

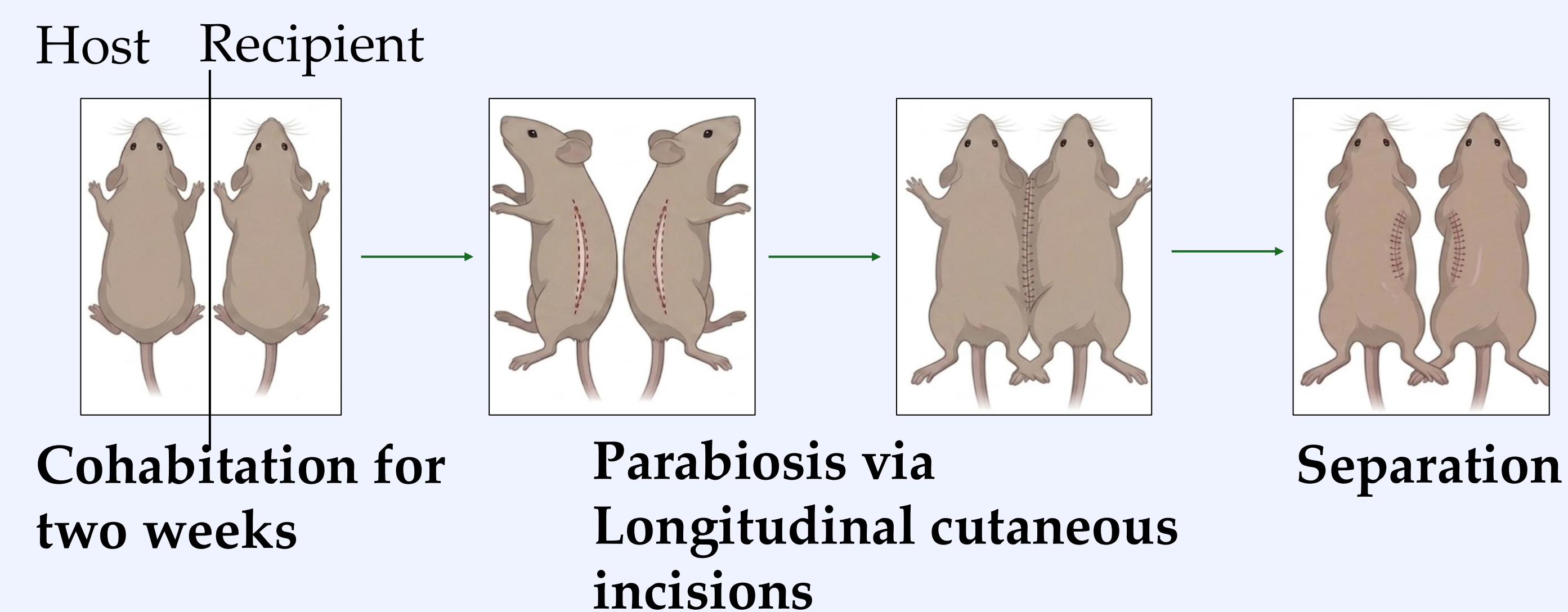
Evaluation of Parabiosis as a Model to Assess Distant Metastasis past Pulmonary Microvasculature

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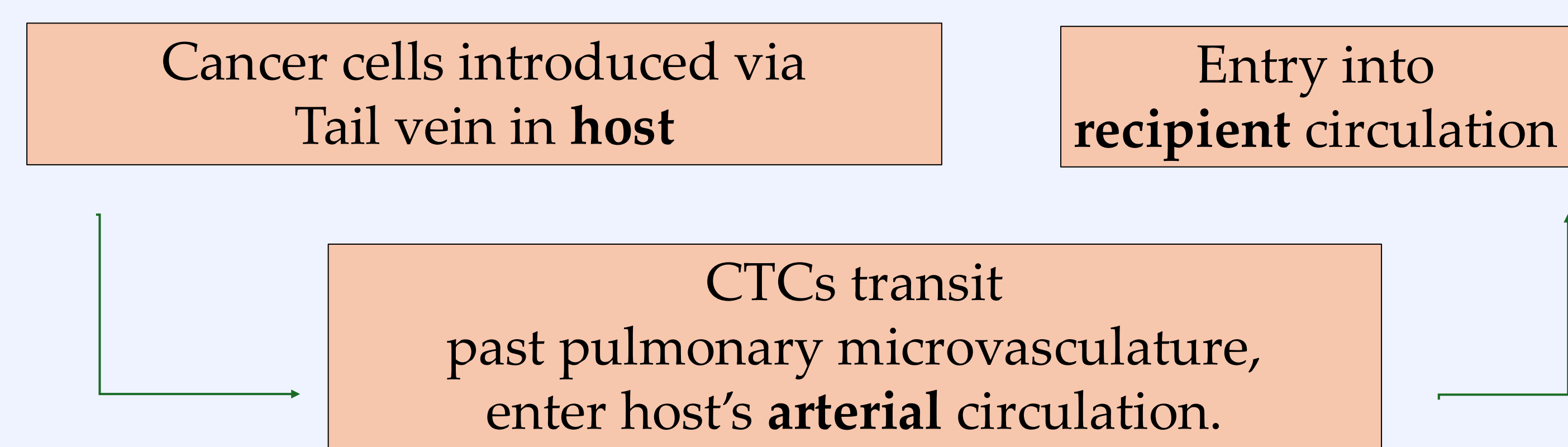
Background

