local buildup of HCl, mediated by hydrogen bond donors and acceptors and basic amino acids,^{4,5} accounting for the long but still growing list of oncogenic mutations. Red meat is marked by the presence of myoglobin which carries about 21% positively charged basic amino acids, attracting anions such as Cl⁻ and enhancing the formation of strong acids.⁴ Nasopharyngeal carcinoma is prevalent in the humid southern coastal China, Southeast Asia, and Mediterranean regions, but not in the noncoastal and nonhumid southern Yunnan Province, China, and nonhumid Central China.⁶ The nearly saturated humidity in the so-called *Huinan* period in Guangdong from March to May tend to induce the expression of proteins with extensive hydrogen bonding to water and protons, augmenting the formation of HCl and causing mutations.

Frequent nose bleeding and nasal discharge are symptoms of nasopharyngeal carcinoma, and might also render normal

individuals more susceptible to the onset of nasopharyngeal cancer. This type of phenomena has been documented in colorectal cancer.⁷ Given that the EBV virus harbors high content of hydrogen bond donors and acceptors as well as hydrophilic amino acids such as alanine, the moist environment may help the virus to colonize the nasal cavity, compounding the analysis as both virus and high humidity are likely to contribute to carcinogenesis.

Interestingly, nasopharyngeal carcinoma cases have been in the decline in recent years in South China as well as in Southeast Asia,^{8–10} as the *Huinan* period shortens and the humidity lessens to some extent in Guangdong due to global warming.

In summary, the EBV virus can be the driver, passenger, or both in the onset and progression of nasopharyngeal carcinoma. The discovered associations by Xu et al warrant further investigation to discern the dominant effects of the virus and the near-saturated humidity in the *Huinan* season in Guangdong Province of China.

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Author Contributions

QL contributed to the conception and design of the work. QL, YW, SA, YZ, and MT contributed to the analysis and interpretation of data for the work. QL and YW drafted the manuscript with input from all authors.



ORCID iDQiuyun Liu  <https://orcid.org/0000-0001-5533-0128>**REFERENCES**

1. Xu M, Yao Y, Chen H, et al. Genome sequencing analysis identifies Epstein-Barr virus subtypes associated with high risk of nasopharyngeal carcinoma. *Nat Genet.* 2019;51:1131-1136.
2. Chan SH. Aetiology of nasopharyngeal carcinoma. *Ann Acad Med Singapore.* 1990;19:201-207.
3. Buell P. The effect of migration on the risk of nasopharyngeal cancer among Chinese. *Cancer Res.* 1974;34:1189-1191.
4. Tang M, Zhou Y, Li Y, et al. Hydrogen donors and acceptors and basic amino acids jointly contribute to carcinogenesis. *Med Hypotheses.* 2017;98:42-44.
5. An S, Li X, Tang M, et al. Functional duality of ethanol on cancer. *Med Hypotheses.* 2019;122:124-125.
6. Zou J, Wan Y, Zhuang Z, Wan H, Liu Q. Re: "Active and passive smoking and risk of nasopharyngeal carcinoma: a population-based case-control study in southern China." *Am J Epidemiol.* 2018;187:398.
7. Wan Y, Wen L, Liu Q. Who will benefit from colorectal cancer prevention measures. *Eur J Cancer Prev.* 2019;28:459-460.
8. Li K, Lin GZ, Shen JC, Zhou Q. Time trends of nasopharyngeal carcinoma in urban Guangzhou over a 12-year period (2000-2011): declines in both incidence and mortality. *Asian Pac J Cancer Prev.* 2014;15:9899-9903.
9. Chong VH, Telisinghe PU, Lim E, Abdullah MS, Idris F, Chong CF. Declining incidence of nasopharyngeal carcinoma in Brunei Darussalam: a Three Decade Study (1986-2014). *Asian Pac J Cancer Prev.* 2015;16:7097-7101.
10. Lee AW, Foo W, Mang O, et al. Changing epidemiology of nasopharyngeal carcinoma in Hong Kong over a 20-year period (1980-99): an encouraging reduction in both incidence and mortality. *Int J Cancer.* 2003;103:680-685.