Wu et al. Figure I

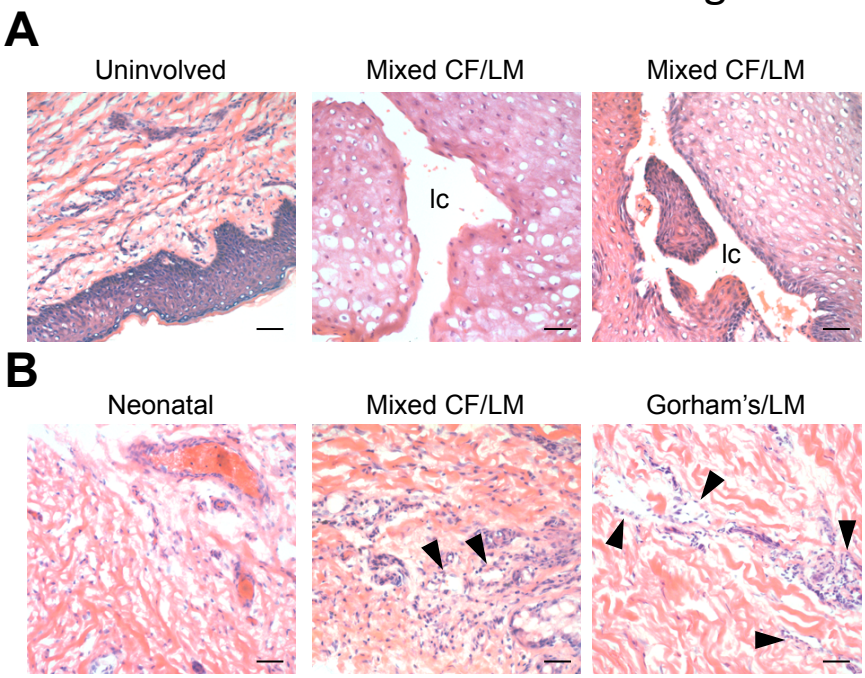

Figure S1. LM tissues histology. (**A**) H&E staining of patient-matched uninvolved and mixed cervicofacial (Mixed CF) LM tissues. (**B**) H&E staining of neonatal control tissue, Mixed CF LM or Gorham's tissues. Arrowheads mark abnormal lymphatic vessels. Scale bars: 50 μm. lymphatic channel (lc)

