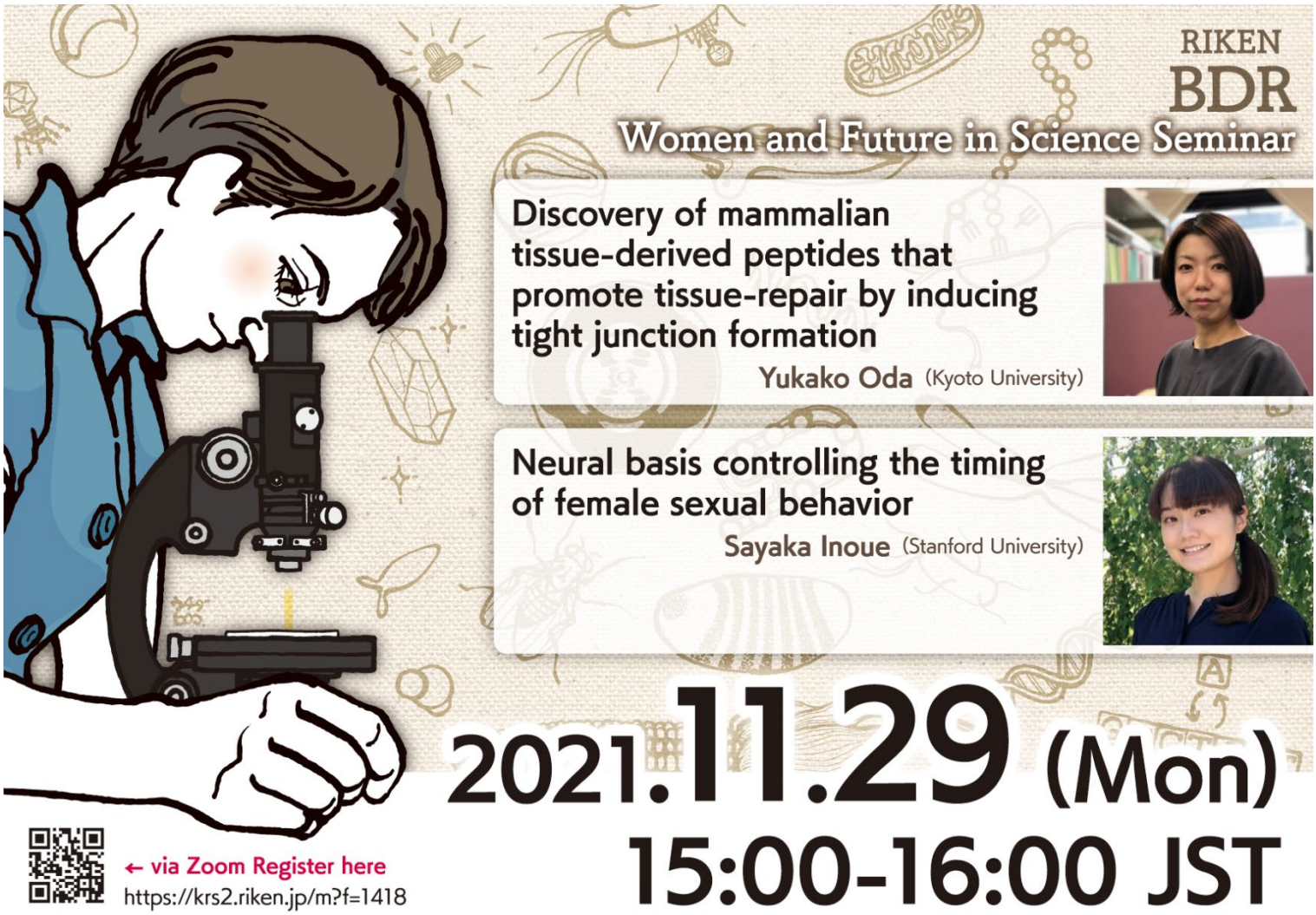

Discovery of mammalian tissue-derived peptides that promote tissue-repair by inducing tight junction formation

【Abstract】

Tight junctions (TJs) are epithelial barriers that prevent dehydration and pathogen invasion, and their disruption leads to various inflammatory diseases and tissue destruction. However, a therapeutic strategy to overcome TJ disruption in diseases has not been established because of the lack of clinically applicable TJ-inducing molecules. Here, we discovered TJ-inducing peptides (JIPs) in mice and humans, which corresponded to 35–40 residue peptides of the C-terminus of alpha 1-antitrypsin (A1AT), an acute phase anti-inflammatory protein abundant in circulating blood. JIPs inserted into the plasma membrane of epithelial cells, which induced TJs by directly activating the heterotrimeric G protein G13. In a mouse intestinal epithelial injury model established by dextran sodium sulfate (DSS), inhibition of JIPs impeded the restoration of TJs in regenerating intestinal epithelial cells, whereas mouse or human JIPs administration restored TJ integrity and strongly prevented colitis. Our study has revealed TJ-inducing anti-inflammatory physiological peptides that play a critical role in tissue repair and proposes a novel therapeutic strategy for TJ-disrupted diseases.

Neural basis controlling the timing of female sexual behavior

【Abstract】

Behaviors are associated to the internal physiological state. In many species, including mice, females dramatically change their sexual behaviors along the state of ovulation. Females are sexually receptive exclusively during the estrus, ovulatory phase of the estrous cycle, while they are not receptive during other phases. Sex hormones such as estrogen and progesterone are required for both ovulation and female sexual behavior. Although central and peripheral mechanisms of ovulation is well characterized, neural circuit mechanisms underlying the estrus-associated change of the behavior is poorly understood. We have previously shown that progesterone receptor (PR) expressing neurons in the ventromedial hypothalamus (VMH) are essential for female sexual behavior. Here we examined whether PR+ VMH neurons play a role in the estrus-associated change of female sexual behavior. We find that PR+ VMH neurons significantly strengthen their functional connections during estrus with the anteroventral periventricular nucleus. We further find that these projections are essential for female sexual receptivity during estrus. These findings demonstrate that periodic remodeling in this behaviorally salient connections play a critical role in associating female sexual behavior with internal physiological state. We will present these and recent findings to discuss hypothalamic circuit mechanisms that control the timing of female sexual behavior.

Contact information : bdr_diversity_po@ml.riken.jp