The plasminogen activator system is composed of two plasminogen activators (tissue type and urokinase type), two specific inhibitors (type 1 and 2), and a membrane-anchored urokinase-type plasminogen-activator-specific receptor (uPAR). This system plays an important role in various biological processes including synaptic plasticity and remodeling in the central nervous system. In the mesolimbic dopaminergic system, these two mechanisms represent a crucial part in the development of drug dependence. Previous studies have shown that psychostimulants induce both tissue type- (tPA) and urokinase-plasminogen activator (uPA) in acute and chronic drug delivery (Bahi et al., 2007), but uPA induction is specific to cocaine. However the function of this induction is still unknown in cocaine addiction. With a specific doxycline-regulatable lentiviral expression system, we will characterize the role of uPA in the development of cocaine addiction. Over-expression or suppression of uPA will show the role of uPA in a rat self-administration behavioral paradigm. We will also show by molecular biological technics like qRT-PCR, Western-blot, immunohistochemistry and in situ hybridization approaches, which intracellular pathways are involved in the function of uPA in cocaine addiction. These new knowledge will allow to implicate uPA as a new target for therapeutic researches against cocaine addiction.