Diverse Patterns of Simian Foamy Virus (SFV) Transmission to Humans

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Simian foamy viruses (SFVs) are retroviruses that are enzootic but non-pathogenic in most non-human primates (NHPs). Humans are not infected with their own foamy virus variant; however, SFVs are transmitted from NHPs to humans more frequently than any other retrovirus. Therefore, SFV transmission provides an excellent model to explore factors that permit viruses to cross species barriers. Historically, this research has primarily focused on humans that were infected by SFV through occupational contact with primates, including laboratory workers and African bushmeat hunters. However, in a recent study published in *Emerging Microbes and Infections*, the laboratories of Drs. Lisa Jones-Engel (University of Washington) and Maxine L. Linial (Basic Sciences Division) along with an international team of collaborators in Bangladesh shift this focus to Asia, where human interactions with macaques are frequently part of everyday life.

To investigate the zoonotic transmission of SFVs to humans, the researchers tested humans from five urban sites and one group of nomadic people in Bangladesh for evidence of infection with SFV. More than 50% of the people sampled by the research team reported at least one previous bite from a rhesus macaque, reflective of the frequent contact between humans and macaques in this region. Approximately 8% of the people tested were positive for SFV by Western blot or PCR, and there was a positive correlation between age and PCR-positive status ($p=0.0085$). No other factors in the study population, including sex and geographic location, were found to significantly correlate with persistent SFV infection. However, it is unclear from this study whether the increased risk with age is caused by cumulative exposure over time or if it is due to altered immune function in older individuals or some other factor.

To determine whether some virus variants were preferentially transmitted to humans, the researchers sequenced a highly variable region of the SFV gag gene that allows identification of six different core strains of the virus in rhesus macaques (Feeroz et al., 2013; Soliven, et al., 2013). With one exception, all of the human sequences matched one of these six previously defined core strains. Every SFV-positive human was infected with the core strain that was most abundant in the macaques in that geographical region. In addition, the researchers found four people that were also additionally infected with an SFV strain from a more distant geographical region. This is the first time co-infection has been found in humans. Some of these individuals were infected with two virus

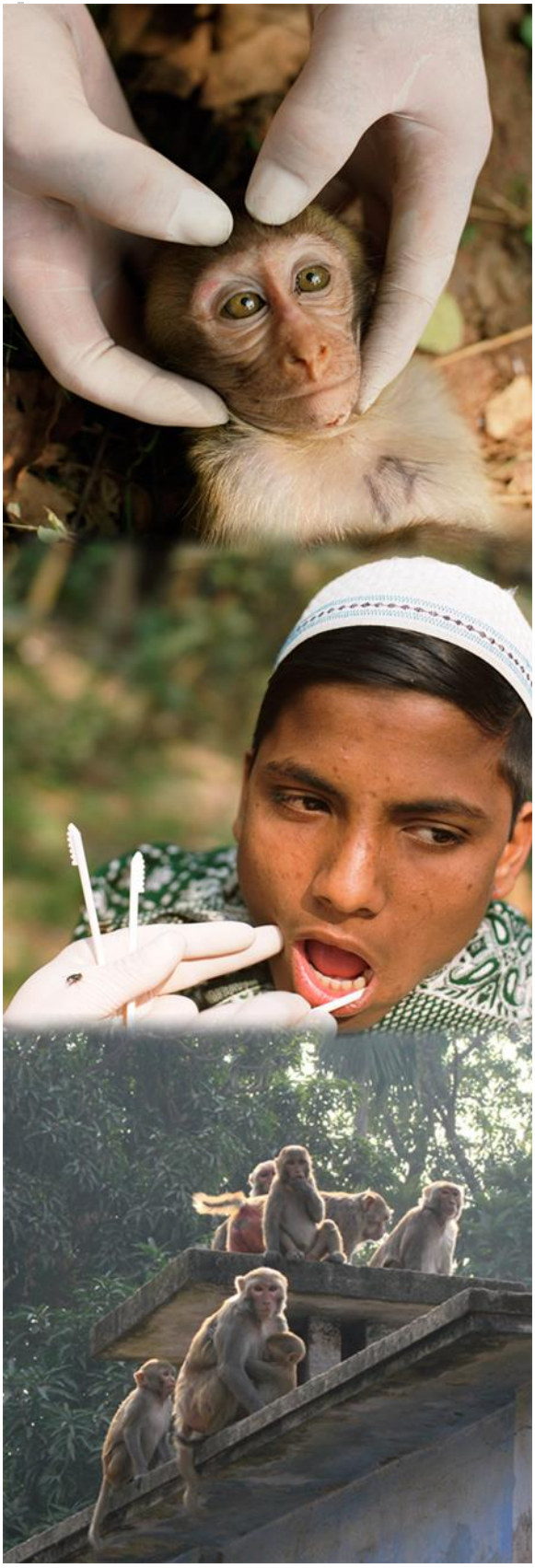
strains known to be predominant in regions hundreds of kilometers apart with no contiguous monkey habitat between the two regions, raising the possibility that human-facilitated movement of these animals may contribute to the diversity of strains infecting humans. An additional report revealed that SFV may undergo at least one round of replication in humans (Matsen, et al., 2014), an observation that raises the possibility that viral recombination may drive viral diversity in co-infected humans and macaques.