Wu et al. Figure II

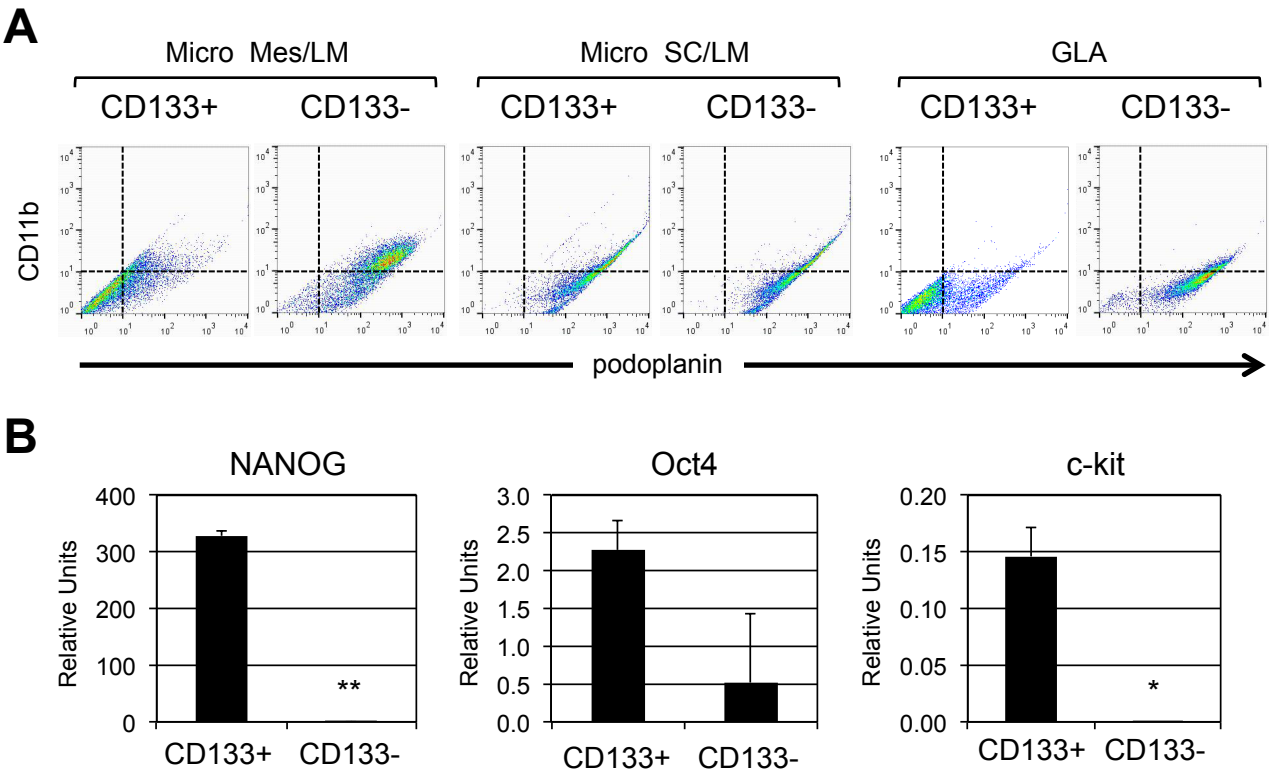

Figure S2. Analysis of progenitor and stem cell markers in C$\mathbf{D133^{+}}$ and $\mathbf{CD133^{-}}$ LM cells. (**A**) CD11b and podoplanin FACS of patient-matched $CD133^{+}$ and $CD133^{-}$ LM cells isolated from microcystic mesenteric (Micro Mes) LM, microcystic subcutaneous (Micro SC) LM and general lymphatic anomaly (GLA) specimens. (**B**) NANOG, Oct4 and c-Kit qRT-PCR of RNA isolated from patient-matched $CD133^{+}$ and $CD133^{-}$ LM cells isolated from a macrocystic mesenteric LM. Data normalized to β-actin qRT-PCR and represented as mean ± s.e.m. * $p < 0.01$, ** $p < 0.0005$.

Wu et al. Figure III

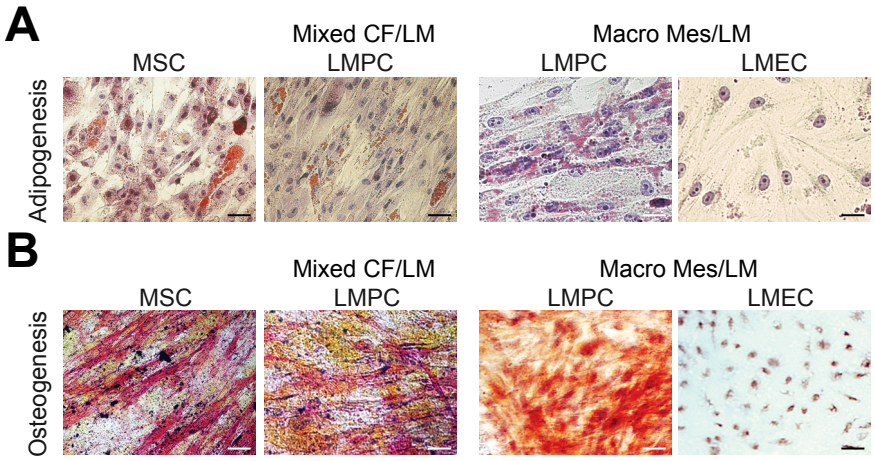

Figure S3. LMPCs and not LMECs were multipotent.
(**A**) Oil Red O staining of MSCs, LMPCs isolated from mixed cervical facial (Mixed CF) LM and patient-matched LMPCs and LMECs isolated from macrocystic mesenteric (Macro Mes) LM after 2 weeks in adipogenic media. (**B**) Alkaline phosphatase staining of MSC, LMPCs isolated from Mixed CF LM and patient matched LMPCs and LMECs isolated from Macro Mes LM after 2 weeks in osteogenic media. Scale bars: 50 μm.

