

Sleepiness and Motivation



The Lazarus/Oishi Lab

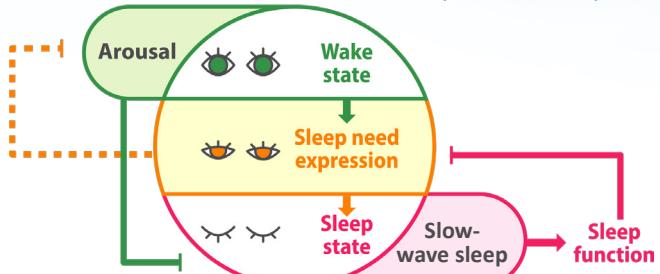
International Institute for Integrative Sleep Medicine (WPI-IIIS)

Drug discovery to treat insomnia and schizophrenia

Regulation of sleep homeostasis by arousal



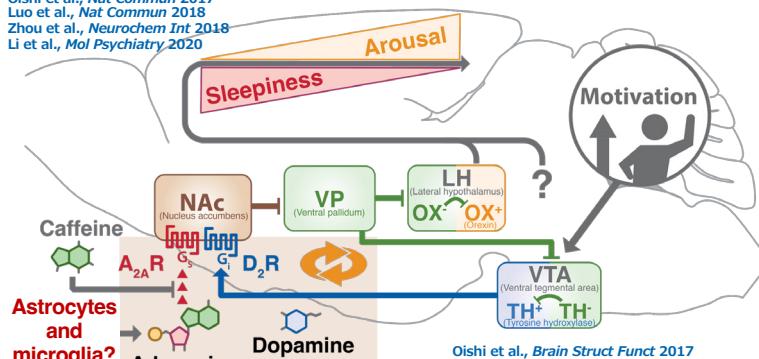
Lazarus M., Oishi Y., Bjorness T., Greene R., *Front Neurosci*, 2019



The neural mechanisms of sleepiness are widely unknown. Sleep is established in the absence of arousing inputs, for example, motivation.

Nucleus accumbens (NAc)/midbrain is a sleep/reward circuit

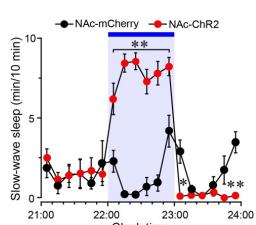
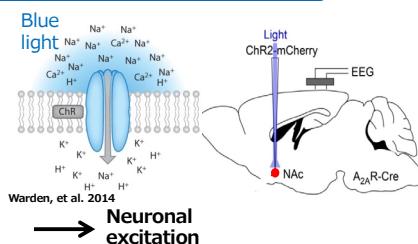
Lazarus et al., *J Neurosci* 2011
Oishi et al., *Nat Commun* 2017
Luo et al., *Nat Commun* 2018
Zhou et al., *Neurochem Int* 2018
Li et al., *Mol Psychiatry* 2020



Oishi et al., *Brain Struct Funct* 2017
Takata et al., *J Neurosci* 2018
Yang et al., *PLoS Biology* 2018
Zhang et al., *Current Biology* 2019
Honda et al., *iScience* 2020

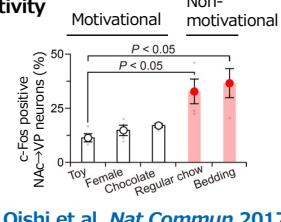
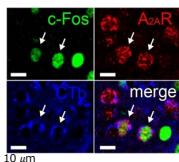
Adenosine A_{2A} receptors (A_{2A}R) are co-expressed with dopamine D₂ receptors (D₂R)

