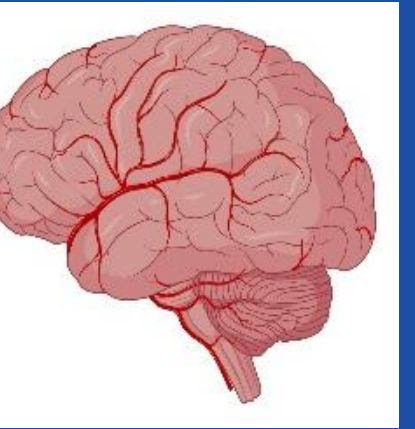


Radiolabeling of human mesenchymal stem cells for imaging of intraarterial delivery to the brain

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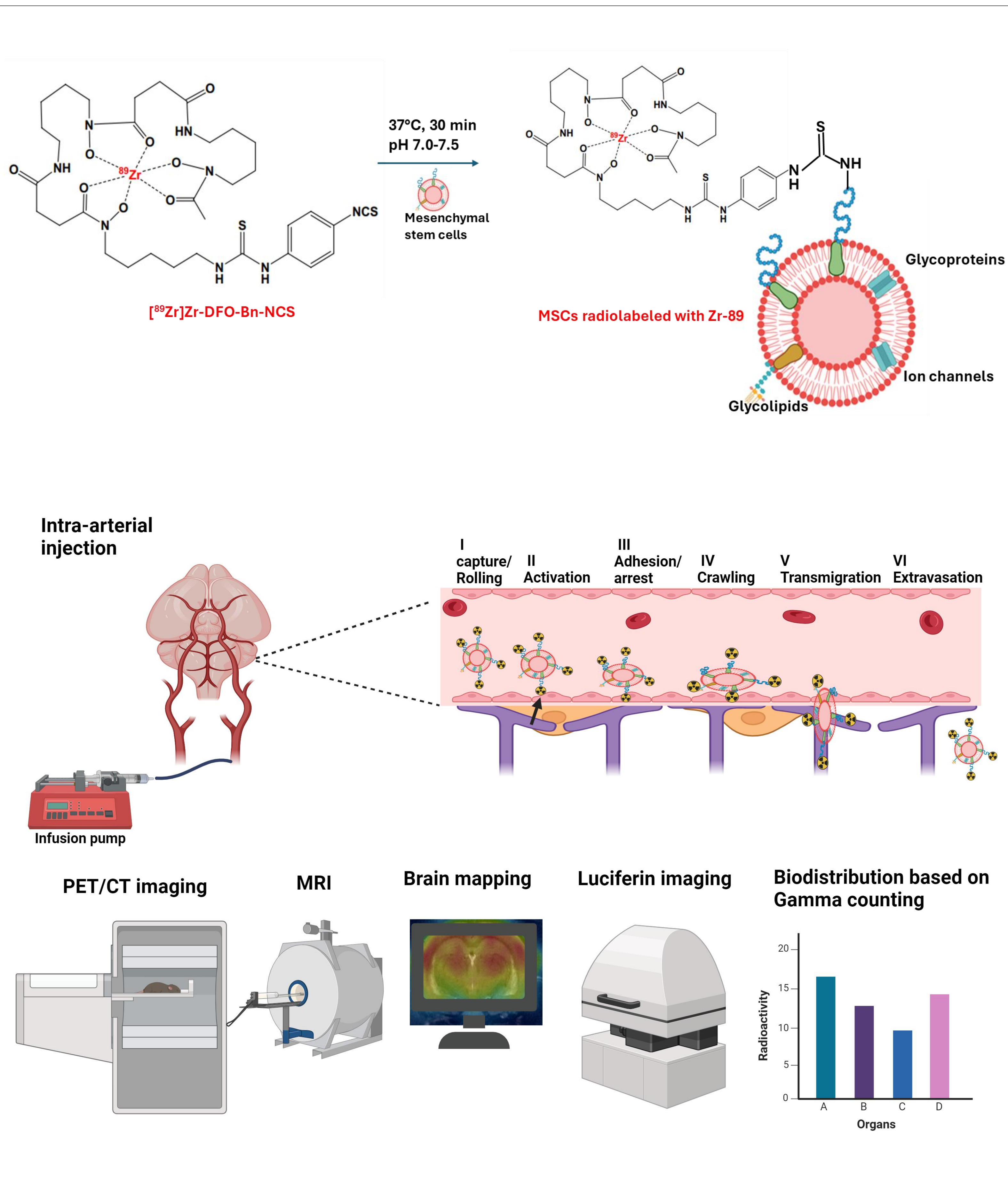
Abstract

Intra-arterial delivery of cellular therapies might be highly beneficial due to the first-pass effect, lowering total cell dose; however, imaging might be instrumental in achieving high precision. Magnetic labeling was used for this purpose, but it interferes with diagnostic MRI and has low specificity on follow-up scans. Radiolabeling and PET imaging may address both drawbacks, although radiolabeling conditions were never studied systematically, and efficiencies needed to be higher to adapt methods of low-dose intra-arterial interventions. We hypothesize that radiolabeling of human mesenchymal stem cells (hMSCs) might be beneficial by yielding higher sensitivity over a longer period and will provide quantitative results. Therefore, the goal of the current project is to investigate clinically applicable methods for cell tracking. Moreover, we employ a modern radioisotope ^{89}Zr , which allows for long-term (up to 2 weeks) cell biodistribution in the body. Specifically, the radiolabeling will reveal the retention capacities of transfected cells in the target organ (brain) but can also assess the off-target destination of transplanted cells in live animals.

