Sarah C. Heilshorn
Stanford University

Adaptable hydrogels for organoid culture

The term “organoid” refers to an artificially grown collection of cells that resembles aspects of a native organ. While organoid culture has the potential to revolutionize our understanding of human biology, current protocols rely on the use of Matrigel, a complex, heterogeneous material with large batch-to-batch variations that hinder reproducibility. In response, several groups have begun designing synthetic hydrogel systems to enable the reproducible culture of organoids. Recently, the matrix stress relaxation rate (i.e. the ability of a hydrogel to remodel its network connectivity in response to an applied stress) has been demonstrated to have profound effects on encapsulated cells. To date, the role of matrix stress relaxation on organoid cultures has been underexplored. Here we present the design of a family of double-network hydrogels that undergo two stages of crosslinking: the first stage uses reversibly dynamic covalent chemistry bonds, while the second stage reinforces the hydrogel through thermal-induced polymer aggregation. This double-network of physical interactions results in a gel with a broad dynamic range of tunable mechanical properties, where the gel stiffness is set by the number of crosslinks and the gel stress relaxation rate is independently set by the kinetics of the crosslink binding and unbinding. These novel, double-network hydrogels are being used to study the role of mechanotransduction in the culture of several different types of patient-derived, human organoids.