- Circulating tumor cells (CTCs, 15 – 25µm diameter) must traverse pulmonary microvasculature (5 – 8µm diameter) to cause distant metastasis – a poorly understood phenomenon.
- Parabiosis offers a novel solution for mechanistic elucidation: recipient animals receive CTCs after successfully navigating host pulmonary microvasculature.

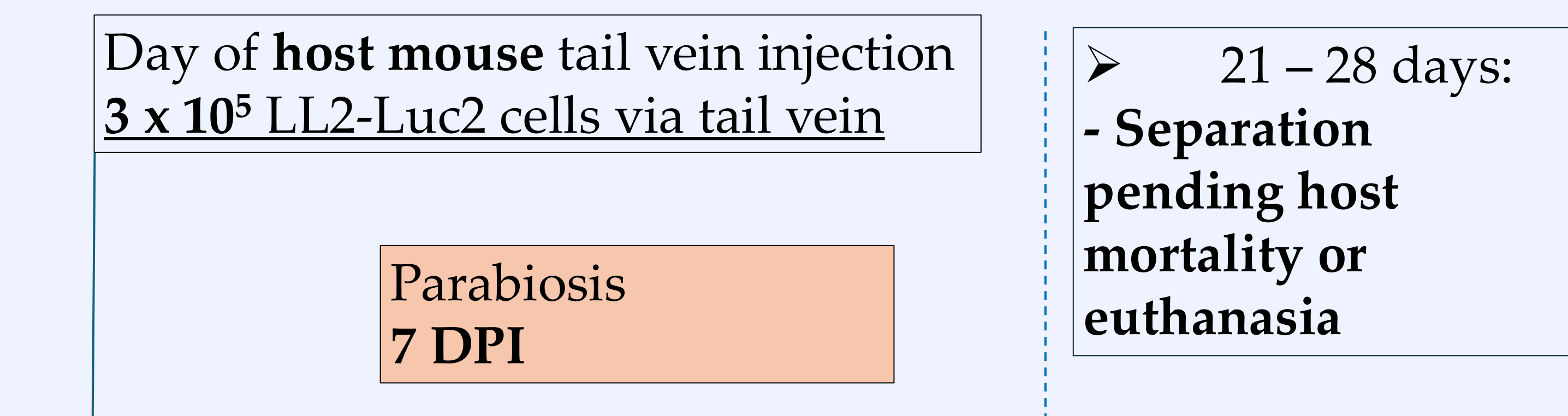
Conceptual Schematic



Rationale



Experimental Design



LAGO (Live animal imaging) 3-4 DPI (Days post injection), and every 7 days after Parabiosis.

