

## Optogenetic Approach to Regulate Vasopressin Neuron for Breakthrough of a Novel Sodium • Water Balance Mechanism

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### Summary

Arginine vasopressin (AVP) is synthesized in the magnocellular neurosecretory cells (MNCs) in the supraoptic (SON) and the paraventricular nuclei (PVN) of the hypothalamus. The MNCs project their axon terminals in the posterior pituitary and secrete AVP in the systemic circulation. Plasma AVP acts on the kidney as an anti-diuretic hormone. Recently, optogenetics provides a powerful tool to regulate neuronal activity by light-sensitive ion channels such as channelrhodopsin 2 (ChR2). In the present study, we have generated a transgenic rat that expresses an AVP-ChR2-enhanced green fluorescent protein (eGFP) fusion gene in the MNCs of the hypothalamus and the posterior pituitary. The eGFP fluorescence that indicates the expression of ChR2-eGFP was observed in the SON and in the magnocellular division of PVN that are known to contain AVP-secreting neurons. The eGFP fluorescent MNCs and fibers were scattered in the SON and the PVN and few in the posterior pituitary under normal condition. On the other hand, the eGFP fluorescent intensities in the SON, the PVN and the posterior pituitary were markedly increased after chronic salt loading (2% NaCl in drinking water for 5 days). ChR2-eGFP was localized mainly in the membrane of AVP-positive MNCs in the SON and the PVN in salt-loaded transgenic rats. Whole-cell patch-clamp recordings were performed from single MNCs isolated from the SON of the transgenic rats. In current clamp mode blue light evoked membrane depolarization and repetitive action potentials.

Our work provides for the first time an optogenetic approach to selectively activate AVP neurons in the rat. This novel transgenic rat gives us a new tool to study the physiological relationships between activated AVP neurons and sodium/water balance mechanisms.