

an additive effect of the two agents when administered together. These results will be presented. In addition, results from on-going PKPD studies of TMZ in combination with two other small molecule inhibitors, RG7388, an MDM2 inhibitor, and GDC0068, an AKT inhibitor, will also be presented. **DISCUSSION/SIGNIFICANCE OF IMPACT:** Our long-term goals are to further elucidate SOC-induced responses in GBM and establish combination treatment regimens that are safe and significantly improve therapeutic efficacy. Collectively, our studies will broadly influence chemotherapy of GBM by establishing a process to rationally design combination approaches that mitigate resistance development. These studies will ultimately provide opportunities to study other targeted agents tailored to individual molecular signatures of GBM, as well as other tumor types.

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An Evaluation of Machine Learning and Traditional Statistical Methods for Discovery in Large-Scale Translational Data

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OBJECTIVES/SPECIFIC AIMS: To examine and compare the claims in Bzdok, Altman, and Brzywinski under a broader set of conditions by using unbiased methods of comparison. To explore how to accurately use various machine learning and traditional statistical methods in large-scale translational research by estimating their accuracy statistics. Then we will identify the methods with the best performance characteristics. **METHODS/STUDY POPULATION:** We conducted a simulation study with a microarray of gene expression data. We maintained the original structure proposed by Bzdok, Altman, and Brzywinski. The structure for gene expression data includes a total of 40 genes from 20 people, in which 10 people are phenotype positive and 10 are phenotype negative. In order to find a statistical difference 25% of the genes were set to be dysregulated across phenotype. This dysregulation forced the positive and negative phenotypes to have different mean population expressions. Additional variance was included to simulate genetic variation across the population. We also allowed for within person correlation across genes, which was not done in the original simulations. The following methods were used to determine the number of dysregulated genes in simulated data set: unadjusted p-values, Benjamini-Hochberg adjusted p-values, Bonferroni adjusted p-values, random forest importance levels, neural net prediction weights, and second-generation p-values. **RESULTS/ANTICIPATED RESULTS:** Results vary depending on whether a pre-specified significance level is used or the top 10 ranked values are taken. When all methods are given the same prior information of 10 dysregulated genes, the Benjamini-Hochberg adjusted p-values and the second-generation p-values generally outperform all other methods. We were not able to reproduce or validate the finding that random forest importance levels via a machine learning algorithm outperform classical methods. Almost uniformly, the machine learning methods did not yield improved accuracy statistics and they depend heavily on the a priori chosen number of dysregulated genes. **DISCUSSION/SIGNIFICANCE OF IMPACT:** In this context, machine learning methods do not outperform standard methods. Because of this and their additional complexity, machine learning approaches would not be preferable. Of all the approaches the second-generation p-value appears to offer significant benefit for the cost of a priori defining a region of trivially null effect sizes. The choice of an analysis method for large-scale translational data is critical to the success of any statistical

investigation, and our simulations clearly highlight the various trade-offs among the available methods.

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An Injectable Sulfonated Reversible Thermal Gel for Controlled and Localized Delivery of Vascular Endothelial Growth Factor to Promote Cardiac Protection After a Myocardial Infarction

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OBJECTIVES/SPECIFIC AIMS: This study aims to evaluate an injectable sulfonated reversible thermal gel (SPSHU-PNIPAM) for angiogenic growth factor delivery by examining the vascularization and cardioprotective properties of the polymer system. This study could lead to clinical translation by moving into larger animal studies and eventually clinical trials. The success of this study was determined by analyzing the results of echocardiography data on cardiac function (ejection fraction, fractional shortening, and left ventricle inner diameter) and assessment of histological staining on cardiac tissue (fibrotic tissue formation, infarct size, wall thinning, blood vessel cell counts, and vessel size quantification) after MI. Five groups were compared for this study: saline, VEGF, SPSHU-PNIPAM, SPSHU-PNIPAM loaded with VEGF, and no injection (sham). Significant statistical differences between control groups and polymer injection groups, when $p < 0.05$, indicates successful outcomes from this study. **METHODS/STUDY POPULATION:** SPSHU-PNIPAM Polymer Synthesis: SPSHU-PNIPAM was synthesized as previously described. Briefly, PSHU was synthesized with N-BOC serinol, urea, and HDI at 90 °C for 7 days. PSHU was deprotected in DCM and TFA at room temperature for 45 min. PNIPAM was conjugated to the deprotected PSHU using EDC and NHS at room temperature for 24 h. PSHU-PNIPAM was sulfonated with 1,3-propanesultone and potassium tert-butoxide at 60 °C for 3 days. **Surgical Procedure:** Male C57BL/6 mice weighing 24-28 g were anaesthetized using isoflurane and artificial ventilation provided. A small left thoracotomy incision was made at the left fourth intercostal space to expose the heart, and the proximal left anterior descending coronary artery was ligated for 45 min. The coronary artery was then released and 30 µl injections of saline, SPSHU-PNIPAM (1% w/v), bolus VEGF (200 ng), or SPSHU-PNIPAM + VEGF (1%, 200 ng) were injected intramyocardially at the infarcted site and the incision closed. **Echocardiography and Histological Staining:** Standard serial transthoracic echocardiography was performed while simultaneously recording ECG to assess cardiac morphology and left ventricular function. Immunohistochemistry and histology staining procedures were used to identify: fibrotic tissue formation, infarct size, wall thinning, blood vessel cell counts, and vessel size quantification. These were performed according to manufacturer instructions or by previously published criteria. **Statistical Analysis:** Two-tailed t-test assuming unequal variances was used to determine significant differences between two groups. Analysis of variance (ANOVA) was used to determine significant differences between three or more groups followed by Tukey-Kramer to determine significant differences between two groups as appropriate. Statistical significance was considered when $p < 0.05$. **References:** Lee, D. J., Rocker, A. J., Bardill, J. R., Shandas, R. and Park, D. (2018), A sulfonated reversible thermal gel for the spatiotemporal control of VEGF delivery to promote therapeutic angiogenesis. *J Biomed Mater Res.* doi:10.1002/jbm.a.36496. **RESULTS/ANTICIPATED RESULTS:** Echocardiography results: Ejection fraction improved for