清华团队 Nature 揭示寨卡病毒感染暴发机制

Tsinghua University Has Reported the Evolutionary enhancement of Zika virus infectivity in Aedes aegypti mosquitoes

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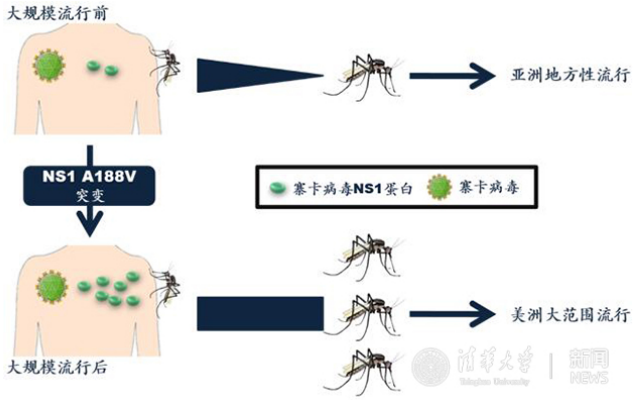
5 月 25 日，Nature 发表了题为《进化导致寨卡病毒在埃及伊蚊上感染力增强》(Evolutionary enhancement of Zika virus infectivity in Aedes aegypti mosquitoes)的研究论文。该研究发现，由于病毒位点发生突变，导致亚洲系寨卡病毒感染埃及伊蚊的能力增强。这项发现为解释近年来寨卡病毒暴发流行提供了科学依据。

蚊媒传染病是通过蚊虫叮咬传播给人类及动物宿主的一大类疾病。近年来，多种新发及再发病毒性蚊媒传染病，包括寨卡病毒（ZIKV）、登革病毒（DENV）和乙型脑炎病毒（JEV）等，对人类健康产生了严重威胁。寨卡病毒在进化过程中分为两个世系:一个是非洲世系，主要在非洲的丛林中循环传播；另一个是亚洲世系，主要在东南亚等地区流行。2015 年起，由亚洲系寨卡病毒主导的寨卡疫情在南美洲暴发，并迅速扩散到 40 多个国家，引起胎儿小头畸形和格林巴氏综合症，造成上百万人感染。2016 年世界卫生组织宣布，寨卡病毒的暴发流行已是全球紧急公共卫生事件。



寨卡病毒 NS1 蛋白 188 位点氨基酸突变导致蚊虫带毒率上升，促使寨卡病毒大范围流行。在自然界中，蚊媒病毒在“宿主-蚊虫”之间传播循环。蚊虫可以通过吸血从已被感染的宿主血液中吸取病毒，并获得感染。之前的研究表明，登革病毒和乙型脑炎病毒的非结构蛋白 NS1 可以被大量分泌到感染宿主的血液中。病毒分泌的 NS1 蛋白会与病毒同时被吸食到蚊虫体内，通过抑制蚊虫中肠的免疫系统来辅助病毒感染蚊虫。在程功课题组的研究中，研究者发现寨卡病毒的 NS1 蛋白同样也具有辅助病毒感染蚊虫的功能。亚洲系寨卡病毒非结构蛋白 NS1 上的一个氨基酸位点突变 (NS1 A188V) 导致 NS1 蛋白的分泌能力增强，使得病毒可以更高效地感染蚊虫、导致蚊虫病毒感染率大幅上升，这可能是造成寨卡病毒大范围流行的原因。这一研究为解释近年来寨卡病毒暴发流行提供了科学依据。

Evolutionary enhancement of Zika virus infectivity in Aedes aegypti mosquitoes

进化导致寨卡病毒在埃及伊蚊上感染力增强

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Zika virus (ZIKV) remained obscure until the recent explosive outbreaks in French Polynesia (2013–2014) and South America (2015–2016)1, 2, 3. Phylogenetic studies have shown that ZIKV has evolved into African and Asian lineages. The Asian lineage of ZIKV was responsible for the recent epidemics in the Americas1, 3. However, the underlying mechanisms through which ZIKV rapidly and explosively spread from Asia to the Americas are unclear. Non-structural protein 1 (NS1) facilitates flavivirus acquisition by mosquitoes from an infected mammalian host and subsequently enhances viral prevalence in mosquitoes4. Here we show that NS1 antigenaemia determines ZIKV infectivity in its mosquito vector Aedes aegypti, which acquires ZIKV via a blood meal. Clinical isolates from the most recent outbreak in the Americas were much more infectious in mosquitoes than the FSS13025 strain, which was isolated in Cambodia in 2010. Further analyses showed that these epidemic strains have higher NS1 antigenaemia than the FSS13025 strain because of an alanine-to-valine amino acid substitution at residue 188 in NS1. ZIKV infectivity was enhanced by this amino acid substitution in the ZIKV FSS13025 strain in mosquitoes that acquired ZIKV from a viraemic C57BL/6 mouse deficient in type I and II

interferon (IFN) receptors (AG6 mouse). Our results reveal that ZIKV evolved to acquire a spontaneous mutation in its NS1 protein, resulting in increased NS1 antigenaemia. Enhancement of NS1 antigenaemia in infected hosts promotes ZIKV infectivity and prevalence in mosquitoes, which could have facilitated transmission during recent ZIKV epidemics.