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МУЛЬТИМОДАЛЬНАЯ МАГНИТНО-РЕЗОНАНСНАЯ И ФЛУОРЕСЦЕНТНАЯ ВИЗУАЛИЗАЦИЯ ТРАНСПЛАНТАЦИИ ИНДУЦИРОВАННЫХ ПЛЮРИПОТЕНТНЫХ СТВОЛОВЫХ КЛЕТОК В МОЗГ[1]

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Понимание характеристик пересаженных клеток, таких как выживание, рост и распределение, необходимо для оптимизации клеточной терапии, а мультимодальная визуализация на анатомическом и молекулярном уровнях предназначена для достижения этой цели. Нами сконструирован лентивирусный вектор, несущий гены тяжелой цепи-1 ферритина (*FTH1*), флуоресцентного белка ближнего инфракрасного диапазона (*iRFP*) и усиленного зеленого флуоресцентного белка (*egfp*). Создана культура индуцированных плюрипотентных стволовых клеток (iPSCs), стабильно экспрессирующих эти три репортерных гена. Эти iPSCs флуоресцировали в зеленой и ближней инфракрасной области спектра, а также обладали способностью поглощать железо *in vitro*. После трансплантации меченых iPSCs в мозг крысы прижившиеся клетки можно было до 60 суток визуализировать *in vivo* с помощью магнитно-резонансной (MRI) и флуоресцентной спектроскопии в ближней инфракрасной области (NIF) на анатомическом уровне. Кроме того, эти клетки можно было обнаружить с помощью иммуноокрашивания EGFP и окрашивания берлинской лазурью. Разработанную нами технологию можно рассматривать как новый инструмент для изучения поведения трансплантированных клеток мультимодальным способом, что важно при оценке эффективности и безопасности клеточной терапии.

Ключевые слова: мультимодальная визуализация, магнитно-резонансная визуализация, флуоресцентная визуализация, клеточная терапия, мозг

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MULTIMODAL MAGNETIC RESONANCE AND FLUORESCENCE IMAGING OF THE INDUCED PLURIPOTENT STEM CELL TRANSPLANTATION IN THE BRAIN

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The understanding of the engrafted cell behaviors such as the survival, growth and distribution is the prerequisite to optimize cell therapy, and a multimodal imaging at both anatomical and molecular levels is designed to achieve this goal. We constructed a lentiviral vector carrying genes of ferritin heavy chain 1 (*FTH1*), near-infrared fluorescent protein (*iRFP*) and enhanced green fluorescent protein (*egfp*), and established the induced pluripotent stem cells (iPSCs) culture stably expressing these three reporter genes. These iPSCs

showed green and near-infrared fluorescence as well as the iron uptake capacity *in vitro*. After transplanted the labeled iPSCs into the rat brain, the engrafted cells could be *in vivo* imaged using magnetic resonance imaging (MRI) and near-infrared fluorescent imaging (NIF) up to 60 days at the anatomical level. Moreover, these cells could be detected using EGFP immunostaining and Prussian blue stain at the cellular level. The developed approach provides a novel tool to study behaviors of the transplanted cells in a multimodal way, which will be valuable for the effectiveness and safety evaluation of cell therapy.

Keywords: multimodal imaging, magnetic resonance imaging, fluorescent imaging, cell therapy, brain