

489a Degradable Polymersomes That Create New Pathways for Anti-Cancer Drugs

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Carrier-mediated delivery of drugs into cells is often limited by release from either the carrier or an internalizing endosome. Here we describe delivery and release of degradable polymersomes with drug cocktails that induce apoptosis in xenografted tumors. Mechanisms identified in cell culture as well as by molecular simulation reveal pinocytotic entry of (Polyethylene-glycol)-(Polyester) polymersomes into cells followed by endosomal rupture and release of soluble and insoluble cytotoxic drugs. While the polymersomes retain their drug load for over a month at 4°C, they break down into copolymer micelles over dozens of hours at 37°C and low pH. Above a critical polymer concentration easily achieved in endosomes, the micelles disrupt lipid membranes and enhance drug activity by up to 40-fold relative to free drug. Polymersomes and other macro-surfactants can thus create novel pathways for controlled release and delivery.