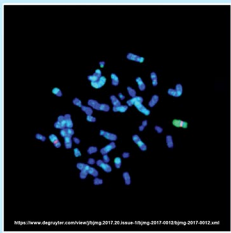


SHAN YU

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Active (blue/pink) & inactive (green/pink)
female X chromosome

Expression Levels of *XIST* RNA Predict PTSS and Chronic Pain Outcomes in Women Experiencing Motor Vehicle Collision

Posttraumatic stress symptoms (PTSS) and chronic posttraumatic pain (CPTP) are frequent co-morbid sequelae of trauma that are more prevalent in women than in men. X chromosome inactivation (XCI) is one candidate mechanism contributing to increased PTSS and CPTP burden in women, and the long non-coding RNA, X-inactive specific transcript (*XIST*) is known to be a major regulator of XCI. Previous studies have shown that 1) *XIST* RNA is over-expressed in females with major affective disorders, and 2) genes that escape XCI are associated with depression, bipolar disorder, and mental impairment. In the current study, we hypothesized that high *XIST* levels predict PTSS and CPTP in women experiencing motor vehicle collision (MVC), one of the most common forms of life-threatening trauma exposure in industrialized nations. African American women age 18 to 65 present in the emergency department after MVC were enrolled, and blood RNA were collected and sequenced (Illumina HiSeq, n=120). PTSS and CPTP were assessed 6 weeks, 6 months, and 1 year after MVC using standardized questionnaires. Repeated measures linear regression analyses were used to evaluate the relationships among *XIST* RNA, escapee transcripts, and clinical outcomes. *XIST* RNA expression levels predicted both PTSS (F=4.436, p=0.036) and CPTP severity (F=4.514, p=0.034). For both outcomes, higher *XIST* RNA expression levels were associated with increased risk. This relationship was also observed in blood and central nervous tissue from rat animal models. Further, of the 97 genes shown previously to be escapees of XCI, 74/97 (76%) exhibited evidence of escape in this cohort, 16/74 (22%) significantly predicted PTSS, and 47/74 (64%) significantly predicted CPTP (p<0.05). These data suggest that *XIST* and related X-chromosome transcript levels predict PTSS and CPTP outcomes in women experiencing MVC trauma.