PLOS Science Wednesday: Hi reddit, we're Ke Lan, Xing Wang, and Zhe Zou and our findings help explain why men are more susceptible to Kaposi's sarcoma herpes virus infection than women – Ask Us Anything!

PLOSScienceWednesday [1] and r/Science AMAs[1]

[1]Affiliation not available

April 17, 2023

Abstract

Hi Reddit, My name is Ke Lan and I am a professor and the Director of the State Key Laboratory of Virology at Wuhan University, Wuhan, P.R. China. My researches focus on the mechanism of latent infection and oncogenesis caused by Kaposi's sarcoma-associated herpes virus. Dr. Xing Wang and Mr. Zhe Zou who worked in my lab before will join me to answer questions. Dr. Xing Wang is now a professor at the Department of Gastroenterology, Xinqiao Hospital affiliated to the Third Military Medical University, Chongqing, P.R. China. And, Mr. Zhe Zou is now a technician at the Department of Gastroenterology, Xinqiao Hospital affiliated to the Third Military Medical University, Chongqing, P.R. China. We recently published an article titled "Male hormones activate EphA2 to facilitate Kaposi's sarcoma-associated herpesvirus infection: Implications for gender disparity in Kaposi's sarcoma" in PLOS Pathogens. Previous studies have shown that the incidence of Kaposi's sarcoma is higher in males, however the reason has not been addressed. In our study, we found that male hormones and its receptor (AR) can promote KSHV infection by activating an important cellular signaling pathway. Our findings suggested that males are more vulnerable to infection of KSHV due to the male hormones, providing an explanation to the higher incidence of Kaposi's sarcoma in males. We will be answering your questions at 1pm ET – Ask Us Anything!

the WINNOWER

REDDIT

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PLOSSCIENCEWEDNESDAY R/SCIENCE

Hi Reddit,

My name is Ke Lan and I am a professor and the Director of the State Key Laboratory of Virology at Wuhan University, Wuhan, P.R. China. My researches focus on the mechanism of latent infection and oncogenesis caused by Kaposi's sarcoma-associated herpes virus.

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Hi all, and thank you for doing this AMA.

How robust is the data suggesting that Kaposi sarcoma is more common in men? My recollection is that early studies suggested women only accounted for ~10% of KS cases, but now they account for nearly half. The way this was explained to me was that KS manifests differently in women - they are younger at time of presentation and have more extensive cutaneous disease - so they were not given a KS diagnosis. How about outcomes data? Is there robust evidence for a gender bias here?

SirT6

Ke & Xing & Zhe: Kaposi's sarcoma (KS) is classified into 4 clinical types, at least the classical and endemic types with KSHV infection and without HIV coinfection, occurs disproportionately in men. As we mentioned in our paper, a number of previous epidemiology studies showed that the age-standardized incidence rate of KS was 12.3 and 4.6 per 100,000 in African males and females, respectively. In older age groups, KS was about 10 times more common in males. Regarding the gender-associated seroprevalence of KS-associated herpesvirus (KSHV), the causative agent of KS, a recent evidence-based meta-analysis indicated that KSHV preferentially infects males in Africa, and a

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significantly higher quantity of KSHV DNA has been detected in men than women. Reference: 1. Parkin, D. M. et al. Part I: Cancer in Indigenous Africans--burden, distribution, and trends. The Lancet. Oncology 9, 683-692, doi:10.1016/S1470-2045(08)70175-X (2008). 2. Begré, L., Rohner, E.,Mbulaiteye, S. M., Egger, M. & Bohlius, J. Is human herpesvirus 8 infection more common in men than in women? Systematic review and meta-analysis. International Journal of Cancer,doi:10.1002/ijc.30129 (2016).

Hello! Thank you for doing this AMA, and for your research.
Bearing in mind this is very much not my field, can you explain how it is that male hormones introduce this vulnerability?

StonedPhysicist

Ke: In our study, we have confirmed the role of both AR and its ligand in promoting KSHV primary infection in target cells. Meanwhile, AR inhibition led to a dramatically decreased number of perinuclear-accumulated virus particles during early KSHV entry stage. Mechanically speaking, the effect was resulted from the interaction of AR with a known KSHV entry receptor EphA2. We found that AR can promote the phosphorylation of EphA2 at residue Ser897, which is critical for successful KSHV infection.

Hello. Can this receptor be influenced or modified to reject the bad code. Like a firewall or a moat. I have little knowledge in this area so please forgive.

yesmaybeyes

Ke & Xing: Thanks for asking. In theory, it can be influenced. But the risk would be high if the receptor to be directly editted. The clinical implications of these findings include two aspects: Firstly, the reasonable inhibition to male sex steroids in those advanced KS patients may lead to clinical advantage. Because in KS lesion, the vast majority of KS spindle cells are latently infected with KSHV, however the virus in a small proportion of the infected cells can undergoes lytic replication spontaneously leading to the production of mature virus. Our finding postulated a novel role of male hormones as internal stimuli that facilitate the secondary infection by those newly made virus which contribute to the pathogenesis. Secondly, we found that the phosphorylation of the Ser897 of KSHV entry receptor EphA2 may provide a potential therapeutic target for KS patient.

Given the potential infection-promoting role of AR, would it be possible to retrospectively examine the incidence of KSHV infection in populations that have been using AR inhibitors? I suppose this information might not be available.

RhyDonCorleone

It would be interesting to examine. To our knowledge, the information is not available as you said. Thank you.

Can we still ask a question?

mom4tabj

Yes.