

Driving incident HIV infections to 0 is the goal of many if not all regional departments of public health. This requires knowledge of which populations may serve as an important promoters of HIV transmissions in the region, and interventions that may prevent those transmissions. While we have a general idea of what types of interventions prevent infections, we don't have a good understanding of the relative benefits of one program over another. To most efficiently prevent HIV transmission, we need to know more than if something works, we need to know how well it works, not just how well we can administer it. Molecular epidemiology is a tool that may provide some of these answers. Combining these analyses with detailed collection of demographic and risk data, data about existing prevention programs, and incidence testing, could provide a road-map for a more efficient and effective public health response.

Prevention requires early diagnosis, engagement and treatment of people with HIV (PWH) as well as behavioral and biomedical prevention interventions among vulnerable persons without HIV infection (PWoH). Here we propose a study to use ME to better understand the impacts of existing prevention programs in LA County. We will characterize and estimate the impact of selected regional providers contracted to provide prevention and treatment services (e.g., homeless outreach).

**Specific Aim 1. Identify groups that are high priority for prevention and engagement efforts.** To identify these priority populations we will use 3 approaches. First, we will standard epidemiologic techniques to identify geographic and demographic hotspots across the county with higher numbers of new diagnoses and incident infections. Second, we will use network analysis to identify clusters of genetically linked infections and identify the demographic and geographic factors associated with newly diagnosed, linked infections (over the past 2 years). Third, we will use phylodynamic approaches to characterize the relative flow of HIV into/out of specific regions or groups to determine which of these populations are disproportionately contributing to transmissions throughout the LA County.

*Hypothesis: A high priority population (i.e., PWID, TW, geographic groups, etc.) will be associated with at least two of the three measures of transmission activity (epidemiologic hotspot, clusters of newly diagnosed, linked infections, flow into/out-of the identified region) compared to non-priority populations that are associated with  $\leq 1$  of these measures.*

**Specific Aim 2. Evaluate the effectiveness of LA County prevention programs directed to PWH and PWoH.** We will measure program effectiveness by changes in the following metrics before and after 6-month periods of program activity: 1) number of new HIV diagnoses, 2) number of incident infections, 3) new linked infections, and 4) changes in phylodynamic flows into/out of the specific populations prioritized by the prevention program. We will weight the outcomes of these contracted services by number of clients reached and further adjust by funding allocated to the program.

*Hypothesis: A harm reduction program directed to PWID in the Skid Row neighborhood of LA will demonstrate a reduction in new linked infections and transmissions from Skid Row to the rest of LA County.*

**Specific Aim 3. Model the cost effectiveness of scaling programs that meet effectiveness thresholds in Aim 2 within key populations.**

*Hypothesis:*