氏名	大高彩美（おおたかあやみ）
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学位論文名	ROLE OF THE LATS FAMILY KINASES DURING MEIOSIS IN FISSION YEAST （分裂酵母におけるLATSリン酸化酵素ファミリーの減数分裂での役割について）
論文審査委員	（主査） 教授　野島　博 （副査） 教授　平岡　泰　教授　升方　久夫

論文内容の要旨

Mitotic exit network (MEN) is responsible for the critical step to divide a cell into two daughter cells. We previously reported that the mammalian Lats2 kinase localizes at the centrosome and regulates the exit from mitosis. Although *LATS2* gene is also induced during mouse spermiogenesis, little is known about its meiotic functions. In *S. pombe*, amino acid sequences of two protein kinases, Sid2 and Mug27 (also known as Slk1 and Ppk35), are similar to Lats2. Indeed, Sid2 plays a pivotal role in septation initiation network (SIN) that is equivalent to MEN. We report here that a novel meiosis-specific protein kinase Mug27 is expressed after horsetail phase, and its expression is maintained until the second meiotic division. Green fluorescent protein (GFP)-tagged Mug27 appears at the start of prometaphase I, localizes to the spindle pole body (SPB: equivalent to centrosome) and then translocates to the forespore membrane (FSM) at late anaphase II. We found that Mug27, like Sid2 and its scaffold protein Sid4, localized at SPB with a non-crescent morphology when the SPB itself is transformed into a crescent morphology in meiosis II. Moreover, unlike Sid2, Mug27 moves to the forespore membrane (FSM) that assembles around the haploid nuclei to become a scaffold for spore wall formation. In the *mug27* null mutant (*mug27Δ*) cells, development of the FSM was defective and the spore size was smaller than that of wild type. The spore viability of *mug27Δ* strain was reduced to about half of wild type. Furthermore, its protein kinase activity appears to be important for its function because similar phenotypes to *mug27Δ* cells are also observed in the putative *mug27* kinase dead mutant. Interestingly, over-expression of Sid2 can rescue the abnormal

meiotic phenotypes of *mug27Δ* cells. Taken together, our results suggest that Mug27 plays a pivotal role in accurate FSM development during meiosis at least partially through the same signaling pathway as that of Sid2.

論文審査の結果の要旨

減数分裂は、生殖細胞を形成する過程であり有性生殖には重要であるが、その制御機構には不明な点が多い。申請者は核分裂後の配偶子形成制御について、分裂酵母をモデル実験系とし、分子遺伝学的および細胞生物学的手法を用いて研究を進めた。具体的には、細胞質分裂を制御するシグナル伝達経路であるSeptation Initiation Network(SIN)の最終段階で働くLatsファミリーのメンバーである機能未知のMug27に注目し、その減数分裂過程での機能を解析した。その結果、Mug27のリン酸化酵素活性が、有糸分裂での制御メカニズムとは異なった形で配偶子形成制御に必須であることを明らかにした。一方、Mug27は既知のSINと部分的に機能相補することも明らかにし、これらを総括して有糸分裂と減数分裂におけるLatsリン酸化酵素の役割についてモデルを提唱した。本研究で得られた成果は、配偶子形成制御に重要な知見をもたらすことで分子細胞生物学の進歩に貢献した。それゆえ、申請者は学位の授与に値するものと考える。