1. **No.**

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2. **Title**

   Role of Nicotinic Acetylcholine Nervous System in the Brain of Down Syndrome

3. **Period**

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4. **Summary**

Down syndrome, also known as trisomy 21 is a developmental disorder with mental retardation. Previous reports revealed that an abnormality in the acetylcholine nervous system in brains of Down syndrome patients. In order to elucidate the pathogenic mechanism of Down syndrome, a direct reprogramming method to differentiate from disease-derived fibroblasts to neurons was established, and the relevance of Dow's syndrome to the acetylcholine nervous system was examined. For the establishment of the experimental system of direct reprogramming, we used lentivirus shRNA for knockdown of pyrimidine-tract-binding protein (PTB) in mouse skin fibroblast derived A9 cell line. PTB shRNA-A9 cells expressed Tuj1, an immature neuronal marker on DIV17 and MAP2, a marker of mature neurons on DIV24. Furthermore, the activation of the voltage-dependent Na+ channel was observed in PTB shRNA-A9 cell, but not in control shRNA-A9 cells. In addition, spontaneous activity was observed in PTB shRNA-A9 cell co-cultured with rat glial cells on DIV24. We have established a direct reprogramming method for neurons in mouse skin fibroblasts. Similar investigations will be carried out on human fibroblasts and fibroblasts derived from Down syndrome, and the responsiveness of drugs involved in the acetylcholine nervous system will be examined.