

## Development of a screening system for the compounds that induce the cell cycle activity in mammalian cardiomyocytes

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### 【Background and Objective】

Since mammalian cardiomyocytes exit from cell cycle immediately after birth, the regenerative activity is limited in adult mammalian hearts. The aim of this study is to construct a screening system of the compounds that induce the cell cycle activity in mammalian cardiomyocytes, using Geminin-mAG1, a Fluorescent Ubiquitination-based Cell Cycle Indicator (FUCCI) that is stabilized in S/G2/M phases.

### 【Methods and Results】

We generated adenovirus vector expressing the FUCCI and infected the vector in neonatal rat cardiomyocytes. The frequency of FUCCI-positive cardiomyocytes increased in a FBS concentration dependent manner, concomitant with Ki-67-positive cells. Importantly, the cells transfected with miR-294, which was reported to be involved in cardiomyocyte proliferation, exhibited increased frequency of FUCCI-positive cells. In the presence of the proteasome inhibitor MG-132 that stabilizes FUCCI, more than 90% of the cells were positively identified, which is the limitation of this screening system.

### 【Conclusion】

We constructed a novel screening system for the compounds that induce the cell cycle activity in cardiomyocytes, though false positive samples cannot be completely excluded.