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Bioluminescence imaging to monitor the prolongation of stem cell survival by pharmaceutical intervention

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Purpose: The rapid donor cell death and rejection owing to humoral and cellular immune reactions are a basic limitation encountered in stem cell therapy for treatment of cardiovascular disease. We investigated the potential for longitudinal bioluminescence imaging to monitor the survival of transplanted stem cells prolonged by immunosuppressive agents. **Methods:** Embyonic rat H9c2 cardiomyoblasts were transfected with adenovirus containing luciferase reporter gene (Ad-CMV-Fluc) in different MOI (1,10,100) and various cell doses ($1x10^5$ - $5x10^6$)followed by injection in the thigh muscle of nude mice (n=6 per group). Other mice (n=18) were undergone transient immunosuppression provided by either Cyclosporine (5mg/kg) or Tacrolimus (1mg/kg) or Dexamethasone (4mg/kg) beginning 3 days prior to and continuing to 2 weeks after transplantation. Optical bioluminescent imaging was then daily carried out using cooled CCD camera (Xenogen) **Results:** Viral transfection at MOI 100 and the $5x10^6$ cell dose implantation resulted in optimal transgene efficiency. Mice received immunosuppressive agents displayed long-term in vivo reporter gene expression for a time course of 14 days. Tacrolimus (Prograf) and Cysclosporine successfully suppressed the transplanted cell loss in animals, that obviously observed until day 8 as compared to Dexamethasone-treated and non-treated mice (day 1: 1.00E+08 (Prograf), 9.47E+07 (Cys), 5.25E+07 (Dex), and 1.25E+07 p/s/cm^2/sr (control); day 8: 3.27E+05 (Prograf), 1.02E+05 (Cys), 6.17E+04 (Dex) and 2.73E+04 p/s/cm^2/sr (control)) and continued expressing bioluminescence until day 13 (6.42E+05 (Prograf), 4.99E+05 (Cys), and 4.10E+04 p/s/cm^2/sr. **Conclusion:** Induction of immune tolerance using pharmaceutical agents during cardiomyoblast transplantation improved long-term donor cell survival in murine muscles. Optical imaging technique is capable of being used for tracking implanted stem cells in myocardium of living subjects over time.

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Monitoring Bacteriolytic Therapy of Salmonella Typhimurium with Optical Imaging System

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Purpose: Systemically administrated Salmonella has been studied for targeting tumor and developed as an anticancer agent. In Salmonella, because msbB gene plays role in the terminal myristoylation of lipid A and induces tumor necrosis factor α(TNF-α)-mediated septic shock, Salmonella msbB mutant strain is safe and useful for tumor-targeting therapy. Here we report that Salmonella msbB mutant strain induce oncolysis after intravenous injection in tumor bearing mice. **Methods:** The CT26 mouse colon cancer cells were stably transfected with firefly luciferase gene and subcutaneously implantated in Balb/C mice. After establishing subcutaneous tumor mass, we intravenously injected 1x108 cfu Salmonella msbB mutant strain or MG1655 E coli strain. Not only tumor size but also total photon flux from the tumor mass were monitored everyday and compared among experimental groups (No treatment, Salmonella treatment, E. coli MG1655 treatment group). After intraperitoneal injection of D-luciferin (3 mg/animal), in vivo optical imaging for firefly luciferase was performed using cooled CCD camera. **Results:** Imaging signal from Salmonella injected group were significantly lower than that of no treatment or E. coli treatment group on day 2 after injection. On day 4 after injection, imaging signal of salmonella-injected group was 43.8 or 20.7 times lower than that of no treatment or E. coli treatment group, respectively (no treatment: 2.78E+07 p/s/cm^2/sr, Salmonella treatment: 6.35E+05 p/s/cm^2/sr, E. coli treatment: 1.29E+07 p/s/cm^2/sr, $P<0.05$). However, when we injected E.coli MG1655 into tumor bearing mice, the intensity of imaging signal was not different from no treatment group. **Conclusion:** These findings suggest that Salmonella msbB mutant strain retains its tumor-targeting properties and have therapeutical effect. Bioluminescent tumor bearing animal model was useful for assessing tumor viability after bacteriolytic therapy using Salmonella.