

## ABSTRACT

**Background:** Altered susceptibility to HIV-1 infection has been observed in a commercial sex worker (CSW) cohort in Nairobi, Kenya, where a subset of women are classified as HIV-1 exposed yet seronegative (HESN). A gene expression analysis conducted showed differential regulation of the glycolysis/gluconeogenesis pathway in HESN CSWs. The first and potentially critical regulatory step in glucose metabolism is its entry into lymphocytes, where glucose binds to Hexokinase-1 that prevents it from leaking out. Together with the Glucose Transporter 1, Hexokinase-1 regulates the first rate-limiting steps of the entire glucose metabolism by phosphorylating glucose into glucose-6-phosphate, which is the starting material for glycolysis.

**Methods:** The study population was randomly selected from the Pumwani Sex Worker Cohort, Nairobi including: HIV highly exposed yet seronegative (HESNs) CSWs (>7 years); newly enrolled HIV-uninfected (<3 years) CSWs, 85% of whom would likely seroconvert to HIV-1 positive; and lowly-exposed HIV negative antenatal clinic attendees with low exposure to HIV. Total RNA was extracted from PBMCs using Trizol; cellular Hexokinase-1 mRNA levels were quantified by quantitative real time PCR using SYBR Green. Statistical analysis was performed using Mann-Whitney U Test. Differences were considered to be significant if  $P < 0.05$ . Each assay was normalized using 18s rRNA gene.

**Results:** We observed significantly lower level of Hexokinase-1 mRNA expression in HESNs when compared to that in newly enrolled HIV uninfected CSWs (Hexokinase-1  $p = 0.0323$ ).

Furthermore, the levels of Hexokinase-1 mRNA in HESN and the HIV negative antenatal clinic attendees were quite similar (Hexokinase-1  $p = 0.6448$ ).

**Conclusions:** Lower expression of Hexokinase-1 in HESN might suggest lower regulation of glucose uptake. Hexokinase is a rate-limiting enzyme in the glycolysis pathway. Following studies of expression and uptake are underway to understand its role in glucose metabolism in HIV resistance.