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In vivo manipulations of single cells using an all-optical platform

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The hematopoietic stem cell niche is a specialized bone marrow microenvironment where blood-forming cells reside. Interactions between these rare cells and their niche need to be studied at the single-cell level. While live animal cell tracking with optical microscopy has proven useful for this purpose, a more thorough characterization requires novel approaches. This can be accomplished by using an integrated optical platform for cell and tissue manipulations (cell transplantation and extraction) in the skull bone of live mice. The platform integrates a non-damaging laser ablation microbeam for bone removal and tissue cutting, optical tweezers for single cell trapping, and a video-rate multiphoton scanning microscope. For single cell delivery, a narrow channel is ablated through bone under imaging guidance. Cells are then transferred from a micropipette into an optical trap, which brings cells into the bone marrow through the channel. The survival and proliferation of implanted cells can be tracked in vivo by imaging and using standard blood analysis approaches. Critically, our approach uniquely enables the imaging of early stem cell division at the microscopic level, well before extensive proliferation and differentiation have occurred.

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