Gene and cell therapy on the acquisition and relapse-like binge drinking in a model of alcoholism: translational options

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Studies reviewed show that lentiviral gene therapy directed either at inhibiting the synthesis of brain acetaldehyde generated from ethanol or at degrading brain acetaldehyde fully prevent ethanol intake by rats bred for their high alcohol preference. However, after animals have chronically consumed alcohol, the above gene therapy did not inhibit alcohol intake, indicating that in the chronic ethanol intake condition brain acetaldehyde is no longer the compound that generates the continued alcohol reinforcement. Oxidative stress and neuroinflammation generated by chronic ethanol intake are strongly associated with the perpetuation of alcohol consumption and alcohol relapse ?binge drinking?. Mesenchymal stem cells, referred to as guardians of inflammation, release anti-inflammatory cytokines and antioxidant products. The intravenous delivery of human mesenchymal stem cells or the intranasal administration of mesenchymal stem cell-generated exosomes reverses both (i) alcohol-induced neuro-inflammation and (ii) oxidative stress, and greatly (iii) inhibits (80?90%) chronic alcohol intake and relapse binge-drinking. The therapeutic effect of mesenchymal stem cells is mediated by increased levels of the brain GLT-1 glutamate transporter, indicating that glutamate signaling is pivotal for alcohol relapse. Human mesenchymal stem cells and the products released by these cells may have translational value in the treatment of alcohol-use disorders.