Novel Iron-Regulating Hydrogel for the Treatment of Diseases with Iron Dyshomeostasis

Henein, Marc

Elevated levels of highly-reactive non-transferrin bound iron (NTBI) are common in many diseases with iron dyshomeostasis and are a marker of their progression. Chelation therapy is an effective way to treat these diseases. However, excess iron must be removed without depriving cells of the essential iron needed for normal metabolism. In this study, a hydrogel was engineered to detect the amount of NTBI in its environment and release doses of chelator in response to elevated levels. The chelator, deferoxamine (DFO), which deprotonates when it binds to Fe (III), was physically entrapped in a P(NIPAAm-co-AAc) hydrogel, selected among ten other candidates that were tested for pH-sensitivity and for pores with a low molecular weight cutoff. The release of DFO from the hydrogel was studied in PBS with ferric ammonium citrate using UV/Vis spectroscopy and in an iron-overloaded cell culture by looking at changes in transferrin mRNA and ferritin levels using Northern Blot and immunoprecipitation respectively. In the first four hours, the hydrogel was shown to release only 4% of DFO in a control environment with no NTBI and 46% in an iron-overloaded environment with 10 micro-mol/L NTBI. Finally, the hydrogel swelling and diffusion were mathematically modeled in order to also use the hydrogel as an assay that could more accurately measure NTBI levels in a blood sample. This novel hydrogel could open the doors to safely treating many diseases, like tumor angiogenesis and neurodegenerative diseases, with targeted chelation therapy and to using NTBI as a biomarker in a clinical setting.