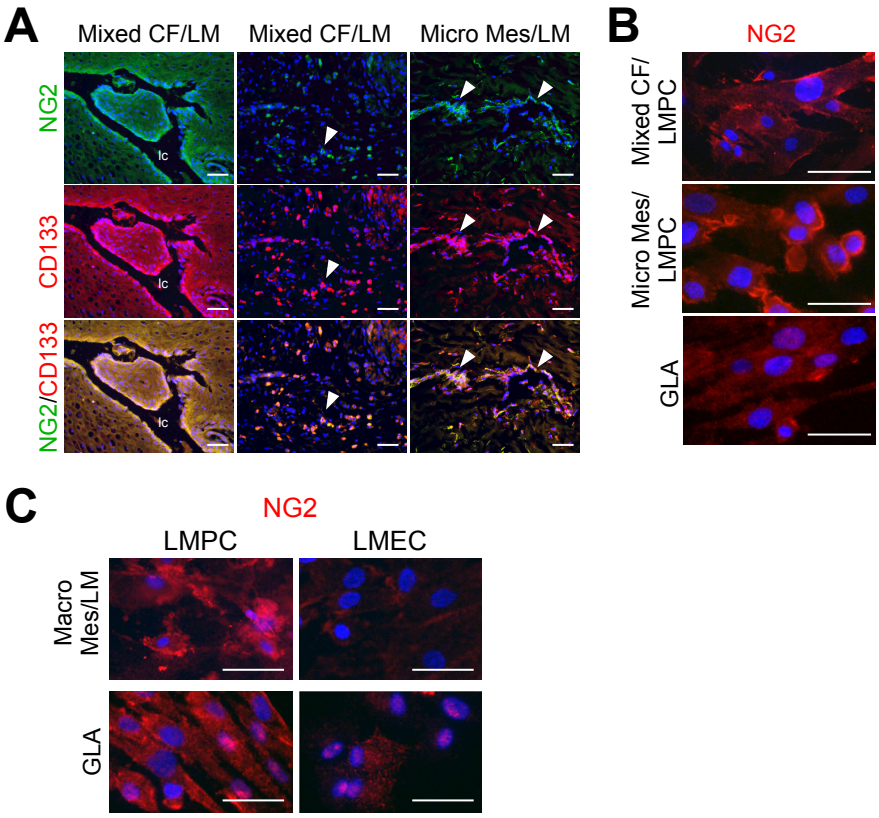

Figure S4. LMPCs expressed NG2. (**A**) NG2 and CD133 staining of mixed cervical facial (Mixed CF) and microcystic mesenteric (Micro Mes) LM tissues. White arrowheads mark abnormal lymphatic vessels. (**B**) NG2 staining of $CD133^+$ LM cells isolated from Mixed CF LM, Micro Mes LM tissues and generalized lymphatic anomaly (GLA) specimens. (**C**) NG2 staining of patient-matched $CD133^+$ LMPCs and $CD133^-$ LMECs isolated from macrocystic mesenteric (Macro Mes) LM and GLA. Scale bars: 50 μm. lymphatic channel (lc)

