Vasopressin (ADH)

Secreted from the pituitary gland in response to:

Low blood plasma volume (detected by baroreceptors in veins and atria)

High blood blood plasma osmotic pressure (detected by osmoreceptors in the hypothalamus)

Presence of angiotensin II (a peptide hormone present in the blood which regulates blood pressure)

ADH is released from the posterior pituitary and sent into the blood stream, where it will promote vasoconstriction in blood vessels and allow the kidneys to pull water from urine to increase blood volume

V1 Receptor

- V1R is located on vascular smooth muscle cells and are responsible for relaying the signal for vasoconstriction
- ADH binds to a specific G-protein which follows the Gq/11 pathway

- G-protein activates Phospholipase C (PLC)

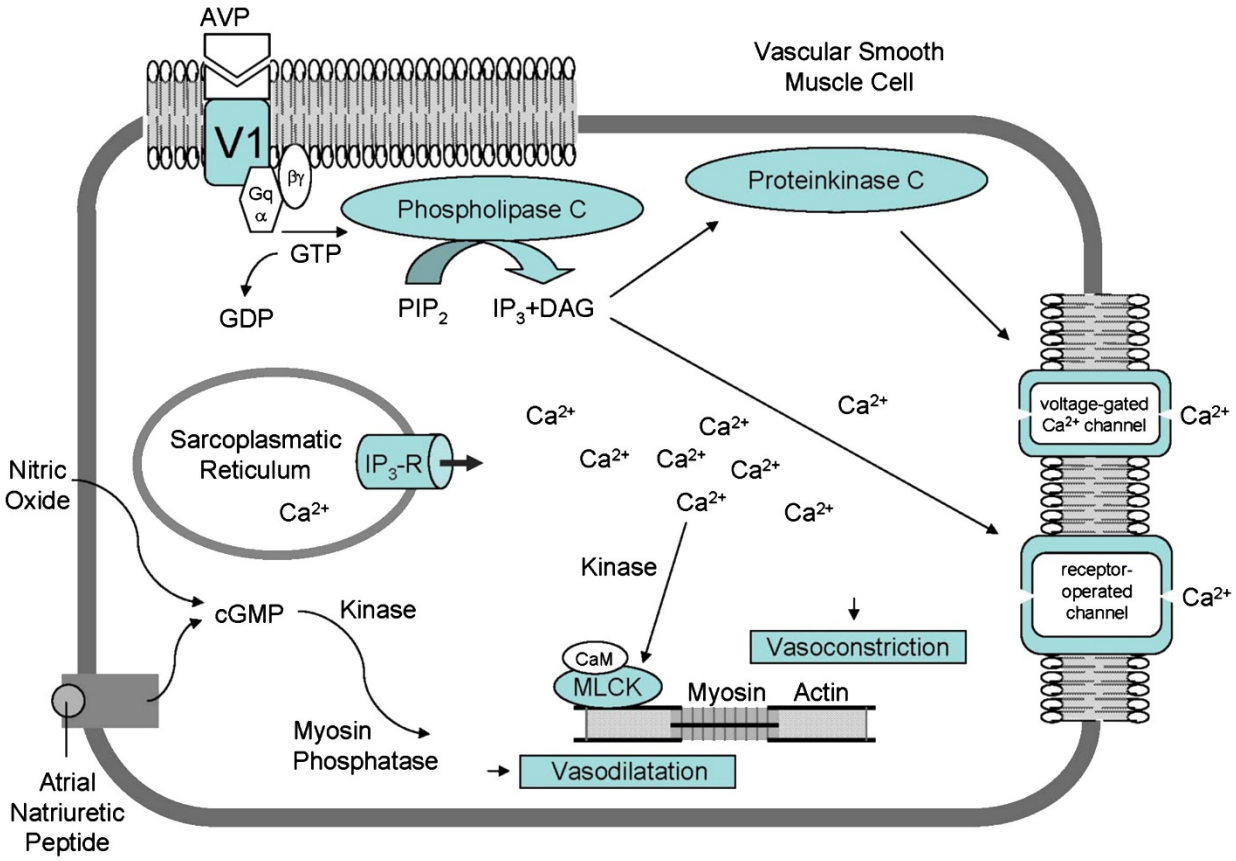
- PLC cleaves PIP2 into IP3 + DAG

- DAG activates Protein kinase C, which then activates calcium ion channels, letting calcium into the cytosol

- At the same time, IP3 activates an IP3 receptor on the sarcoplasmic reticulum which releases stored calcium ions into the cytosol

- The influx of calcium forms complexes with calmodulin (CaM), which then activates myosin light-chain kinase (MLCK)

- MLCK phosphorylates myosin, which goes on to activates myosin ATPase by actin, inducing vasoconstriction.



