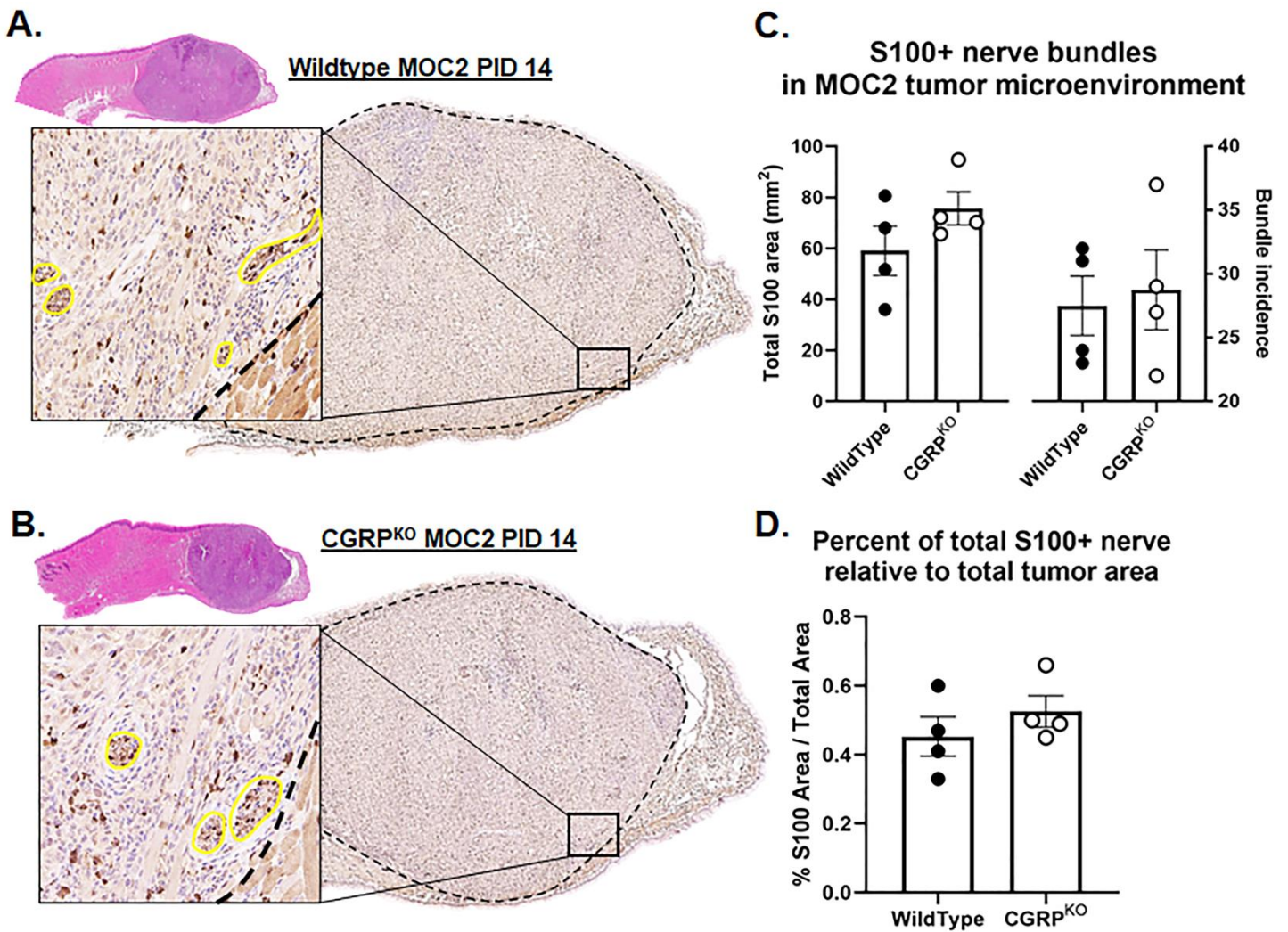


Supplemental Figure 1. Correlation between patient-reported pain and CGRP immunoreactivity (IR). A simple linear regression was run between patient-reported pain and the percent of total α CGRP-IR nerve area relative to total S100-IR nerve area across tumor tissue sections from 11 HNSCC patients with PNI pathology reported by an oral and maxillofacial pathologist. Patient demographics are located in **Table 1**. Pain was measured by the FACT-H&N Additional questions number 12, "I have pain in my mouth, throat or neck". The response to this question is rated on a scale of 0 (not at all) to 4 (very much). Pearson Correlation $p > 0.05$.



Supplemental Figure 2. S100-immunoreactive nerve presence in tumor-bearing mice. Representative images of anti-S100 staining in MOC2 tumor tissue from in wildtype mice (**A**) and CGRP^{KO} mice (global *Calca* knockout) (**B**) at PID 14. Images were collected from 5 μ m sections at 1.6x and 10x (inset) magnification. Tumors are outlined in black dotted lines. **C**) Quantitative analysis of S100-immunoreactive (IR) nerve bundles in MOC2 tumor tissue (n=4/genotype). The total number of S100-IR bundles were counted across four sections, and the total nerve area was calculated using ImageScope software per section and averaged per sample. Student's t test, p>0.05. **D**) The percent of total S100-IR nerve area was calculated relative to the total tumor area assessed per section and averaged for each sample. Student's t test, p>0.05.