FUNDING PROGRAM FOR NEXT GENERATION WORLD-LEADING RESEARCHERS

Project Title: Molecular study on the formation of aneuploidy in gamates for evaluation on risk of miscarriage	
Name: Miki SHINOHARA	**Institution**: Osaka University

1. Background of research

From a statistical analysis, about 10% of the pregnant women will experience the miscarriage. It is known that abnormality of the chromosome number, aneuploidy, in the embryo causes the miscarriage. Some aneuploidy of embryo is induced by failure in reductional segregation of chromosomes to a half during meiosis-I, a specific process to generate haploid gametes (eggs and sperms). However, detailed mechanisms on accurate reduction of chromosome numbers in meiosis-I have poorly understood.

2. Research objectives

I will analyze the function of proteins and structures of meiotic chromosomes involved in chiasma formation in budding yeast, a useful model organism that has similar molecular mechanism with which humans distribute meiotic chromosomes in gametes. I would like to show the mechanism to make all of the homologous chromosomes segregate accurately during meiosis-I.

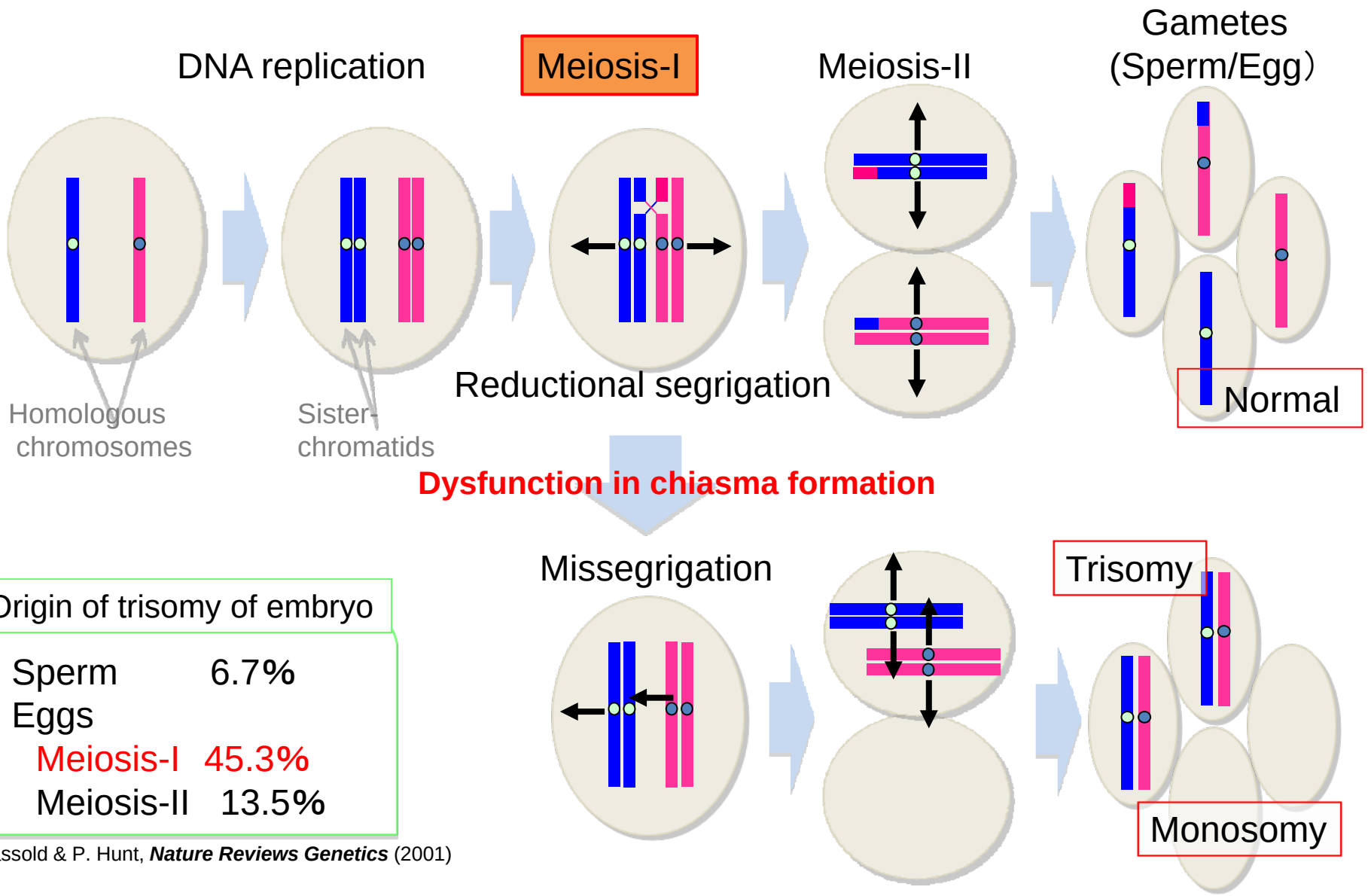
3. Research characteristics (incl. originality and creativity)

