the SPSHU-PNIPAM groups compared to the saline, VEGF, and no injection controls (Figure 1). SPSHU-PNIPAM either loaded with or without VEGF seemed to have very similar treatment effects for ejection fraction and fractional shortening. This indicates that the more significant component of the cardioprotective effects of the hydrogel system is the biomaterial itself rather than the release of VEGF (Figure 1). However, the only statistically significant improvement for ejection fraction, fractional shortening, and left ventricular inner diameter that was observed compared to the saline, VEGF, and no injection controls was the SPSHU-PNIPAM + VEGF group (Figure 1). Histology Results: After analyzing Masson trichrome staining, SPSHU-PNIPAM + VEGF demonstrated the smallest infarct size after MI reperfusion injury and was statistically reduced compared to the saline, VEGF, and no injection controls (Figure 2). Furthermore, left ventricular wall thickness showed that the SPSHU-PNIPAM + VEGF treatment group reduced the wall thinning resulting from MI. The SPSHU-PNIPAM group without VEGF displayed a thicker ventricular wall as well, which may be attributed to the increased mechanical stability with the intramyocardial injection of the biomaterial (Figure 2). The immunohistochemical results for vascularization show that the SPSHU-PNIPAM + VEGF group significantly increased the number of functional vascular endothelial cells compared to the saline, VEGF, SPSHU-PNIPAM, and no injection controls (Figure 3). Additionally, the SPSHU-PNIPAM + VEGF group showed a significant increase in total vessel formation compared to the control groups, although there was no significant difference compared to SPSHU-PNIPAM without VEGF (Figure 3). The promotion of angiogenesis, without the delivery of VEGF, may be attributed to inflammation induced vascularization, including VEGF dependent vascularization that is initiated via signal transducer and activator of transcription 3 (STAT3) pathway that is induced by the pro-inflammatory cytokine interleukin 6. DISCUSSION/SIGNIFICANCE OF IMPACT: The SPSHU-PNIPAM loaded with VEGF was evaluated for therapeutic angiogenesis to protect cardiac function after MI. Treatment with SPSHU-PNIPAM showed improved cardiac function and vascularization; however, the additional delivery of VEGF showed inadequate additional therapeutic benefits. Further investigation will include optimizing VEGF release characteristics including both loading amount and release rate. The decline of ejection fraction and fractional shortening after MI were reduced, while left ventricular internal diameter showed reduced ventricular dilation. Both infarct size and left ventricular wall thinning decreased while an increase in the vessel formation was observed. These results demonstrate the SPSHU-PNIPAM biomaterial has cardioprotective and increased vascularization properties for the treatment of MI.

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Analysis of High-Dimensional Patient Data in Characterizing Alzheimer's Disease Progression

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OBJECTIVES/SPECIFIC AIMS: Our research hypothesis is that resting state fMRI (rsfMRI) data can be used to identify regions of the brain which are associated with cognitive decline in patients – thereby providing a tool by which to characterize AD progression in patients. METHODS/STUDY POPULATION: We used data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) to analyze Mini-Mental State Examination (MMSE) questionnaire scores from 14 patients diagnosed with AD at two measurement occasions. RsfMRI data was available at the first of these occasions for these patients. These rsfMRI data were summarized into 264 node-based graph theory measures of clustering coefficient and eigenvector centrality. To address our research hypothesis, we modeled changes in patient MMSE scores over time as a function of these rsfMRI data, controlling for relevant confounding factors. This model accounted for the high-dimensionality of our predictor data, the longitudinal nature of the outcome, and our desire to identify a subset of regions in the brain most associated with the MMSE outcome. RESULTS/ANTICIPATED RESULTS: The use of either the clustering coefficient or eigenvector centrality rsfMRI predictors in modeling MMSE scores for patients over time resulted in the identification of different subsets of brain regions associated with cognitive decline. This suggests that these predictors capture different information on patient propensity for cognitive decline. Further work is warranted to validate these results on a larger sample of ADNI patients. DISCUSSION/SIGNIFICANCE OF IMPACT: We conclude that different rsfMRI graph theory measures capture different aspects of cognitive function and decline in patients, which could be a future consideration in clinical practice.

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Bacterial biotransformation of chemotherapeutics may promote diversity among the intestinal microbiota

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OBJECTIVES/SPECIFIC AIMS: This study aims to test the hypothesis that bacterial biotransformation of chemotherapeutics promotes gut microbial diversity by enhancing persistence of drug-sensitive taxa. METHODS/STUDY POPULATION: The impacts of doxorubicin on a model community of gut bacteria was investigated in vitro in anaerobic batch culture. The synthetic community was composed of specific members predicted by genomic analysis to be sensitive to the therapeutic (i.e., Clostridium innocuum, Lactobacillus sp.), resistant via putative biotransformation (i.e., Escherichia coli, Klebsiella pneumoniae), or resistant via putative efflux (i.e., Enterococcus faecalis). Bacterial growth was monitored in monocultures by measuring OD600 and standard plate counts, and in mixed cultures by strain-targeted qPCR. Doxorubicin concentration was detected via absorbance assay. RESULTS/ANTICIPATED RESULTS: Strains with predicted resistance to doxorubicin by drug biotransformation significantly lowered concentrations of the drug in culture media. In contrast, E. faecalis proved resistant without evidence of drug transformation. Predicted sensitive strains were growth-repressed by the doxorubicin, but able to grow in spent media where biotransformation had occurred. However, they remained growth-repressed in spent media from E. faecalis where drug transformation had not been observed. Bacterial growth kinetics in mixed batch culture were dependent on starting bacterial concentrations and timing of drug exposure. DISCUSSION/SIGNIFICANCE OF IMPACT: This work will be extended to model microbial community responses to doxorubicin as a factor of microbial interactions and extent of drug transformation prior its exposure to sensitive strains. The resulting model will have translational implications for mitigating health risks during pediatric cancer treatment.