

## Description of Additional Supplementary Files

File Name: Supplementary Movie 1

Description: **Saphenous vessel imaging after intraventricular infusion of P40D680.** Noninvasive imaging of the saphenous vein region on the left leg of a Prox1-GFP mouse starting 5 min after intraventricular infusion of 2.5  $\mu\text{L}$  of 200  $\mu\text{M}$  P40D680. No P40D680 signal is seen at start of movie at  $t = 0$  min, signal becomes first apparent by eye at around  $t = 25$  min and continues to increase throughout the experiment. Images are acquired at 1 frame per 15 s at 25x magnification.

File Name: Supplementary Movie 2

Description: **Mandibular lymph node and afferent collecting lymphatic vessel imaging after intraventricular infusion of P40D680.** Noninvasive imaging of the neck of a Prox1- GFP mouse starting 5 min after intraventricular infusion of 2.5  $\mu\text{L}$  of 200  $\mu\text{M}$  P40D680. No P40D680 signal is seen at start of movie at  $t = 0$  min, signal becomes first apparent in lymphatic vessels and lymph nodes at around  $t = 7$  min (12 min after infusion). Note signal in lymph node on right side of movie (left side of mouse) is apparent before superficial afferent lymphatic vessel is observed, indicating a connection from the deep cervical region. Images are acquired at 1 frame per 1 s at 6x magnification.

File Name: Supplementary Movie 3

Description: **Posterior facial vein imaging after intraventricular infusion of P40D680.** Imaging of ROI shown in Supplementary Figure 5a of a C57BL/6J-*Tyr<sup>C-J</sup>* mouse starting 10 min after intraventricular infusion of 2.5  $\mu\text{L}$  of 200  $\mu\text{M}$  P40D680. Background signals decline over time from intracranial P40D680, however, no signal is apparent within the posterior facial vein.

File Name: Supplementary Movie 4

Description: **Saphenous vessel signals in a young (2-month-old) mouse after intraventricular infusion of P40D680.** Imaging of a region on the left leg of a young mouse starting 5 min after intraventricular infusion of 2.5  $\mu\text{L}$  of 200  $\mu\text{M}$  P40D680. No P40D680 signal is seen at start of movie at  $t = 0$  min, signal becomes first apparent at around  $t = 22$  min and continues to increase throughout the experiment. Images are acquired at 1 frame per 15 s at 25x magnification.

File Name: Supplementary Movie 5

Description: **Saphenous vessel signals in an aged (18-month-old) mouse after intraventricular infusion of P40D680.** Imaging of a region on the left leg of an aged mouse starting 5 min after intraventricular infusion of 2.5  $\mu\text{L}$  of 200  $\mu\text{M}$  P40D680. No P40D680 signal is seen at start of movie at  $t = 0$  min, signal becomes first apparent at around  $t = 32$  min and enhances to a lesser degree than in young mice over time. Images are acquired at 1 frame per 15 s at 25x magnification.