SUPPLEMENTAL MATERIAL

Analytical Considerations of Local and Global Gradients in c_{O_2}

To justify the continuum treatment of the concentration distribution within our scaffolds, we must show that the typical gradient associated with a single cell is small compared to that of the full distribution of cells in the geometries considered. We estimate the average global gradients in c_{O_2} as

$$\nabla c_{\text{global}} \sim c_0/\lambda_k \sim \sqrt{\frac{c_o \rho_{\text{cell}} R_{O_2,\text{cell}}}{D}},$$

where $\lambda_k \sim \sqrt{Dc_0/\rho_{\text{cell}} R_{O_2,\text{cell}}}$ is the Krogh length scale for global changes in c_{O_2} in a zeroth order model, and typical local gradients in c_{O_2} around a single cell as

$$\nabla c_{\text{local}} \sim \frac{c_{\text{local}}(r = 0.5\rho_{\text{cell}}{}^{-1/3}) - c_{\text{local}}(r = r_{\text{cell}})}{0.5\rho_{\text{cell}}{}^{-1/3}},$$

where we have taken the average intercellular spacing as the length scale that defines the cell's local environment. The local concentration profile in the vicinity of a single cell can be found by solving:

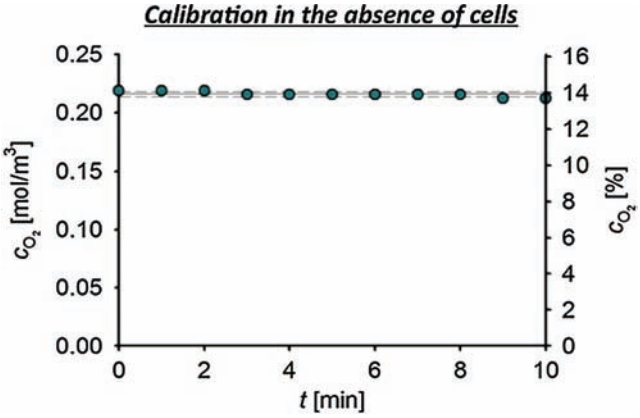
$$D\nabla^2 c = \rho_{\text{cell}} R_{O_2,\text{cell}}, \text{ assuming } c(r \to \infty) = c_\infty.$$

We therefore find, for a cellular point sink assumption, that

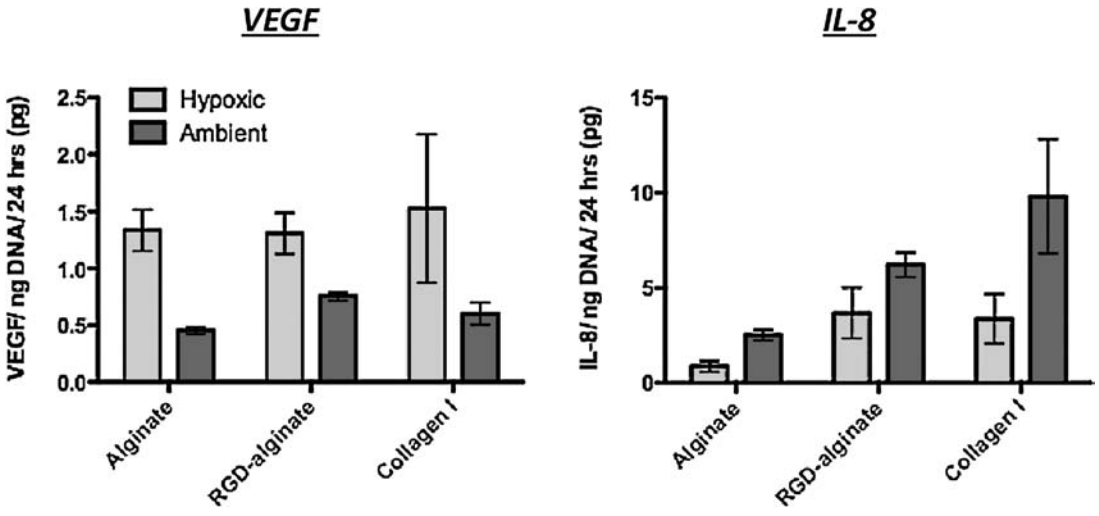
$$\nabla c_{\text{local}} \sim \frac{(R_{O_2,\text{cell}}/4\pi D r_{\text{cell}})}{0.5\rho_{\text{cell}}{}^{-1/3}}$$

and for $r_{\text{cell}} \sim 8\,\mu\text{m}$, and $\rho_{\text{cell}} \sim 60\times10^6\,\text{cell/mL}$, we find

$$\frac{\nabla c_{\text{local}}}{\nabla c_{\text{global}}} \sim 0.03.$$



SUPPLEMENTAL FIG. S1. Control O_2 consumption measurement. O_2 concentration was measured in a sealed, magnetically stirred vial containing 2 mL Dulbecco's modified Eagle's medium, identical to the system used for cellular O_2 consumption measurements, with negligible change in concentration observed over 10 min. Data points represent individual measurements; the solid and dotted lines represent the mean and standard deviation of all measurements taken over the 10-min interval presented.



SUPPLEMENTAL FIG. S2. Summary of oral squamous cell carcinoma secretion data. Summary of oxygen partial pressure (pO_2) and extracellular-matrix-dependent vascular endothelial growth factor (VEGF) and interleukin-8 (IL-8) secretions for three-dimensional cultured oral squamous cell carcinoma, cultured at hypoxia (1%) and ambient ($18 \pm 1\%$) O_2, and in three different scaffold systems: nonmodified alginate, RGD-modified alginate, and type I collagen. Alginate cultures were in free-floating 200-μm-thick disks, whereas the collagen culture was in <100 μm of scaffold material, in a poly (dimethylsiloxane)-supported microwell format. Alginate data represent 24-h secretion periods, at a day-3 timepoint. Collagen data represent 24-h secretion periods, at a day-2 timepoint.