Wu et al. Figure V

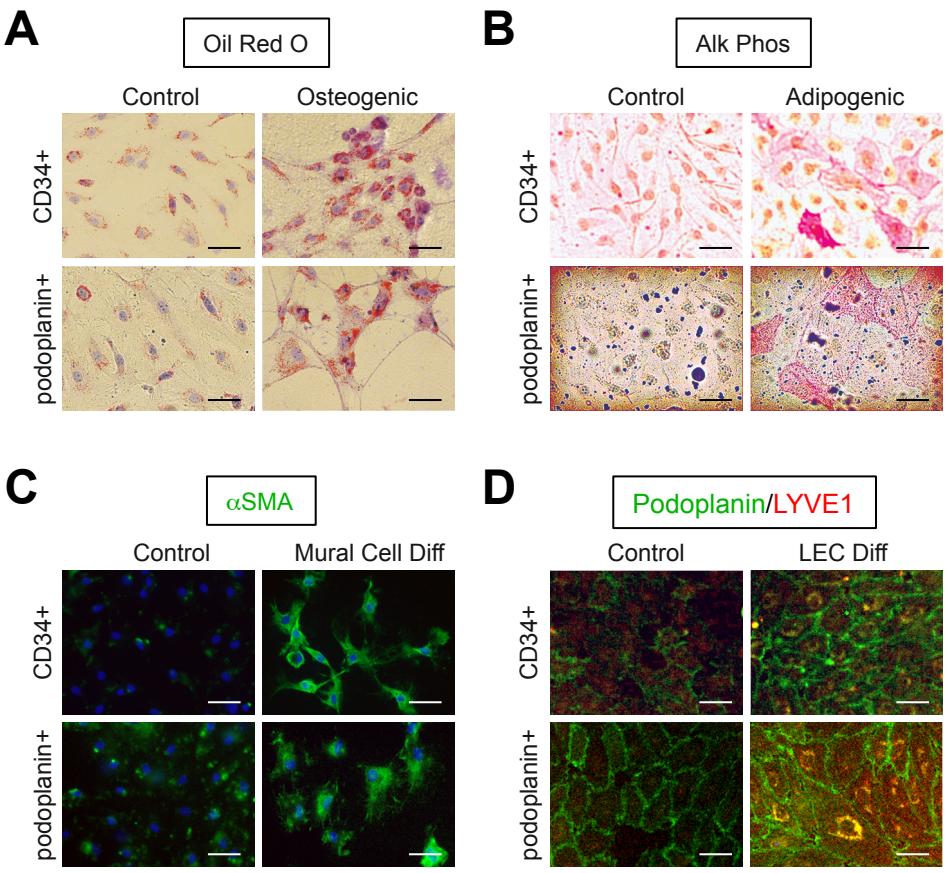

Figure S5. CD34+ and podoplanin+ LMPCs were multipotent. LMPCs isolated from a microcystic subcutaneous were sorted for CD34 or podoplanin positivity and induced to differentiate into fat, bone, VSMCs and LECs. (**A**) Oil Red O staining of CD34$^+$ or podoplanin$^+$ LMPCs after 2 weeks in growth media (control) or adipogenic media. (**B**) Alkaline phosphatase (Alk Phos) staining of CD34$^+$ or podoplanin$^+$ LMPCs after 2 weeks in growth media (control) or osteogenic media. (**C**) Alpha smooth muscle actin (αSMA) staining of CD34$^+$ or podoplanin$^+$ LMPCs after 2 weeks in growth media (control) or mural cell differentiation (Diff) media. (**D**) Podoplanin and LYVE1 staining of CD34$^+$ or podoplanin$^+$ LMPCs after 2 weeks in growth media (control) or LEC differentiation (Diff) media. Scale bars: 50 μm.

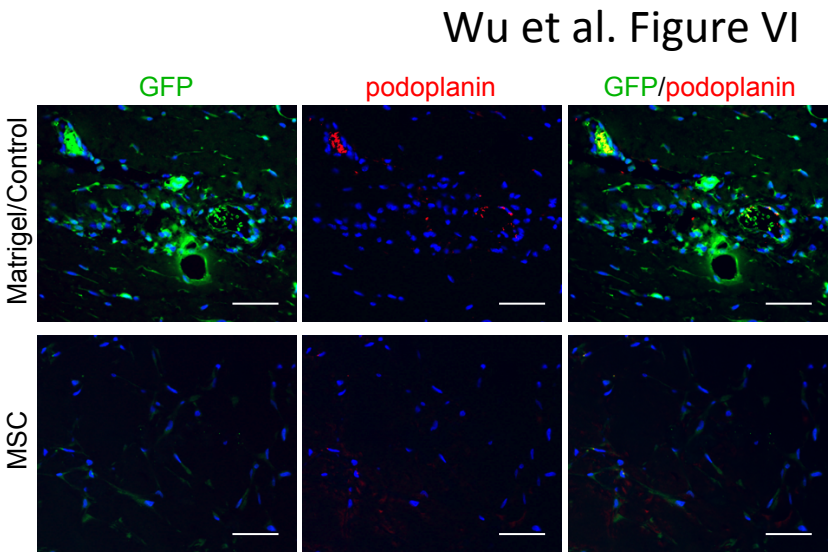

Figure S6. Analysis of control implants. Matrigel alone or MSCs suspended in Matrigel was implanted into GFP-expressing immunocompromised mice. GFP (host cell) and podoplanin staining of xenograft sections. Scale bars: 50 μm.