By analyzing many isolated yeast mutants that showed a defect in chromosome segregation in meiosis-I, I will pick up key proteins/genes and show their critical roles in meiotic chromosome function. Moreover I would like to isolate homologues, proteins involved in similar function, in mammals such as human or mouse to know its functions in us.

4. Anticipated effects and future applications of research

Solving the molecular mechanism of reductional segregation of chromosomes during meiosis-I in detail, we can know the critical step to guarantee accurate segregation. In addition, we will get insight in a step to make a mistake when it creates aneuploid gametes. Results of our research will be applied to diagnosis of persons who have the possibility of habitual miscarriage and to various choices of treatments in early stage of birth.

Many of aneuplidy of human eggs originally are caused by homologous chromosome missegrigation during meiosis-I

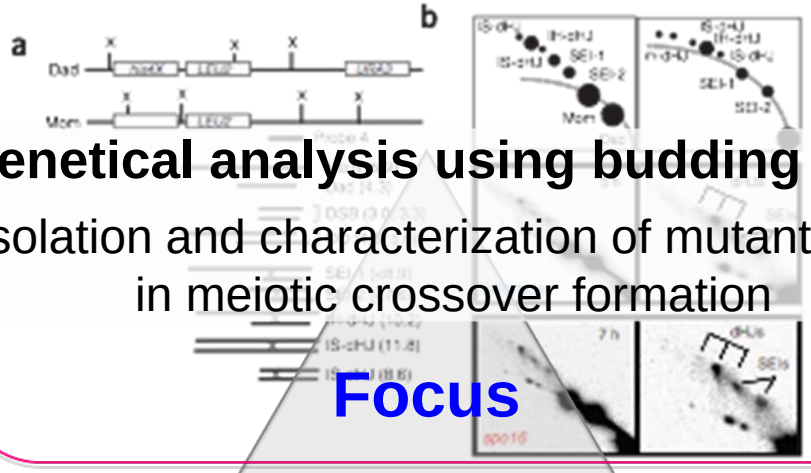


Origin of trisomy of embryo

Sperm	6.7%
Eggs	
Meiosis-I	45.3%
Meiosis-II	13.5%

T. Hassold & P. Hunt, ***Nature Reviews Genetics*** (2001)

To know about chiasma formation
is the way to know about aneuploidy formation of gamates



Genetical analysis using budding yeast

Isolation and characterization of mutant cells in meiotic crossover formation

Focus

<u>International & domestic collaboration</u>

- Analysis in mouse
- Relationship with habitual miscarriage

Progression & dynamic remodeling

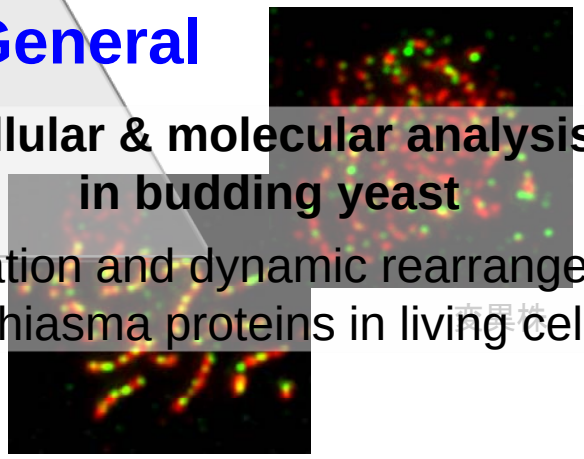
Concrete

Profiling localization of chisma Protein

Rerationship with the other meiotic proteins or Histone modifications

Rerationship to chromosome aberration In human cells

General



Cellular & molecular analysis in budding yeast

Localization and dynamic rearrangement of chiasma proteins in living cells

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