Differentiation of human embryonic stem cells is widely studied as a potential unlimited source for cell replacement therapy to treat degenerative diseases such as diabetes. The directed differentiation of human embryonic stem cells relies mainly on soluble factors. Although, some studies have highlighted that the properties of the physical environment, such as substrate stiffness, affect cellular behavior. Here, mass-produced, injection molded polycarbonate nanopillars are presented, where the surface mechanical properties, i.e., stiffness, can be controlled by the geometric design of the ultrahigh aspect ratio nanopillars (stiffness can be reduced by 25,000X). It is found that tall nanopillars, yielding softer surfaces, significantly enhance the induction of definitive endoderm cells from pluripotent human embryonic stem cells, resulting in more consistent differentiation of a pure population compared to planar control. By contrast, further differentiation toward the pancreatic endoderm is less successful on “soft” pillars when compared to “stiff” pillars or control, indicating differential cues during the different stages of differentiation. To accompany the mechanical properties of the nanopillars, the concept of surface shear modulus is introduced to describe the characteristics of engineered elastic surfaces through micro or nanopatterning. This provides a framework whereby comparisons can be drawn between such materials and bulk elastomeric materials.