

# **A CELL-PERMEABLE PEPTIDE DERIVED FROM CAVEOLIN-1 REDUCES BLOOD PRESSURE IN AWAKE MICE**

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Nitric oxide is a gaseous second messenger molecule that is produced by the enzyme endothelial nitric oxide synthase (eNOS) in vascular endothelial cells and causes vasorelaxation. Recently, we developed a cell permeable peptide which increases eNOS activity *in vitro*, apparently by disrupting tonic negative regulation by the endogenous protein caveolin-1. Here, we sought to determine whether the peptide was active *in vivo*.

We measured blood pressure in awake mice using a tail cuff system. Blood pressure was determined at baseline, and at one hour following intra-peritoneal injection of either a control peptide ("AP") or varying concentrations of active peptide ("AP-Cav-3PM"). Both WT and eNOS KO mice were studied and mean changes in BP following peptide injection are presented.

<u>Mouse</u>	<u>Conc.</u>	<u>Peptide</u>	<u><math>\Delta</math> Mean BP (mmHg) mean (S.E.M.)</u>
WT	4mg/kg	AP	-4.6 (5.6)
WT	4mg/kg	AP-Cav-3PM	-21.3 (3.9)*
WT	1mg/kg	AP	-2.4 (2.1)
WT	1mg/kg	AP-Cav-3PM	-17.1 (6.4)*
WT	0.1mg/kg	AP	-4.1 (4.4)
WT	0.1mg/kg	AP-Cav-3PM	4.2 (3.5)
eNOS KO	4mg/kg	AP-Cav-3PM	2.8 (12.3)

(\*,  $p < 0.04$  for active vs. control peptide)

In summary, the active peptide (but not a control peptide) caused a dose-dependent decrease in blood pressure in awake mice.

The peptide had no effect in eNOS KO mice, which suggests that it acts via an eNOS-dependent mechanism.