Results

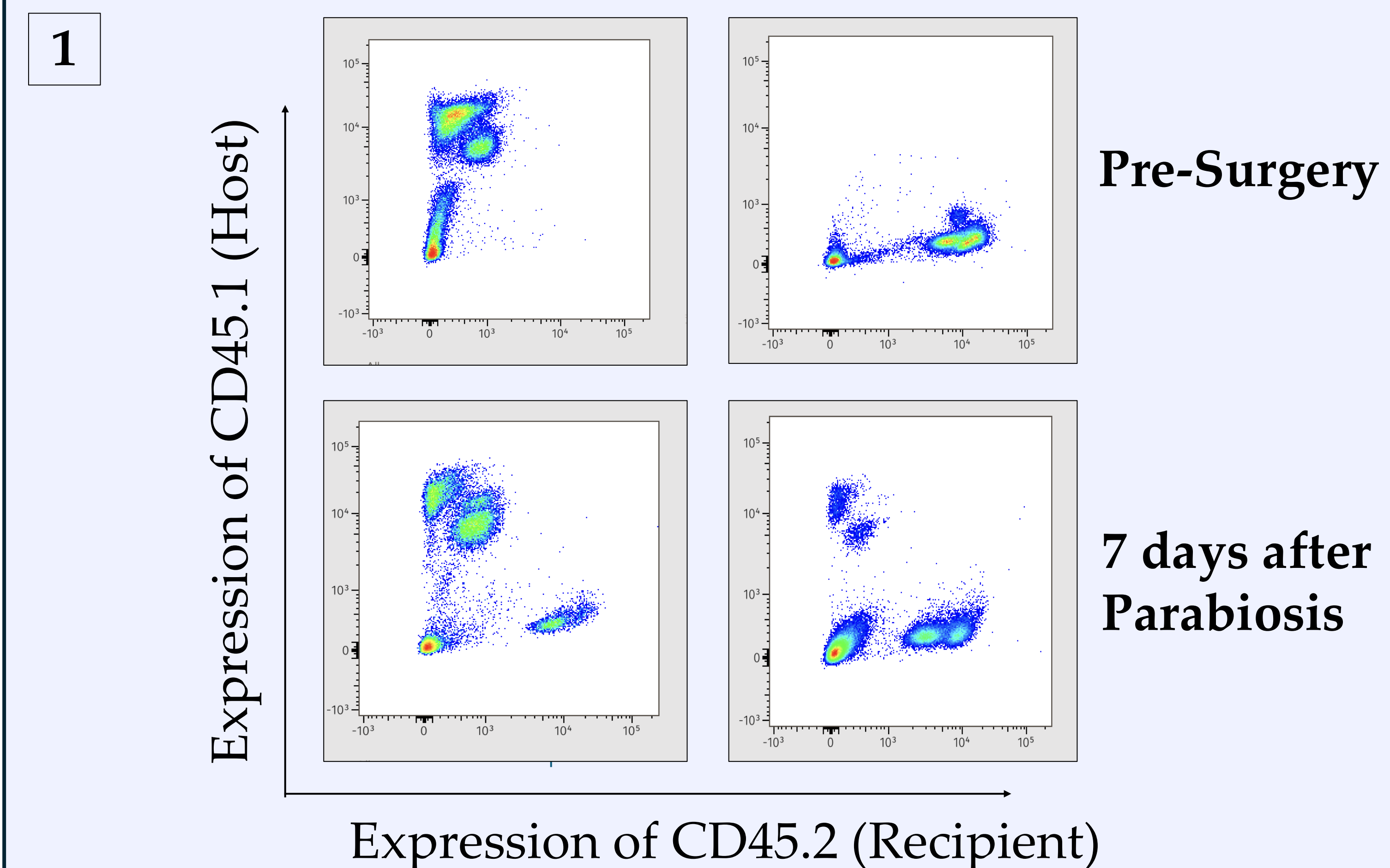


Figure 1: Establishment of chimerism and shared circulation observed 7 days after parabiosis (n = 2 pairs)