V2 Receptor

- V2R is located in the kidneys and is responsible for activating a pathway that pulls water from urine into the blood stream, thereby increasing blood volume
- ADH binds to a specific G-protein which follows the Gs pathway

- G-protein activates adenylyl cyclase, which produces cAMP

- cAMP activates PKA, which goes on to actvate 3 proteins:

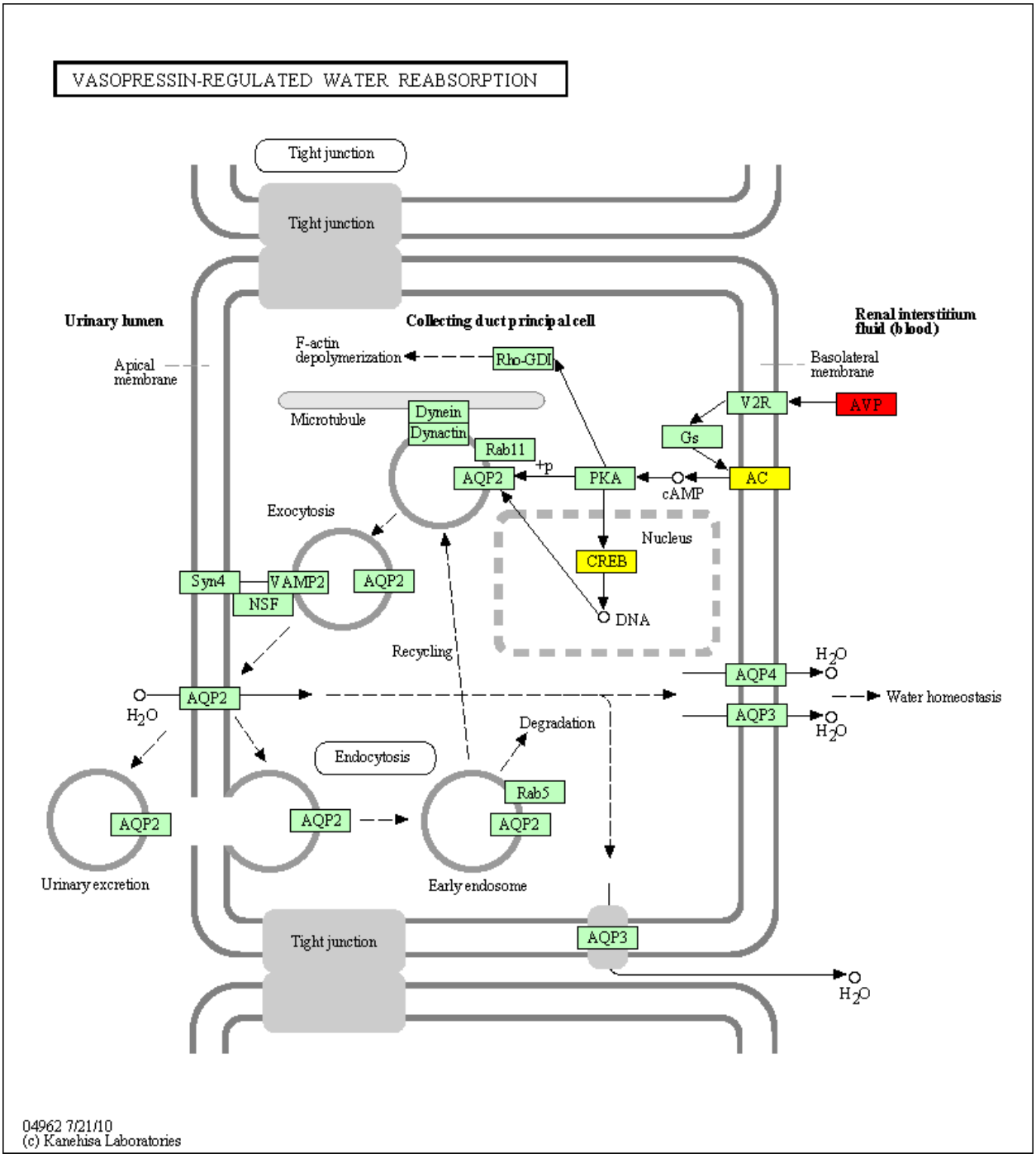
- cAMP response element binding factor (CREB) is activated in the nucleus and aquaporin 2 (APQ2) transcription is increased

- APQ2 vesicles are activated, which proceed along microtubles to the cell surface

-Rho-GDI is activated, which leads to actin depolymerization possibly aiding the transportation of APQ2 vesicles

- APQ2 is transported to the surface, allowing for water to flow from the urine into the cell, which is then passed through the cell into the blood stream
- APQ2 is then either detached from the cell wall and excreted through the urine,

or is taken back into the cell via endocytosis and then degraded



Regulation of the Vasopressin Signal

Vasopressin has a short half-life of 16-24 minutes

Downregulation

GPCRs decrease in responsiveness after ligand-binding.

Caused by phosphorylation and binding of ß-Arrestin proteins

Or degradation of cAMP by phosphodiesterases, coordinated by ß-Arrestins

Desensitzed vasopressin receptors are internalized and then cycled back to surface

V1R, V3R, OTR are recycled rapidly

V2R is cycled more slowly than other receptors

Clinically – by vasopressin receptor antagonists (VRAs) via competitive model (to treat hyponatremia)

Integration of the Vasopressin Signal

V1R – activates Gq/11 family of G-proteins, which in turn activate phospholipase C, which cleaves IP3 from diacylglycerol(DAG); IP3 activates Ca+ channels which, in conjunction with DAG, activates PKC

Pimarily facilitates arterial constriction

Facilitates thrombosis in platelets

Part of reward circuity for pair-bonding in brains

Also found in testis, cervix, and liver

V2R – activates the Gs family, inhibiting adenylyl cyclase and thus increasing concentration of cAMP

Allows for water reabsorption in the kidneys during dehydration

V3R – less specific (Gq/11, Gs, Gi)

Enables secretion of adrenocorticotropic hormones in pituitary gland, which increase production of cortisol

OTR – also Gq/11, activating a number of Ca+ promoted mechanisms

Contraction of the uterus,

Milk production in mammary glands

Part of baby bonding system in brain

P2R – also increases Ca+ promoted mechanisms

Primarily cardiac contraction