京都大学教育研究振興財団助成事業
成　果　報　告　書

2022年　8月　9日

公益財団法人京都大学教育研究振興財団
会 長　藤　　洋 作　様

所属部局・研究科　生命科学研究科

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新幹線代	24,980
宿泊料の一部として	8,040

当財団の助成について	I want to express my gratitude for supporting our group with the grant. This helped us to present our work in one of the most prestigious international scenes and the feedback and connections we made will surely help us to generate better science. In the future, it might be a good idea to be allowed to get the results of the application a little earlier, specially for international students that might need to prepare expensive or long processing time documents such as visas for the United States.

成果の概要／**RODRIGUEZ, Carlos Mario**

GRS and GRC 2022 report

GRS section:
Dates: June 4th – June 5th

The GRS meiosis is a research seminar aimed at graduate students, post docs and other scientists with a comparable level of experience.

During this seminar the young scientists present and discuss their projects and new data on how gametes are produced from diploid cells.

The seminar was divided into three sections:

1. Mechanisms and Control of Meiotic Recombination
   The section was focused on how double strand breaks are generated and repaired during meiosis with emphasis on crossover resolution.

   The discussion leader during this session was Michael Lichten and during the first part of his presentation he discussed how they developed a system to monitor heteroduplex formation of repaired DNA using SNPs close to hotspots. We discussed how template switching is a regular phenomenon that they were able to measure by the presence of mosaic heteroduplexes. He also presented the idea that branch migration is the norm for crossover resolution as they could find heteroduplex segments of usually to one side only of the crossover site indicating that the double holiday junction migrated. He mentioned during discussion that most of the DSBR events included branch migration or template switching which were thought to be rare events during the DSBR process.

   On the second part of his presentation, he also mentioned how they employed a system that utilizes ParB (sequence) and ParS (protein) from bacteria to generate artificial hotspots just by localizing the protein Hop1 to wherever the ParB sequence was inserted.

   The talks from the post docs included mostly unpublished data but the presentations were great insights on different mechanisms such as how chromosomes, and specifically form aneuploid nuclei, can segregate in a non-random manner to elevate levels of euploidy (Ting Gong, University of California, Davis), why crossover formation and viably gametes are decreased in young mice (Parijat Chakrabotry, University of Texas, MD Anderson) and how R-loops are problematic for the germline as they're able to evade DNA damage recognition (Tara Hicks, University of Iowa).

2. Mechanisms of Chromosome Segregation
   During this session Sadie Wignall from the Northwestern University presented their work on the spindle poles. Their publication showed that the protein KLP-18 is required to maintain the spindle bi-polarity. When they shifted a thermos sensitive KLP-18 to a restrictive temperature, they could clearly show a shift from bi-polar spindle to mono-polar spindles by shifting the micro tubules minus ends to the inner part of the spindle.

   Another interesting talk from the session came from Lexy von Diezmann from the University of Utah. She showed their progress and continuation of their publication on single molecule tracking in the chromosomes where they showed that the synaptonemal complex can diffuse through the synapsed chromosome axes.

3. Quality Control during Gametogenesis
   During this session there was an excellent talk from Chenshu Liu that is relevant to the work in Carlton laboratory. The data is still unpublished, but it relates to a technique they developed to chemically induce proximity of proteins that is promising due to the ease of use and wide range of possible applications.

GRC section:
Dates: June 5th – June 10th

The conference encompasses everything related to meiosis. Some of the most prominent meiosis research scientists attend the conference making it a great opportunity to learn about the latest data and work being done on the field.

The conference included the following sessions that were of special interest to the research on the Carlton laboratory:

1. Physical Properties and Organization of the Synaptonemal Complex
   The session was focused mostly on the synaptonemal complex which is the proteinaceous structure that holds homologous chromosomes together during synapsis. One of the main topics of discussion of the conference was the proposed role of the synaptonemal complex as the medium to achieve crossover interference. As it was demonstrated during some of the talks, mutations on the synaptonemal complex often result in an increased number of crossover sites in some organisms. This increase in crossover designation sites can be detrimental to the genomic stability of the organisms.

   Ofer Rog also discussed their published work on how the synaptonemal complex sequence identity is highly divergent between organisms and it is difficult to establish homology through conventional sequence alignments. Instead, the synaptonemal complex has a highly conserved structure. The length of the

transversal elements, the coiled-coil domains and other characteristics are present in most of the members in different species even though the sequences are completely different.

2. Initiation of Meiosis and Induction of Double Strand Breaks
   During this session Scott Keeney from the Sloan Kettering Institute showed some of their previous work on the RMM complex which includes Rec114, Mei4 and Mer2. These proteins seem to be able to make condensates that are functional *in vivo* and work as a scaffold to recruit Spo11 to generate DSBs.
   Another presentation of interest for our laboratory was presented by Monica Colaiacovo from Harvard where she presented their unpublished work on how the DSBs are distributed in *C. elegans*.

   Sarit Smolikov's talk of their unpublished data on the timing of DSBs in *C. elegans* also shed light on how they are regulated during meiosis.

3. DSB processing pathway choice
   During this session, Kei Yamaya from Stanford University presented her still unpublished data on the interplay between RAD-54.L and rad-54.B in *C. elegans*.

4. Spindle Assembly, Chromosome Segregation and Checkpoint Control
   Takashi Akera from the National Institutes of Health talked about the mechanisms by which R2d2, a meiotic drive in mouse is able to be inherited up to 95% of the time by a lagging chromosome mechanism.

   Binyam Mogessie From Yale University showed their work on how Actin filaments are required for proper spindle activity. He discussed their published work on how problems during chromosome segregation still occur even when cohesin is abundant. They were able to demonstrate that maternal decline of actin might be responsible for some of the phenotypes and that the microtubule-actin interactions are required for proper chromosomal and pronucleus movements.

5. Post Translational Modifications in Meiosis
   During this final session, our laboratory presented the now accepted publication regarding double strand break formation regulated by DSB-1 phosphorylation.

   The final talk of the session was given by Yumi Kim from the John Hopkins University where she talked about the protein PLK-2 which phosphorylates and controls Synaptonemal complex components and regulates crossover formation.

The Meiosis GRC of 2022 was a great experience with much unpublished work. We were able to share our research with other high-profile scientists to get feedback and ideas of future experiments.