

Supplementary Information

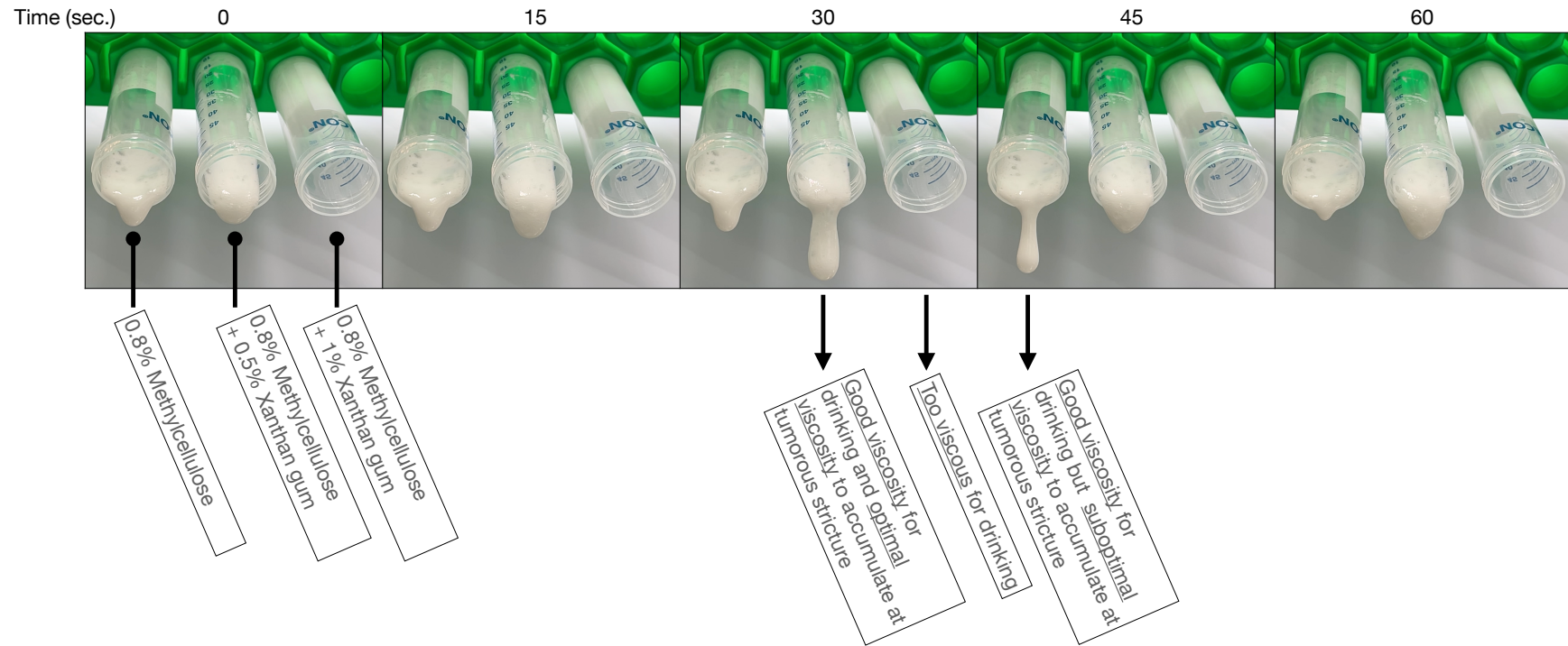
Drinkable gene therapy foam for the treatment of constrictive esophageal carcinoma

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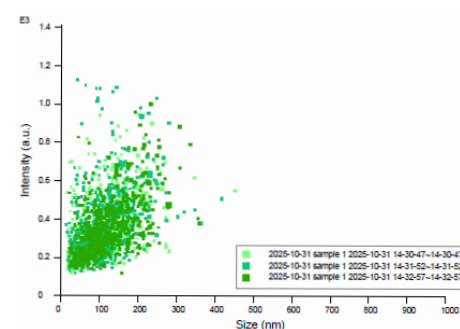
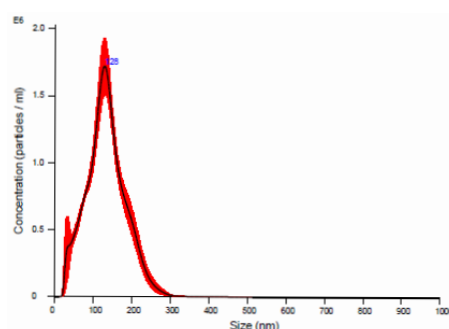
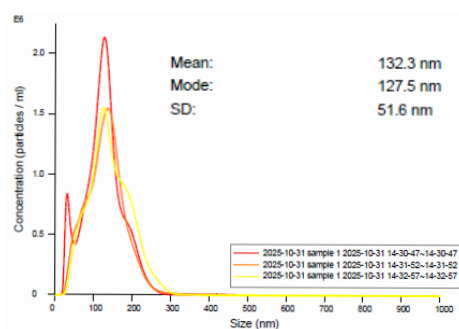
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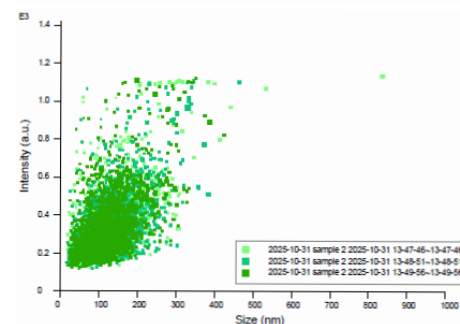
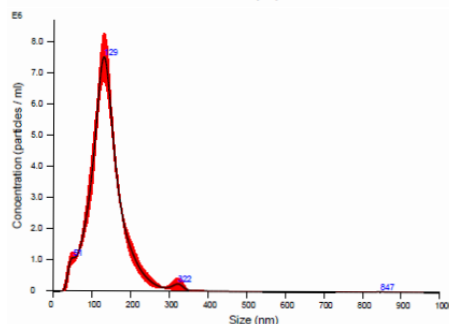
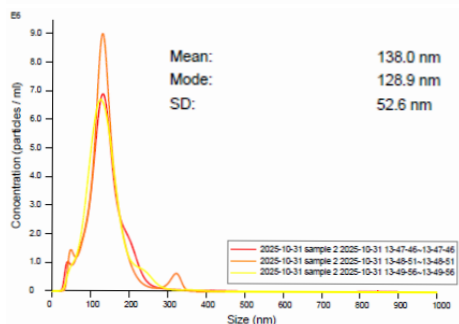
Supplementary Figure 1: Representative frames of a 60-second time lapse video comparing viscosities of foams based on 0.8% Methylcellulose (left tube), 0.8% Methylcellulose + 0.5% Xanthan gum (middle tube), and 0.8% Methylcellulose + 1% Xanthan gum (right tube). Each tube was filled with 4 mL of freshly prepared foam and mounted upside-down at a 45-degree angle inside a 37°C incubator.

