FUNDING PROGRAM FOR NEXT GENERATION WORLD-LEADING RESEARCHERS

Project Title: Development of systematic approach analyses for functional gene networks controlling heart functions in mouse genetic models	
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1. Background of research

By large scale fly heart failure screening, we identified CCR4-NOT complex as a novel regulator of heart functions, which was originally isolated as a transcription regulator from yeast mutants. We first elucidated CNOT3, a component of CCR4-NOT is critically involved in controlling heart functions in mice through epigenetic gene regulation (Cell, 2010), whereas it has recently been suggested as a critical deadenylase for mRNA poly-A tail shortening, implicated important for micro RNA-mediated mRNA decay.

2. Research objectives

We hypothesize that CCR4-NOT complex is a global regulator of cardiac gene expression, which links metabolism of RNA and epigenetic gene regulation and plays crucial roles in coordinating functional gene networks in hearts. We try to dissect the physiological role of CCR4-NOT complex in controlling heart functions and will further elucidate the functional gene networks in pathogenesis of heart diseases.

3. Research characteristics (incl. originality and creativity)

Currently, lower organisms, such as fruitfly and zebrafish are used to investigate multiple gene functions in living organisms. To dissect the CCR4-NOT gene networks in heart diseases, we will map functional interactions of the network genes by means of combined loss or gain of gene functions in mice. Our systematic approach to genetic engineering of mice is highly novel and challenging and will innovate biology and medicine.

4. Anticipated effects and future applications of research

This study is expected to elucidate unknown mechanisms for disease pathogenesis and identify the candidate targets for novel therapeutics. The strategy and results of this study will be translated to broad range of diseases and organs other than heart diseases and may further contribute to development of future medicines, such as iPS cell-based regenerative medicine.