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Development of Molecular Profiles to Predict Treatment Outcomes in Cancer Patients

Lymphoma, a cancer which affects the immune system, is the fifth most common cancer in North America. Rituximab-based chemotherapy (R-CHOP) has become the standard recommended cancer-management course for this disease. Using previously collected data from a 2008 study conducted by Lenz G. Wright and publicly available from the National Center for Biotechnology Information, we used statistical methods to identify genetic characteristics associated with survival in R-CHOP treated patients. Univariate screening reduced the 54,000 recorded genes per patient into a manageable group which displayed strong possible correlation with overall survival. The resulting gene collection was partitioned into clusters of related genes and then scored using principal components. Then, a multivariate Cox-Regression model of these principal components was developed to best predict survival in Lymphoma patients. The resulting model can be used to help identify genetic characteristics of patients who are less likely to response to current therapy and are potential targets for new drug development.

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Genetic Association Analysis of Essential Tremor

Essential tremor (ET) is a disease that causes movement disorder. The exact cause is unknown but is believed to have genetic and neurological components. This disease has been studied by mapping chromosomes to try to find some type of genetic disorder. For this research a pedigree of size twenty-nine was used, but only fourteen subjects were genetically analyzed. Each subject was classified as affected or unaffected with ET. In this sample eight subjects were affected and five were unaffected. Some subjects' affection status was unknown due to uncertainty in the doctor's diagnoses. A Genechip was used to determine the genotype at 909,622 single nucleotide polymorphisms (SNP) locations. Each SNP was examined to detect what alleles it contained and were classified as homozygous or heterozygous. For the analysis the data was divided between affected and unaffected subjects. Using Pearson Chi-Square tests we compared the alleles in each SNP to the subjects' disease status. P-values were calculated for each SNP. These p-values were used to determine the significance of each SNP.

All p-values were below the significance level, however some suggestive peaks were observed. One notable peak was located in 6q21 and corresponded with GPR6 a protein involved in neuron growth and myelination. If more data is collected, there are possibilities for these peaks to become significant. Current studies are still working on this subject.

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Using Actigraphy Watches to Measure Sleep Activity in Subjects with Obstructive Sleep Apnea

Obstructive Sleep Apnea (OSA) is a disorder which partially obstructs the airway as a result of the narrowing in the respiratory passage during sleep, causing loud snoring, excessive daytime sleepiness, and disrupted sleep. It can be potentially fatal for overweight smokers. In this study, we are using actigraphy watches with built-in accelerometers to monitor sleep patterns over a 3-month period. Based on the “low threshold” setting, these watches provided data which allowed a measure of sleep efficiency. To date, 30 subjects with OSA and 16 healthy controls have completed the study. Approximately two weeks after the beginning of the study, OSA subjects began using CPAP devices to treat their condition. Consequently, we made comparisons between groups during the first seven days on study to measure baseline differences, and we compared sleep efficiency profiles during the final month versus baseline to assess within-group differences. We found that the OSA group did, in fact, have less efficient sleep patterns pre-treatment, and that these did not improve significantly over the course of the study. Our results suggest that the actigraphy watches may be an important tool in monitoring sleep patterns in OSA patients, including responses to treatment. The OSA study was funded by NIH grant R01 HL091917.

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Salmonella Infantis: Assessing Causes and Trends

According to the Centers for Disease Control and Prevention, it is estimated that each year foodborne disease is the cause of roughly 48 million illnesses, 128,000 hospitalizations, and 3,000 deaths among American citizens. Of the 31 known pathogens that contribute to domestically acquired foodborne illness, Salmonella is deemed the leading pathogen causing hospitalization and death. Although there has been greater implementation of government regulations, the CDC has confirmed that since 1998 the rate of infection of Salmonella is slightly increasing rather than decreasing. For this reason, Salmonella presents itself as a public health concern that needs to be addressed immediately.

Last year, Diamond Pet Foods recalled a dry dog food product due to a Salmonella Infantis contamination, which caused an outbreak of Salmonella in humans. In order to gain greater intuition on this particular serotype and further understand the outbreak trends of Infantis, the research of this project focuses heavily on using Bayesian statistical methodology to determine changepoints using a Markov Chain Monte Carlo computational method, as well as a Bayesian Poisson Analysis. Furthermore, a simulation study was developed to evaluate how well these methods were able to successfully detect outbreaks, as well as how different factors affect these results. Results showed that the Bayesian Poisson analysis was better at detecting outbreak trends of Salmonella, including the individual strain Salmonella Infantis. The simulation study showed that, when using the Poisson-gamma method, the two most influential factors in detecting the correct number of outbreaks are the frequency of outbreaks and a parameter value that is used to distinguish between outbreaks and background infections.

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Longitudinal Study of Children with a Language Impairment

Language impairment is the difficulty in learning to perceive and/or express language. This research is based on the Longitudinal Study of Children with a Language Impairment which is a study that involves 502 children who were selected from the Child Learning Research Center Project database. All children were separated into two groups, learning impaired or normal using norms established by the Child Language Research Center Project. This longitudinal study was made up of children who completed the Comprehensive Reading and Expressive Vocabulary Test (CREVT) in 2nd, 4th, 8th, and 10th grade. The CREVT is a standardized measure of oral vocabulary in which the child defines up to 25 words. They continued defining these specific words (which increase in difficulty) until the child defines three consecutive words inaccurately or until they reach the last word. We used the results from 502 children in this study to calculate the number of words each child defined correctly at each grade level. The method used to analyze the data from this study is known as a linear mixed effects model which is used for repeated measures. As expected, the number of words defined correctly increases significantly ($\alpha=0.05$) as the children age. In addition normal hearing children performed significantly better than learning impaired, but the difference between the two groups in the number of words correct does not change significantly as the children get older.

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Cochlear Implant Decision Making Study

A cochlear implant is an electronic device that can help a person who is profoundly deaf or hard of hearing to improve their hearing (NIH, 2011). The purpose of this research is to detect whether one cochlear implant (CI) or two CI's are needed in a patient in order to validate theoretical guidelines for CI selection strategies from Perreau et al (2007) and to optimize the candidacy process for binaural and monaural cochlear implantation. The study tested 311 patients with cochlear implants at the University of Iowa Hospital and Clinics. They were given certain assessments prior to implantation, such as the hearing in noise test (HINT) and the consonant nucleus consonant (CNC) monosyllabic word test, to measure how well the patient hears. We utilized the score from those assessments in order to perform logistic regression to predict which group they should fall into. The data was analyzed with the Statistical Analysis System (SAS) software.

Based on the data used, this study found that our model can be significantly determined by the explanatory variables, the better ear score in the pure tone audiometry (PTA) test and years of education, resulting in 67% precision.

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Survival Function Estimation with Recurrent Events: The Case of Neural Firing

Recurrent Events (RE) occur in many scientific disciplines. Some examples of RE involving human subjects are: recurrence of migraine, recurrence of epileptic seizure, cancer tumor recurrence, just to name a few. This project considers an experiment in which (n) random cells within a gridded area of a mouse retina were given constant stimuli with the goal to assess its effect on response transmission to the optic nerve. The observed response to stimuli is the spike arrival times obtained through a computerized system. This experiment is also known as 'neural firing'. In this project the inter-event time survival function of these signals to the optic nerve is estimated. A direct implication of this project is that knowledge about the inter-event times may lead to a better understanding of the neuron's language, the complexity of neural activity, and the transmission of messages to the brain.

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