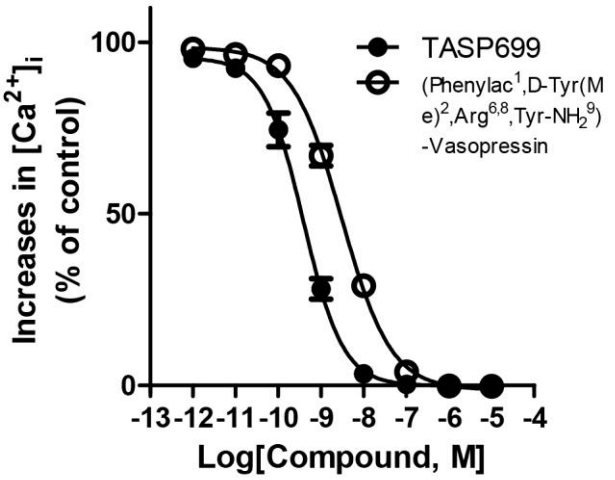


**Supplemental Figure 1**

Inhibitions of AVP-induced increases of $[Ca^{2+}]_i$ as a function of concentrations of TASP699 and [phenylac$^1$,D-Tyr(Me)$^2$,Arg$^{6.8}$,Tyr-$NH_2^9$]-vasopressin as a positive control. Data represent the average percentage of the control response without test compounds from three experiments performed in duplicate. A nonlinear fit was applied to the measured data.

**Supplemental Table 1**

Binding of TASP699 to off-target G protein-coupled receptors, transporters, and ion channels

Values are expressed as the means of the percent inhibition of control-specific binding performed in duplicate.

| Target molecule (species) | % inhibition at 1 μM |
|---|---|
| Adenosine $A_1$ (human) | 2.05 |
| Adenosine $A_{2a}$ (human) | 0.00 |
| Adenosine $A_3$ (human) | 3.67 |
| Adenosine transporter (guinea pig) | 7.03 |
| $\alpha_{1A}$-Adrenergic (rat) | 0.97 |
| $\alpha_{1B}$-Adrenergic (rat) | 0.21 |
| $\alpha_{2A}$-Adrenergic (human) | 6.89 |
| $\alpha_{2B}$-Adrenergic (human) | 6.00 |
| $\alpha_{2C}$-Adrenergic (human) | 0.00 |
| $\beta_1$-Adrenergic (human) | 1.14 |
| $\beta_2$-Adrenergic (human) | 1.69 |
| Angiotensin $AT_1$ (human) | 1.51 |
| Angiotensin $AT_2$ (human) | 4.28 |
| Androgen (rat) | 1.19 |
| Bradykinin $B_1$ (human) | 0.00 |
| Bradykinin $B_2$ (human) | 6.10 |
| Bombesin (rat) | 0.90 |
| $Ca^{2+}$ channel (type L, benzothiazepine) (rat) | 5.09 |
| $Ca^{2+}$ channel (type L, dihydropyridine) (rat) | 1.14 |
| $Ca^{2+}$ channel (type L, phenylalkylamine) (rat) | 1.83 |
| $Ca^{2+}$ channel (type N) (rat) | 0.35 |
| Cannabinoid $CB_1$ (human) | 0.00 |

| | |
|---|---|
| Cannabinoid $CB_2$ (human) | 0.00 |
| CCK $_A$ (human) | 1.53 |
| CCK $_B$ (human) | 3.49 |
| $CRF_1$ (human) | 0.00 |
| Dopamine $D_1$ (human) | 1.57 |
| Dopamine $D_2$ short (human) | 3.49 |
| Dopamine $D_3$ (human) | 1.84 |
| Dopamine $D_{4.2}$ (human) | 1.30 |
| Dopamine $D_5$ (human) | 0.00 |
| Dopamine transporter (human) | 0.46 |
| Estrogen (rat) | 0.00 |
| Endothelin $ET_A$ (human) | 0.00 |
| Endothelin $ET_B$ (human) | 0.00 |
| GABA $_A$ (agonist Site) (rat) | 0.00 |
| GABA $_A$ (benzodiazepine site) (rat) | 0.85 |
| GABA $_A$ (chloride channel) (rat) | 3.50 |
| GABA $_B$ (rat) | 7.74 |
| GABA transporter (rat) | 0.00 |
| Glucocorticoid (human) | 0.06 |
| Glutamate (AMPA) (rat) | 0.00 |
| Glutamate (kainate) (rat) | 0.00 |
| Glutamate (NMDA agonist site) (rat) | 0.00 |
| Glutamate (NMDA glycine site) (rat) | 0.81 |
| Glutamate (NMDA phencyclidine site) (rat) | 0.70 |
| Glutamate (NMDA polyamine site) (rat) | 0.00 |
| Glycine (strychnine-sensitive) (rat) | 0.06 |
| Histamine $H_1$ (human) | 0.00 |
| Histamine $H_2$ (human) | 3.75 |
| Histamine $H_3$ (human) | 9.07 |
| Imidazoline (central) (rat) | 3.26 |
| $IP_3$ (rat) | 1.42 |

| | |
|---|---|
| $K^+$ channel $K_A$ (rat) | 0.00 |
| $K^+$ channel $K_{ATP}$ (rat) | 2.57 |
| $K^+$ channel $SK_{Ca}$ (rat) | 6.24 |
| Leukotriene $B_4$ (guinea pig) | 5.27 |
| Leukotriene $D_4$ (guinea pig) | 0.00 |
| Melatonin $MT_1$ (human) | 0.97 |
| Monoamine transporter (Rabbit) | 1.47 |
| Muscarinic $M_1$ (human) | 0.26 |
| Muscarinic $M_2$ (human) | 0.38 |
| Muscarinic $M_3$ (human) | 4.83 |
| Muscarinic $M_4$ (human) | 1.06 |
| Muscarinic $M_5$ (human) | 6.41 |
| $Na^+$ channel Site 2 (rat) | 2.14 |
| Neurokinin $NK_1$ (human) | 0.18 |
| Neurokinin $NK_2$ (human) | 1.30 |
| Neurokinin $NK_3$ (human) | 0.41 |
| Neuropeptide $Y_1$ (human) | 1.86 |
| Neuropeptide $Y_2$ (human) | 1.11 |
| Neurotensin $NT_1$ (human) | 0.00 |
| Norepinephrine transporter (human) | 2.43 |
| Nicotinic (human) | 0.29 |
| Opiate δ (human) | 3.43 |
| Opiate κ (human) | 1.07 |
| Opiate μ (human) | 0.00 |
| Opiate $ORL_1$ (human) | 5.85 |
| PAF (rabbit) | 8.62 |
| Prostanoid $EP_2$ (human) | 0.44 |
| Serotonin $5HT_{1A}$ (human) | 2.86 |
| Serotonin $5HT_{2A}$ (human) | 7.38 |
| Serotonin $5HT_3$ (human) | 5.52 |
| Serotonin transporter (human) | 3.38 |

| | |
|---|---|
| Sigma $\sigma_1$ (guinea pig) | 3.74 |
| Sigma $\sigma_2$ (guinea pig) | 0.18 |
| $VIP_1$ (human) | 0.00 |

CCK, cholecystokinin; CRF, corticotropin-releasing factor; GABA, 4-aminobutanoic acid; AMPA, 2-amino-3-(3-hydroxy-5-methyl-isoxazol-4-yl)propanoic acid; NMDA, N-methyl-D-aspartate; IP, inositol phosphate; ORL, opioid receptor-like; PAF, platelet activating factor; VIP, vasoactive intestinal peptide.