Peptide-based surface-fill hydrogel facilitates miRNA delivery to treat mesothelioma

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Cancers, such as mesothelioma, that grow as sheets on the surface of organs and tissues having complex anatomical features represent a unique challenge in oncology. In contrast to solid tumor masses, their surgical resection often leaves residual cancer that causes rapid recurrence. We developed a peptide-based hydrogel that can be sprayed or injected to effectively cover large surface areas of organs and tissues having complex anatomical features, including those resulting from surgical resection. Once implanted, the material can shape-change to accommodate real-time changes in tissue morphology. The material locally delivers nanoparticles engineered from intrinsically disordered peptide and miRNA that effectively enter cells, escaping the acidic endosome to target mRNA important for the progression of mesothelioma, an aggressive asbestos-related cancer. Interestingly, endosomal release of the nanoparticles is dependent on the conformational state of the peptide comprising the particle-the peptide must be disordered. We show that with a single application, this gel produces a durable pre-clinical response in three increasingly complex models of mesothelioma. In principle, this regional treatment strategy could be applied to other surface cancers, including ovarian carcinoma and gliomas.