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Oral Sessions

Comprehensive search for cardiomyocyte death-related genes using forward genetic screening

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[Background] Cardiomyocyte (CM) death is an important risk factor in heart failure. Though molecular mechanisms of apoptosis have been well studied, those of necrosis remain to be fully elucidated. To explore novel genes related to non-apoptotic cell death induced by reactive oxygen species, we attempt genome-wide and forward genetic screening using lentiviral shRNA library. For this purpose, we optimized experimental conditions using neonatal mouse CMs.

[Methods] After infection with a pool of lentiviral shRNA library followed by the treatment with or without H₂O₂ (100 μ M), we prepared genomic DNA from neonatal mouse CMs. The sequence of shRNA in the lentiviral vector was analyzed using the next generation sequencer.

[Results] We determined 5359 shRNA sequences targeting approximately 1000 genes. Focusing on difference of reads between 2 groups, 12 candidate genes were obtained. 2 candidates were knocked down in neonatal mouse CMs, but cell death was not suppressed.

[Conclusions] Genome wide lentiviral shRNA screening in cardiomyocytes can be useful for determining novel genes related to cell death. However there are still some problems to be solved because of the low infection efficiency in CMs.