

**TRANSFERRIN INDUCES VASOPRESSIN
RECEPTOR TYPE 2 (V2R) INTERNALIZATION
AND EFFECTS WATER OSMEOSTASIS *IN VIVO*.**

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Vasopressin receptor type 2 (V2R) plays an important role in body fluid homeostasis. Recently, we found that green fluorescent protein tagged V2R (V2R-GFP) was internalized from the plasma membrane of LLC-PK1 cells in the presence of iron-saturated Tfn (Tfn). The presence of Tfn for 4h reduced V2R binding sites by 40% without affecting its main downstream signaling cascade. The co-immunoprecipitation of both receptors increased in a time-dependent manner in the presence of Tfn suggesting a close interaction. Live cell imaging revealed an abundant colocalization of V2R-GFP and rhodamine-tagged Tfn in conditions mimicking the acidic and hypertonic environment observed in the kidney inner medulla. Our *in vivo* preliminary study on catheterized rat ureter showed an increase in urine volume and reduction in osmolarity in rats treated with Tfn but not in sham treated rats suggesting a role of Tfn in water homeostasis. A hemochromatosis rat model (iron overload), which expresses abnormally high levels of Tfn, also showed an increase in urine volume (13.4 ± 4.5 vs 9.7 ± 3.4 g/24h, $p < 0.05$) with slightly lower osmolarity (1155 ± 122 vs 1370 ± 473 mOsm/kg) compared to control rats. These results suggest that Tfn can induce heterologous downregulation of the V2R and they also provide new insights in the role of Tfn in water homeostasis.