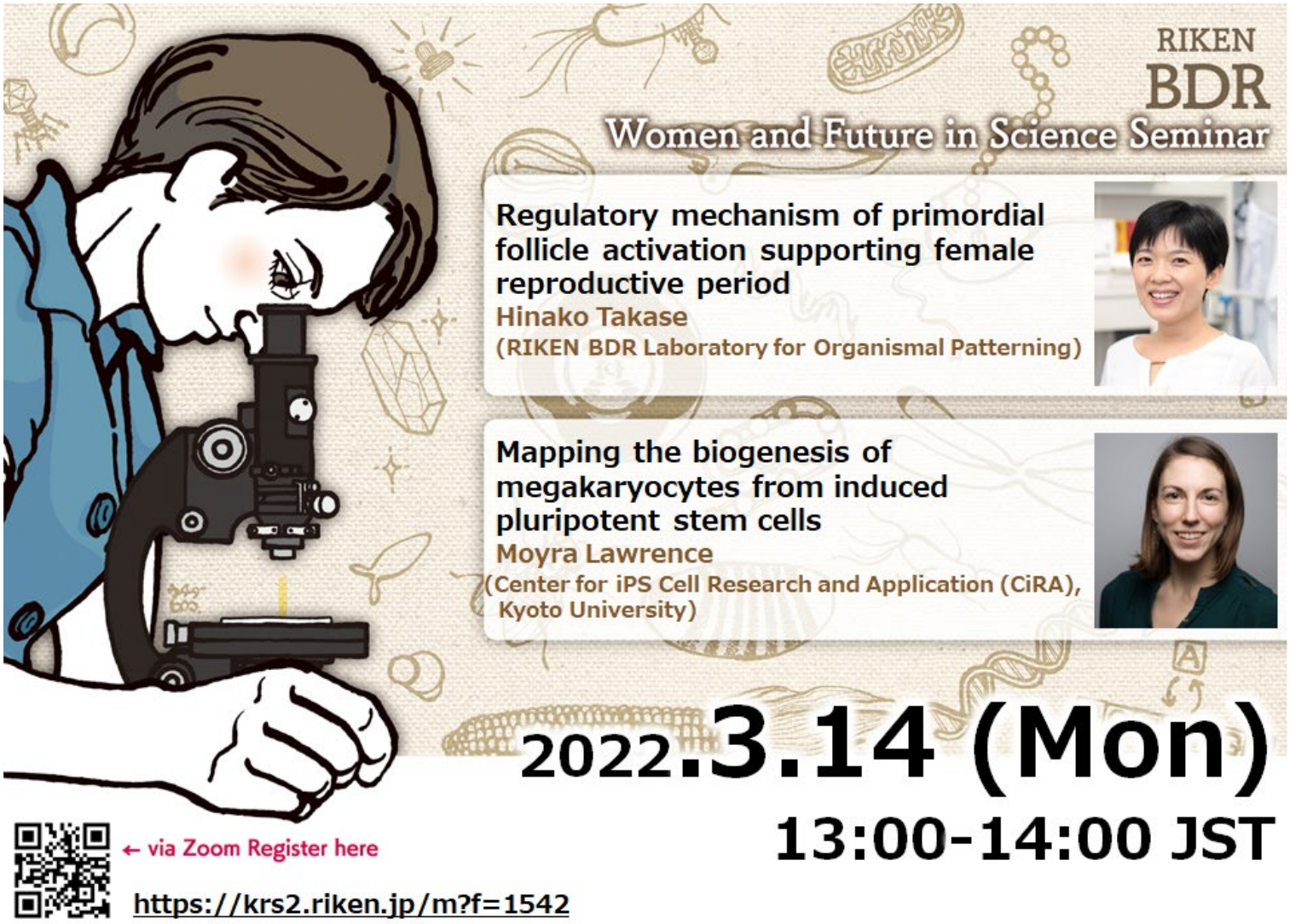

Regulatory mechanism of primordial follicle activation supporting female reproductive period

In the mammalian female, the balance between dormancy and activation of the primordial follicle plays a critical role in the gradual supply of oocytes. When the primordial follicle is activated, pre-granulosa cells and oocytes begin to grow in synchrony. What is the mechanism responsible for the primordial follicle activation (PFA)?

Here, we found that canonical WNT signaling is essential for the activation of pre-granulosa cells and functions in an autocrine manner in PFA; in the absence of WNT signaling, the follicles were unable to continue their growth due to the poorly developed granulosa cell layers which are associated with impaired oocyte maturation. Constitutive stabilization of β-catenin, a core component of canonical WNT signaling, in (pre-) granulosa cells induced no rapid PFA. Thus, our data suggested that WNT is a permissive signal for pre-granulosa cells, leading to successful oogenesis. In this seminar, we would like to discuss the preliminary results of single-cell RNA sequencing on WNT signaling mutants and control mice, to further elucidate the process of oocyte activation.

Mapping the biogenesis of megakaryocytes from induced pluripotent stem cells

Platelet deficiency, known as thrombocytopenia, can cause hemorrhage and is treated with platelet transfusions. We developed a system for the production of platelet precursor cells, called megakaryocytes (MKs), from induced pluripotent stem cells (iPSCs). These cultures can be maintained for >100 days, implying culture renewal by megakaryocyte progenitors (MKPs). However, it is unclear whether the MKP state in vitro mirrors the state in vivo. Additionally MKPs cannot currently be purified using conventional surface markers. We performed single-cell RNA sequencing throughout in vitro differentiation from iPSCs to MKs and mapped each state to its equivalent in vivo, revealing the accelerated formation of MKs without the generation of haematopoietic stem and progenitor cells. We then identified five surface markers that reproducibly purify MKPs, allowing us an insight into their transcriptional and epigenetic profiles as well as their increased telomere length.

Lastly, we performed culture optimisation, increasing MKP production. Together, this study has mapped parallels between the MKP states in vivo and in vitro and allowed the purification of MKPs, accelerating the progress of in vitro–derived transfusion products toward the clinic.

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