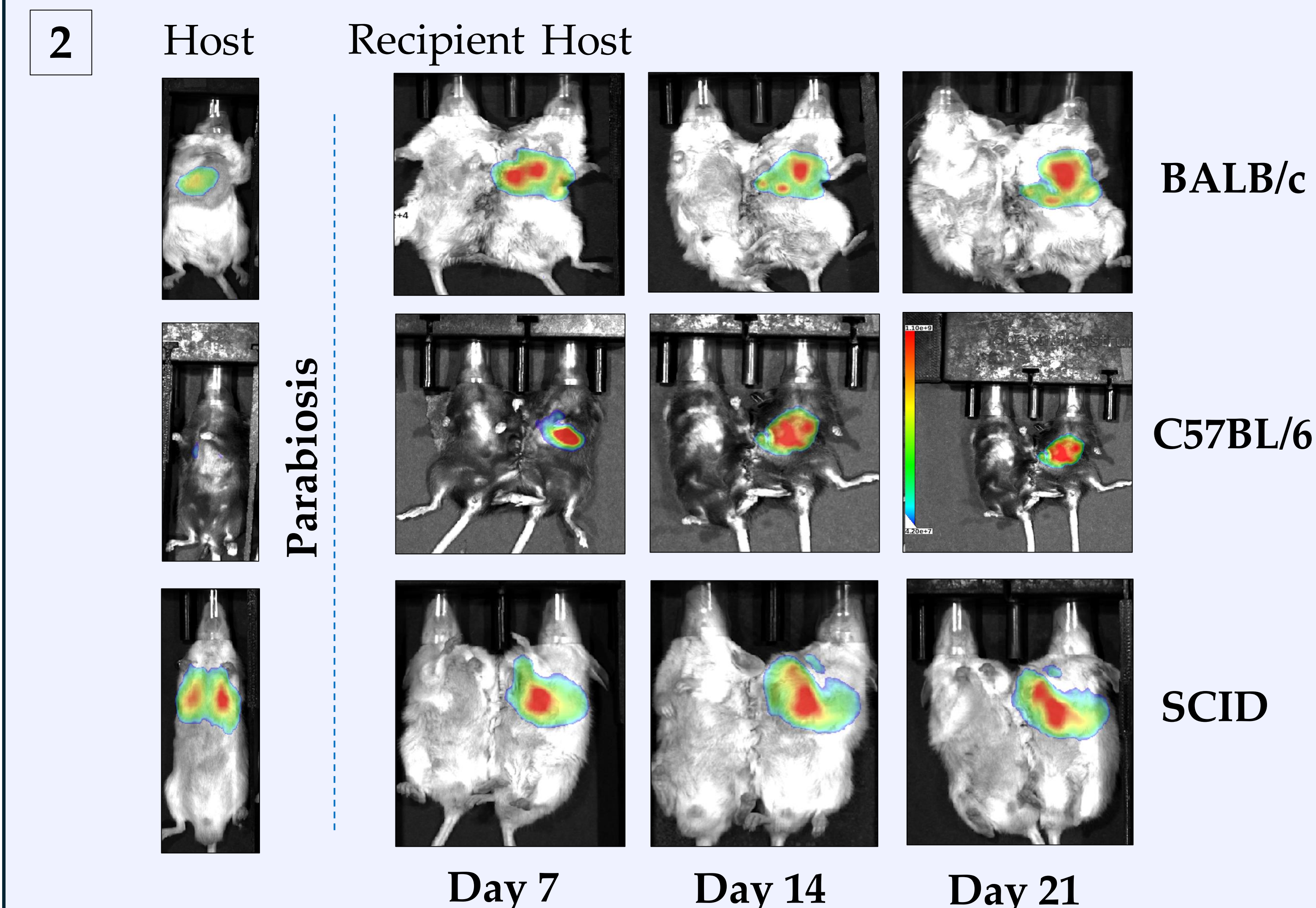


Figure 2: Progression of tumor cells in the host after parabiosis in BALB/c (n = 2 pairs), C57BL/6 (n = 2 pairs), and SCID (n = 4 pairs) strains, up to 3 weeks after parabiosis

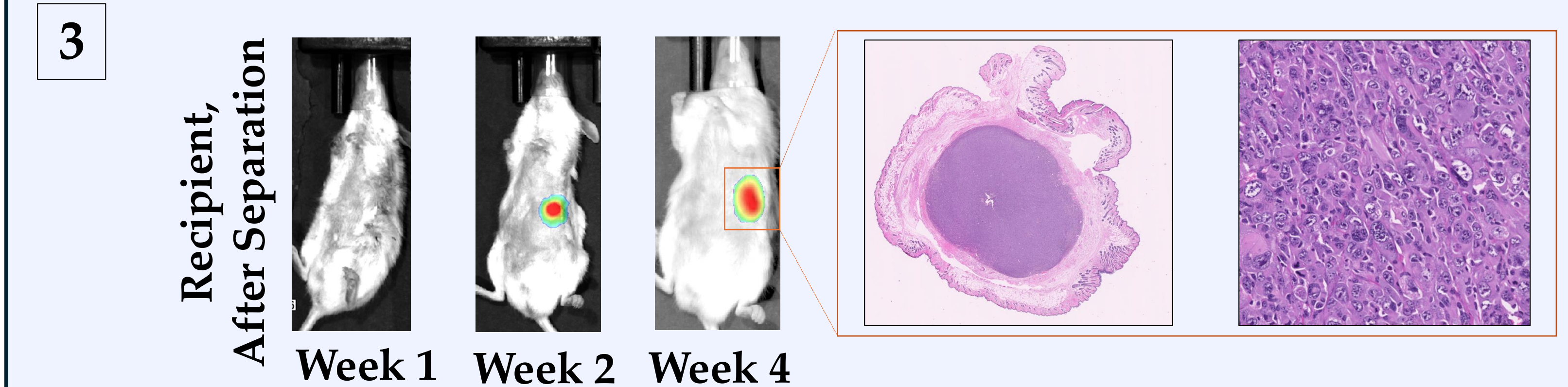


Figure 3: Tumor progression, as monitored in the recipient, weeks after separation, with concordant IHC images in SCID mice (2/4 pairs).