Sleep control by the NAc



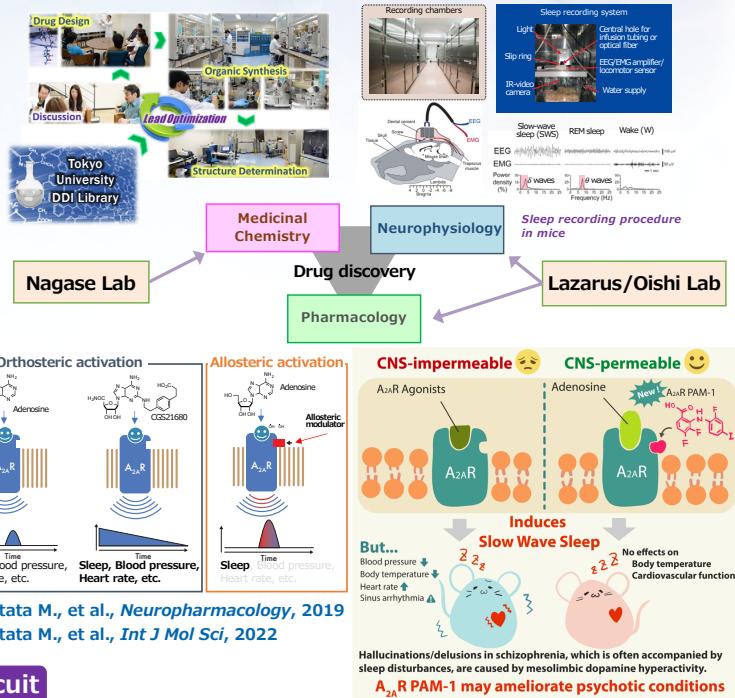
Motivational stimuli regulate NAc activity

NAc-VP pathway activity



Oishi et al. *Nat Commun* 2017

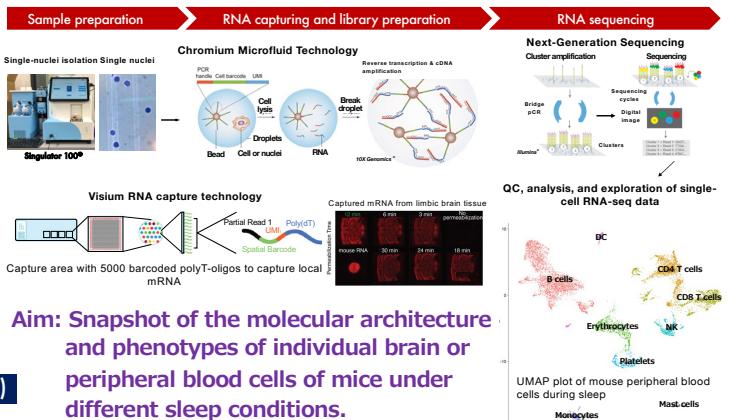
Contact: Michael Lazarus (lazarus.michael.ka@u.tsukuba.ac.jp)



Korkutata M., et al., *Neuropharmacology*, 2019
Korkutata M., et al., *Int J Mol Sci*, 2022

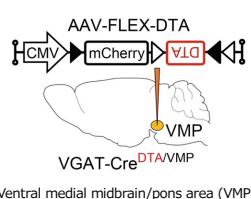
Halucinations/delusions in schizophrenia, which is often accompanied by sleep disturbances, are caused by mesolimbic dopamine hyperactivity.
A_{2A}R PAM-1 may ameliorate psychotic conditions

Hot Science: Single-cell and spatial transcriptomics

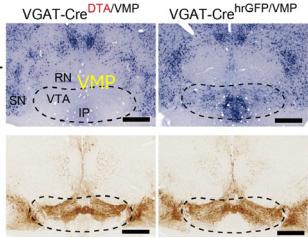


Aim: Snapshot of the molecular architecture and phenotypes of individual brain or peripheral blood cells of mice under different sleep conditions.

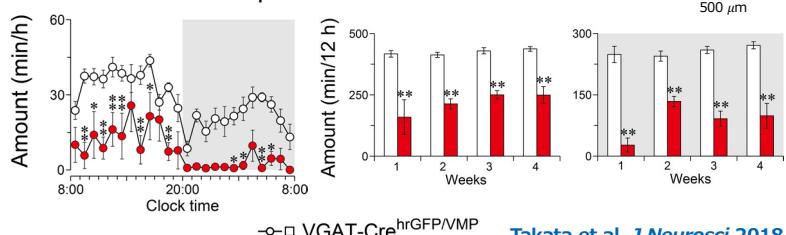
"Short-sleeper" mice by neuronal ablation



Ventral medial midbrain/pons area (VMP)



Slow-wave sleep



Takata et al. *J Neurosci* 2018
Honda et al. *iScience* 2020