- Size Distribution (Nanosight): 138 ± 5 nm; PDI: 0.14
- Zeta Potential: -0.8 ± 0.5 mV
- mRNA Encapsulation: $95.3 \pm 0.5\%$

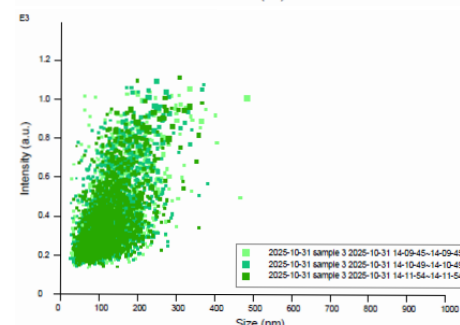
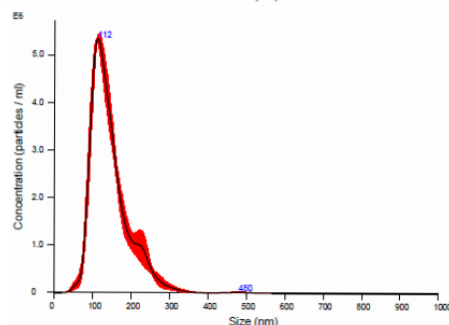
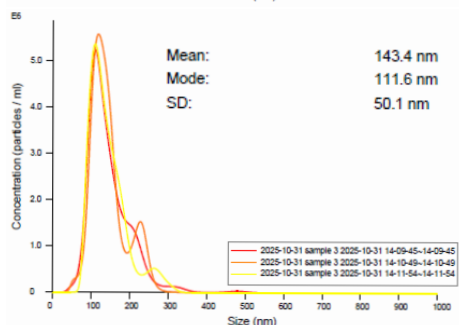
Batch #1



Batch #2



Batch #3



Supplementary Figure 2: Physicochemical characterization of Lipid nanoparticles (LNPs). Size distribution was measured via Nanoparticle Tracking Analysis using a NanoSight NS300 (Malvern) and zeta potential was determined using dynamic light scattering detected with a ZetaPALS instrument (Brookhaven). The particles were diluted 1:100 (v/v) in PBS for size measurements, and 1:33 (v/v) in water for zeta potential quantitation. Size distribution was determined for three independently prepared batches of LNPs. For each batch, three consecutive videos (60 s each) were captured under constant flow conditions. mRNA encapsulation efficiency was determined using a Qubit RNA High Sensitivity Assay Kit (Invitrogen). LNPs were incubated with the Qubit RNA reagent in the presence and absence of 1% Triton X-100. Fluorescence intensities for total mRNA after release from LNPs by Triton X-100 were compared to fluorescence intensities for unencapsulated mRNA measured in the absence of Triton X-100.

Supplementary Movie 1: Workflow for generating methylcellulose/xanthan gum-based gene therapy foam with embedded mRNA lipid nanoparticles (LNPs). LNPs are added to foam precursor in a syringe connected to a second syringe filled with air. The air and foam precursor are mixed by vigorously drawing the syringe plungers back and forth at least 30 times, creating a uniform microfoam consisting of gas bubbles separated by a network of interconnected liquid film structures, called lamellae, that contains highly concentrated vector.

Supplementary Movie 2: Two-hour time-lapse videos showing 4 mL methylcellulose/xanthan gum-based foam entering an esophageal tube narrowed at the bottom by esophageal tumor (OACM5.1 C tumor cells established in 3D collagen plugs). Videos were acquired under a black light and fluorescent UV dye was added to foam for easy detection. Three independent replicates are shown. Representative frames are summarized in **Fig. 3a**.

Supplementary Movie 3: Two-hour time-lapse videos showing 4 mL phosphate-buffered saline (PBS) suspension entering an esophageal tube narrowed at the bottom by esophageal tumor (OACM5.1 C tumor cells established in 3D collagen plugs). Videos were acquired under a black light and fluorescent UV dye was added to liquid for easy detection. Three independent replicates are shown. Representative frames are summarized in **Fig. 3a**.