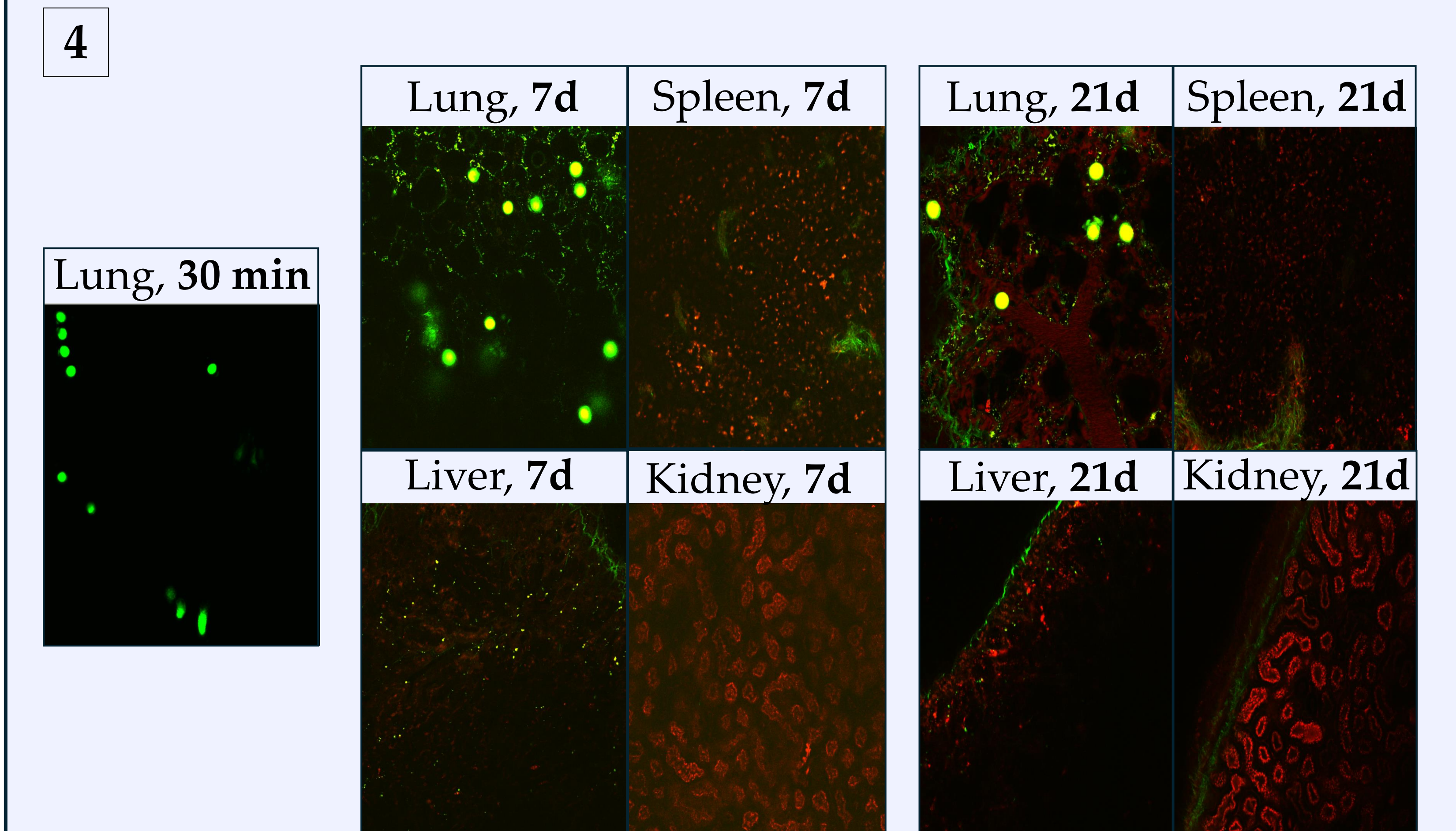


Figure 3: In a separate, standalone experiment, injection of 15µm fluorescent green polystyrene microparticles via the tail vein in C57BL/6 mice demonstrates arrest of particles in the lung at different time points (n = 1 per timepoint).

Conclusion

Data from parabiosis preliminarily suggests that CTCs, and not similar-sized rigid microparticles, can successfully traverse pulmonary microvasculature in SCID mice, though the mechanisms underlying this transit remain to be elucidated.