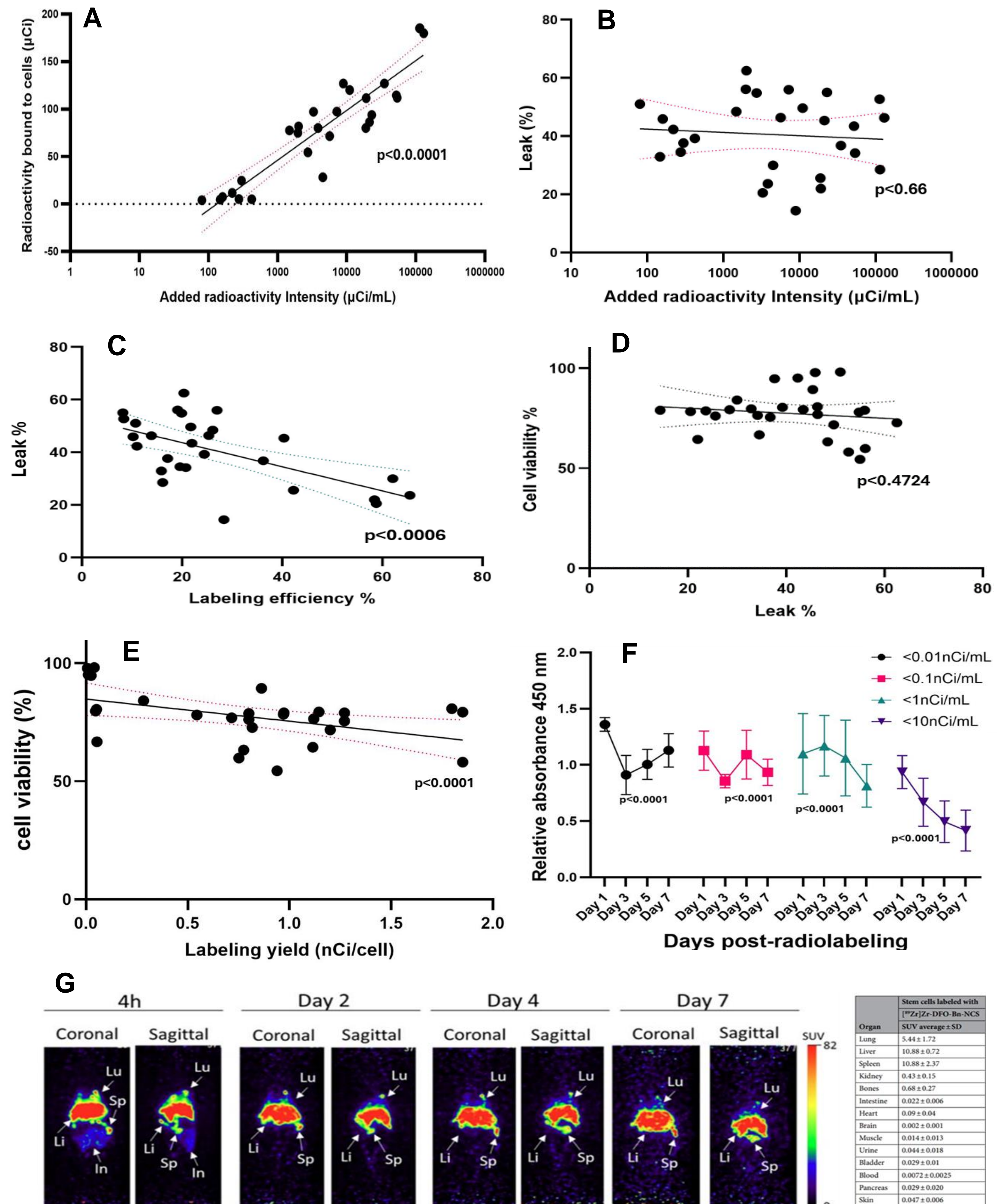
Methods

Radiolabeling of human mesenchymal stem cells (hMSCs) was performed at 37°C for 30 min at pH 7.0-7.5, and then cells were cultured over a week. The independent variables included the radiation intensity ($\mu\text{Ci/mL}$) and cell concentration per mL. Dependent variables included radiolabeling efficacy (%), radioactivity bound to cells (μCi), cell labeling yield (nCi/cell), radiolabeling leak at day 1 and till day 7 (%), cell viability at the end of radiolabeling (%), and cell proliferation and metabolism measured as absorbance in CCK8 assay on days 1, 3, 5 and 7.

Objectives



Results



Conclusion

We found a linear correlation between the logarithm of radioactivity intensity ($\mu\text{Ci/mL}$) and cell-bound radioactivity (A) but not with cell leak (B). Cell leak negatively correlated with radiolabeling efficacy (C) but not cell viability (D). Cell viability negatively correlates with Labeling yield (nCi/cell) (E). Long-term metabolism depends on the uptake of radioactivity (F). I.V administration of radiolabeled stem cells in athymic mice at a concentration of $4 \mu\text{Ci}/10^5$ cells (G) Bansal and Shalini et al. *Sci Rep* 12, 15646 (2022). **We achieved excellent radiolabeling efficiency, but potential radiotoxicity requires further studies.**

References

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