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Title: PEG-GoldMag-pod nanoparticles labeling breast cancer lymphatic endothelial cells and magnetic resonance imaging *in vitro*

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摘要: 目的 运用聚乙二醇 (polyethylene glycol, PEG)、金磁微粒 (GoldMag-Coreshell, GoldMag) 和抗podoplanin抗体构建靶向淋巴管内皮细胞的磁性纳米粒。 方法 在十六烷基三甲基溴化铵 (cetyltrimethyl ammonium bromide, CTAB) 的介导下采用PEG修饰GoldMag制备水溶性的PEG-GoldMag复合微粒, 将抗podoplanin抗体结合到PEG-GoldMag纳米粒上制备PEG-GoldMag-pod分子探针并检测其相关参数。采用小室法体外诱导人真皮淋巴管内皮细胞 (Human dermal lymphatic endothelial cells, HDLECs) 向乳腺癌淋巴管内皮细胞 (lymphatic endothelial cells, LECs) 分化。用铁浓度分别为5、10、15、30、45 $\mu\text{g}/\text{mL}$ 的PEG-GoldMag-pod纳米粒体外标记经诱导的HDLECs, 计算细胞标记率; 对不同浓度铁标记的细胞进行MR成像, 了解标记细胞的信号改变特点, 以未诱导的HDLECs为对照。 结果

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|---|
| 导航/NAVIGATE |
| 本期目录/Table of Contents |
| 下一篇/Next Article |
| 上一篇/Previous Article |
| 工具/TOOLS |
| 引用本文的文章/References |
| 下载 PDF/Download PDF(1179KB) |
| 立即打印本文/Print Now |
| 查看/发表评论/Comments |
| 导出 |
| 统计/STATISTICS |
| 摘要浏览/Viewed 87 |
| 全文下载/Downloads 61 |
| 评论/Comments |

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成功合成了水溶性的PEG-GoldMag-pod纳米分子探针。在铁浓度分别为5、10、15、30、45 $\mu\text{g}/\text{mL}$ 时,诱导后的HDLECs和未诱导的HDLECs的标记效率分别为:(39.65 ± 3.48)%、(71.37 ± 3.07)%、(91.36 ± 4.87)%、100%、100%和(22.61 ± 3.68)%、(36.40 ± 4.06)%、(70.13 ± 3.61)%、(91.40 ± 5.45)%和100%。经乳腺癌细胞诱导后的HDLECs较未诱导的HDLECs具有更高的标记阳性率 ($P < 0.05$)。标记细胞在常规MR上能够产生明显的信号改变,以 T_2^*WI 信号改变最明显。 结论 采用PEG修饰可以有效的构建水溶性的PEG-GoldMag纳米粒,进一步连接PodAb后能有效的标记LECs,通过对标记的LECs进行MR成像可以反映细胞podoplanin的表达情况。

Abstract: **Objective** To build lymphatic endothelial cells (LECs)-targeted PEG-GoldMag-pod nanoparticles with gold magnetic particles (GoldMag) modified by polyethylene glycol (PEG) and anti-podoplanin antibody (PodAb). **Methods** PEG was covalently bound to GoldMag to obtain PEG-GoldMag nanoparticles mediated by cetyltrimethyl ammonium bromide (CTAB). PodAb was covalently bound to PEG-GoldMag to construct PEG-GoldMag-pod nanoparticles. The characteristics of the PEG-GoldMag-pod nanoparticles were tested. Human dermal lymphatic endothelial cells (HDLECs) were incubated with breast cancer cells in Millicell cell culture inserts to acquire breast cancer LECs. The breast cancer LECs were co-cultured with PEG-GoldMag-pod nanoparticles at iron concentrations of 5, 10, 15, 30, and 45 $\mu\text{g}/\text{mL}$ separately for 24 h. The labeling ratio was evaluated by Prussian blue staining. Magnetic resonance (MR) imaging was performed to the labeled breast cancer LECs to investigate the signal characteristics. HDLECs without induction were used as control. **Results** The water-soluble PEG-GoldMag-pod nanoparticles were obtained successfully. Dose-dependence was