This study expands our understanding of cross-species SFV transmission caused by routine human-animal contact. "Foamy viruses so far have not developed into a pathogenic variant, but this is always a possibility. Understanding how to prevent infection is important," said Dr. Maxine L. Linial. Another intriguing finding for the researchers was that owners of pet and performing monkeyss, who are in life-long contact with macaques, have to date shown no evidence of persistent infection with SFV. "This surprising finding raises the possibility that people who come into contact with macaques at a young age develop neutralizing antibodies that prevent infection," said Dr. Maxine L. Linial. "I will be going to Bangladesh this Fall as a Fulbright Scholar to spend several months with the nomadic performing monkey owners to learn more about their movement through the region, their animal acquisition, husbandry and exposures, and to collect additional samples," said Dr. Lisa Jones-Engel.

Engel, G.A., Small, C.T., Soliven, K., Feeroz, M.M., Wang, X., Hasan, M.K., Oh, G., Alam, S.M.R., Craig, K.L., Jackson, D.L., Matsen, F.A., Linial, M.L., Jones-Engel, L. 2013. Zoonotic simian foamy virus in Bangladesh reflects diverse patterns of transmission and co-infection. *Emerg Microbes Infec* 2, e58; doi:10.1038/emi.2013.60

See also: Feeroz, M.M., Soliven, K., Small, C.T., Engel, G.A., Pacheco, MA., Yee JL, Wang, X, Hasan, KM, Oh, G., Levine, K.L., Alam, S.M.R., Craig, K.L., Jackson, D.L., Lee , E.G., Barry, P.A., Lerche, N.W., Escalante, A.A., Matsen, F.A., Linial, M.L., Jones-Engel, L., Wang, X., Hasan, M.K., Oh, G., Alam, S.M.R., Craig, K.L., Jackson, D.L., Matsen, F.A., Linial, M.L., Jones-Engel, L. 2013. Population dynamics of rhesus macaques and associated foamy virus in Bangladesh. *Emerg Microbes Infec* 2, e29; doi:10.1038/emi.2013.23

See also: Soliven K, Wang X, Small CT, Feeroz MM, Lee EG, Craig KL, Hasan K, Engel GA, Jones-Engel L, Matsen FA 4th, Linial ML. 2013. Simian foamy virus infection of rhesus macaques in Bangladesh: relationship of latent proviruses and transcriptionally active viruses. *J Virol* 13628-39.



Images courtesy of Lynn Johnson (top and middle) and Lisa Jones-Engel (bottom)

Casual contact between humans and rhesus macaques in Bangladesh. Collecting saliva samples from a rhesus macaque (top) and a human (middle). Urban monkeys at dawn (bottom).