

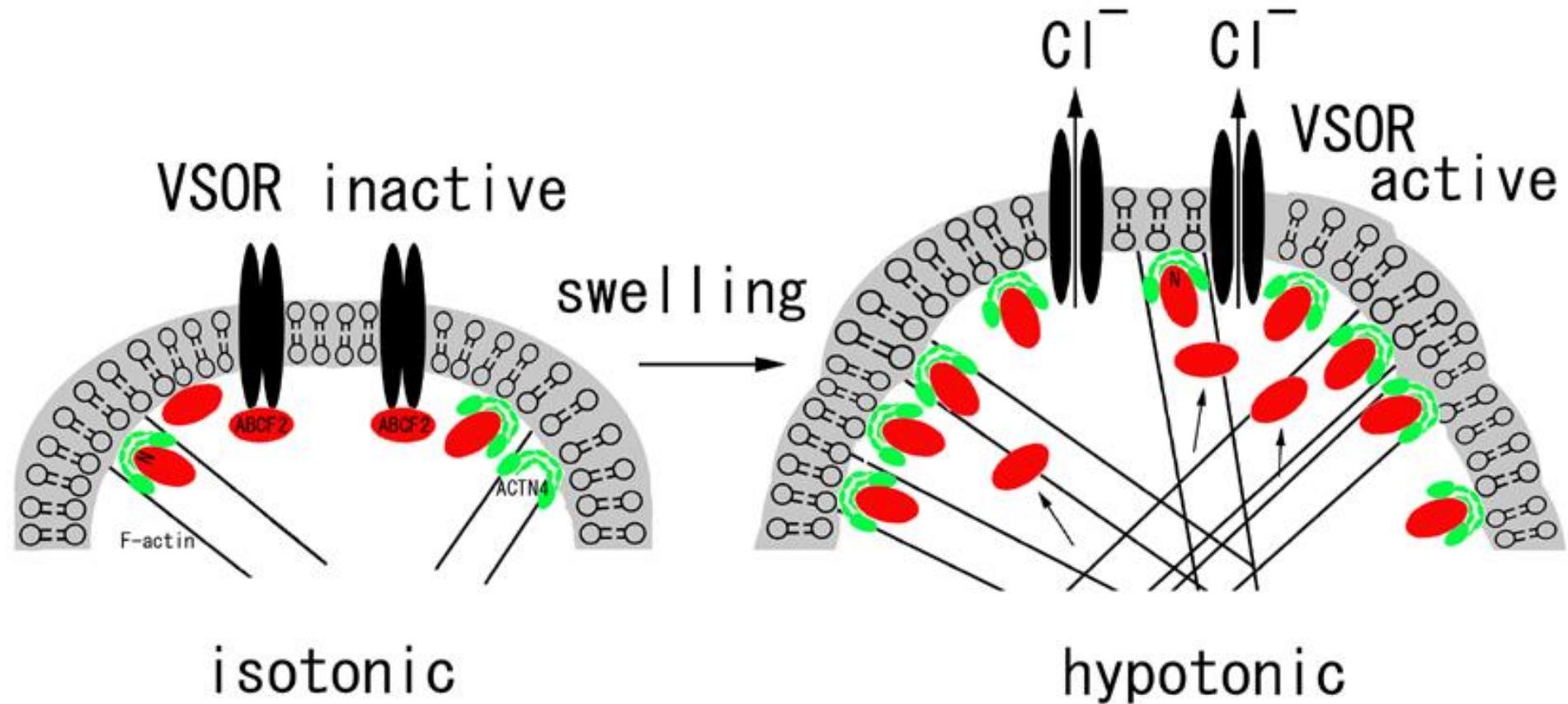
容積感受性外向整流性アニオン チャンネル (VSOR) の働き

～細胞容積調節だけじゃない

薬学科 生理学研究室

赤塚 結子

Schematic model of VSOR activation



Identification of LRRC8 Heteromers as an Essential Component of the Volume-Regulated Anion Channel VRAC

Voss, F.K. et al. (2014). *Science* 344:634-638

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Cell

SWELL1, a Plasma Membrane Protein, Is an Essential Component of Volume-Regulated Anion Channel

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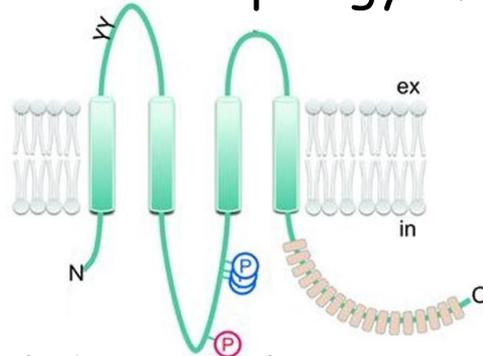
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<http://dx.doi.org/10.1016/j.cell.2014.03.024>

Qiu, Z. et al. (2014). *Cell* 157:447-458

Transmembrane topology of LRRC8A



◎LRRC8A、8C、8Eが免疫沈降法で共沈 (Lutter, D. et al. (2017). *J. Cell Sci.* 130:1122-1133)

◎LRRC8AとLRRC8Cの六量体形成をクライオ(低温)電子顕微鏡で確認
(Denaka, D. et al. (2018). *Nature* 558:254-259)

◎ 低浸透圧刺激によりLRRC8A+LRRC8Dを介してタウリン放出→グリシン受容体やGABA_A受容体にタウリンが結合→膜電位低下→神経の活動電位消失→過興奮から神経を守る。
(Planells-Cases, R. et al. (2015). *EMBO J.* 34:2993-3008)

(Lutter, D. et al. (2017). *J. Cell Sci.* 130:1122-1133)

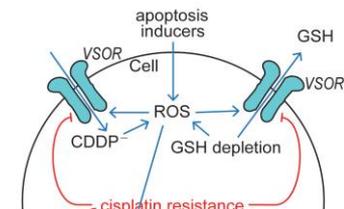
(Ye, H.B. et al. (2013). *Can. J. Neurol. Sci.* 40:628-634)

(Oja, S.S. and Saransaari, P. (2017). *Adv. Exp. Med. Biol.* 975(Pt 1):89-94)

◎GABAはランゲルハンス島β細胞の保護作用があり、糖尿病I型、II型でGABA分泌の不良が見られる。
(Fiorina, P. (2013). *Diabetes* 62:3674-3676)

マウス、ヒトのランゲルハンス島β細胞においてLRRC8Aの発現を抑制すると、GABA放出が消失する。
(Menegaz, D. et al. (2019). *Nat. Metab.* 1:1110-1126)

◎LRRC8A+LRRC8Dは、シスプラチン(CDDP)の通り道
(Planells-Cases, R. et al. (2015). *EMBO J.* 34:2993-3008)



VSOR activation mechanism

