## Tyrosine470 and 88 of human dopamine transporter are responsible for the allosteric modulatory effect of SRI-30827, SRI-20041 and HIV-1 tat protein on dopamine transporter

Jun Zhu [1,*], Wei-lun Sun [2], Subramaniam Ananthan [3], Chang-guo zhan [1,2,3]

[1] *Drug Discovery and Biomedical Sciences, South Carolina College of Pharmacy, University of South Carolina, Columbia, SC, United States*
[2] *Drug Discovery and Biomedical Sciences, University of South Carolina, Columbia, SC, United States*
[3] *Organic Chemistry, Southern Research Institute, Birmingham, AL, United States*

**Aims:** The current study assessed whether SRI-20041 and SRI-30827, via an allosteric modulation of tyrosine470 and 88 sites of human dopamine (DA) transporter (hDAT), pharmacologically block Tat binding to DAT.

**Methods:** Mutations of tyrosine470 and 88 of hDAT (Y470H and Y88F) were generated by site-directed mutagenesis. We performed [$^3$H]DA uptake and [$^3$H]WIN35,428 binding assays in PC12 cells transiently transfected with WT and mutated hDAT in the presence of SRI-20041, SRI-30827, cocaine or Tat.

**Results:** Tat (140 nM) induced a 35% reduction of [$^3$H]DA uptake in WT hDAT but not in Y470H and Y88F. SRI-20041 and SRI-30827 produced a 30% increase in IC50 value for cocaine inhibiting [$^3$H]DA uptake in WT hDAT, however, the effect of the two SRI-compounds on cocaine IC50 was attenuated in Y470H and Y88F. Cocaine-induced dissociation rate in WT was similar to that in Y88F, but was decreased in Y470H. Compared to cocaine alone, the addition of SRI-20041 or SRI-30827 following the addition of cocaine slowed the dissociation rate of [$^3$H]WIN35,428 binding in WT hDAT, however, the effect of SRI compounds on cocaine-induced dissociation was attenuated in Y470H and Y88F.

**Conclusions:** These results indicate that tyrosine470 and 88 may act as allosteric modulatory sites on DAT responsible for SRI-20041, SRI-30827, and Tat. From these findings, developing therapeutic agents targeting tyrosine470 or 88, such as SRI-30827 could provide a viable approach for overcoming HIV infection-induced neurologic impairments.

**Financial support:** NIH grant R01DA035714.

http://dx.doi.org/10.1016/j.drugalcdep.2016.08.613

## Gender disparities in HIV prevalence and risk behaviors among people who inject drugs in Tajikistan

William Zule [1,*], David Otiashvili [2], Alisher Latypov [3], Steffani Bangel [1], Wendee Wechsberg [1]

[1] *RTI International, Durham, NC, United States*
[2] *Addiction Research Center, Alternative Georgia, Tbilisi, GA, United States*
[3] *Management Sciences for Health, Leadership, Management and Governance, Kiev, Ukraine*

**Aims:** HIV among people who inject drugs (PWID) is a serious public health problem in Tajikistan and other Central Asian republics, yet relatively few studies have been conducted among PWID in Tajikistan and almost nothing is known about females who inject drugs. This presentation will examine gender differences in HIV status, injection risk behaviors and sex risk behaviors among PWID in Tajikistan.

**Methods:** Needle and syringe program staff recruited 200 PWID in two Tajikistan cities, Khudjand ($n$ = 100) and Kulob ($n$ = 100), in 2015. All participants completed a brief interview and were tested for HIV. We conducted bivariate analyses to assess gender differences in the sample. We conducted multiple logistic regression analyses to determine if gender was independently associated with HIV status, injection risk, sex risk, and a history of substance abuse treatment.

**Results:** The sample included 27 females and 173 males. HIV prevalence was 44% among females and 24% among males. Among participants who tested positive for HIV, 83% of females and 63% of males were unaware that they were infected with HIV. In multivariable models, female gender was associated with increased odds of testing positive for HIV (odds ratio [OR] = 2.71; 95% confidence interval [CI] = 1.08, 6.80), reporting any direct or indirect needle sharing in the past year (OR = 9.08; 95% CI = 2.31, 35.71), and reporting unprotected sex in the past 30 days (OR = 3.40; 95% CI = 1.08, 10.70). Gender was not significantly associated with a history of substance abuse treatment in the models.

**Conclusions:** Efforts are needed to increase HIV testing among PWID in Tajikistan and to reduce risk behaviors, particularly among females.

**Financial support:** This research was supported by NIH grant number R34DA035094 from the National Institute on Drug Abuse.

http://dx.doi.org/10.1016/j.drugalcdep.2016.08.614

## Drug users' advice on enrollment and retention in health research

Abigail Zulich [*], Amy Elliott, Catherine Woodstock Striley, Linda Cottler

*Epidemiology, University of Florida, Gainesville, FL, United States*

**Aims:** Recruitment and retention are key to the success of health research studies. We gathered advice from drug users in the NIDA-funded study, the Transformative Approach to Reduce Research Disparities Towards Drug Users, to improve enrollment and retention rates in future studies.

**Methods:** Through the HealthStreet community engagement model, participants were recruited for a 90-day intervention to increase drug users' enrollment in research. At 90 days, 209 drug users were asked, through open-ended questions, what researchers should do to make studies easier to enroll in and stay in until completion. Responses were coded and placed into one or more categories.

**Results:** Nearly three-quarters (72%; $n$ = 150) of the sample mentioned something other than being satisfied with the study process or having no advice to give; these comments made up the Analyzable Category (AC) and are reported here. Of these 150 participants, 73% mentioned that logistics like Exclusion Criteria, Flexibility, Contact, Remuneration, or Transportation, were key to increasing enrollment and retention rates. Additionally, 38% of comments in the AC pertained to non-logistics like Advertisement/Outreach, Research Staff Attributes, or Transparency. Contact, Remuneration, and Advertisement/Outreach were mentioned most frequently. Drug users brought up the importance of appointment reminders and regular contact with the study team as well as the amount and the timing of remuneration. Many mentioned that people did not participate in research because they were not aware of the opportunities, emphasizing that advertisement and outreach efforts would increase enrollment.

**Conclusions:** With special attention to the feedback of drug users who have participated in health studies, rates of recruit-