

## Progress Report

The summer student project focused on the relationships between plasma glucose values and the complications of diabetic kidney and nerve disease. The students that have worked on this project are Arjun Sharma (a 11<sup>th</sup> grade high school student), Monica Garde (a sophomore college student) and Varun Sharma (a 11<sup>th</sup> grade high school student). Ms. Garde helped to initiate the project by working with Dr. Sharma (to interpret the urine ACR) with Dr. McIndoe to review the AMDCC database. Varun Sharma helped to identify the nerve parameters to be studied in coordination with Nigel Calcutt. Arjun Sharma has done the brunt of the work by setting up excel data files with the relevant data and generating analysis with a software called spotfire.

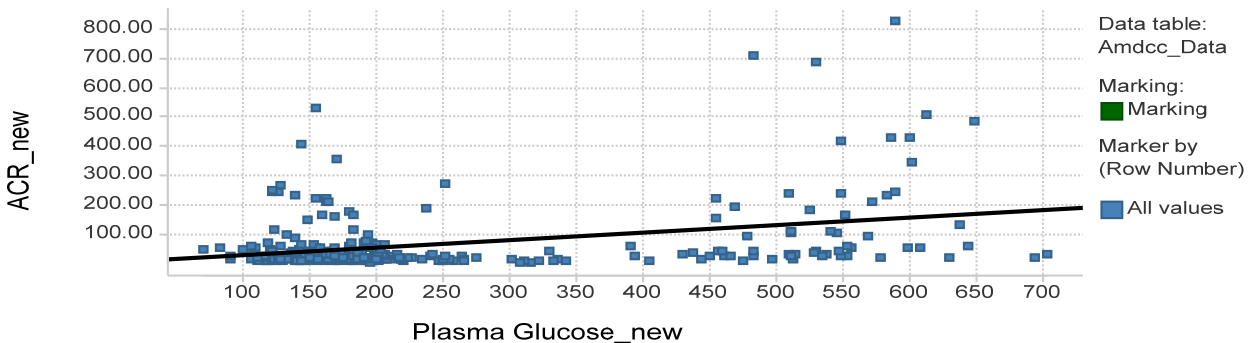
**Results** The following figures were generated by Arjun Sharma for the correlation between urine ACR and the blood glucose values.

**Figure 1: Relationship of urine ACR with plasma glucose across different strains of mice**

### Data Relationships (Linear Regression)

Y (numerical)	X (numerical)	p-value	FStat	RSq	R	Df
ACR_new	Plasma Glucose...	3.96E-009	37.04	0.12	0.35	269

### Data Relationships (Details)



The data that was examined included all the mouse samples where sufficient data existed for both plasma glucose and urine ACR with a similar duration of diabetes. The data shows that there is a highly significant relationship between the plasma glucose and urine ACR (p value  $3.96 \times 10^{-9}$ ,  $r = 0.35$ ).

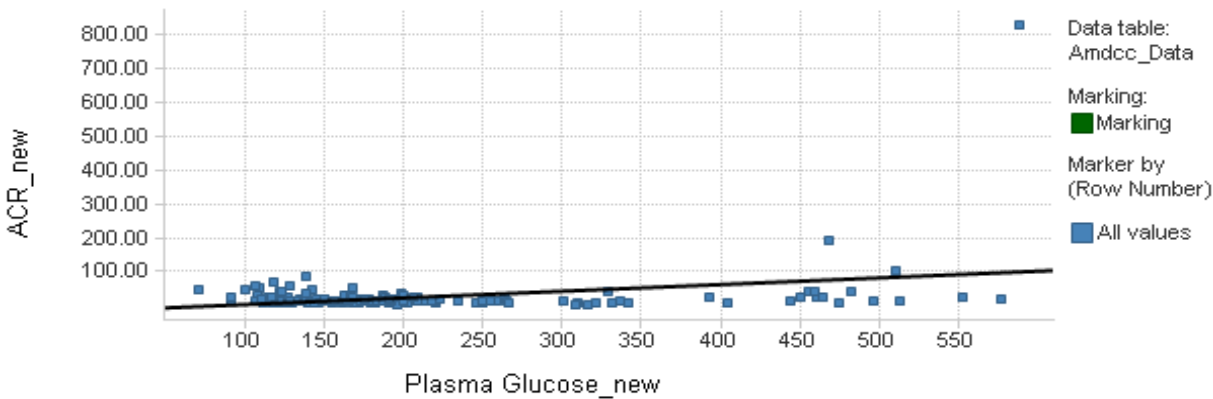
With 269 discrete data points from individual mice it is clear there is an important relationship between the degree of hyperglycemia and urine ACR. However this data included both normal mice with blood glucose values <300 mg/dl and diabetic mice with blood glucose values above 300 mg/dl. In subsequent analyses the students will use a cutoff value of 300 and examine whether the blood glucose will correlate with urine ACR. Additional analyses will also identify whether this relationship holds in models of type1 and type 2 diabetic mice separately.

**Figure 2 Relationship of urine ACR with plasma glucose in female mice only**

**Data Relationships (Linear Regression)**

Y (numerical)	X (numerical)	p-value	FStat	RSq	R	Df
ACR_new	Plasma Glucose...	1.24E-004	15.59	0.10	0.32	141

**Data Relationships (Details)**



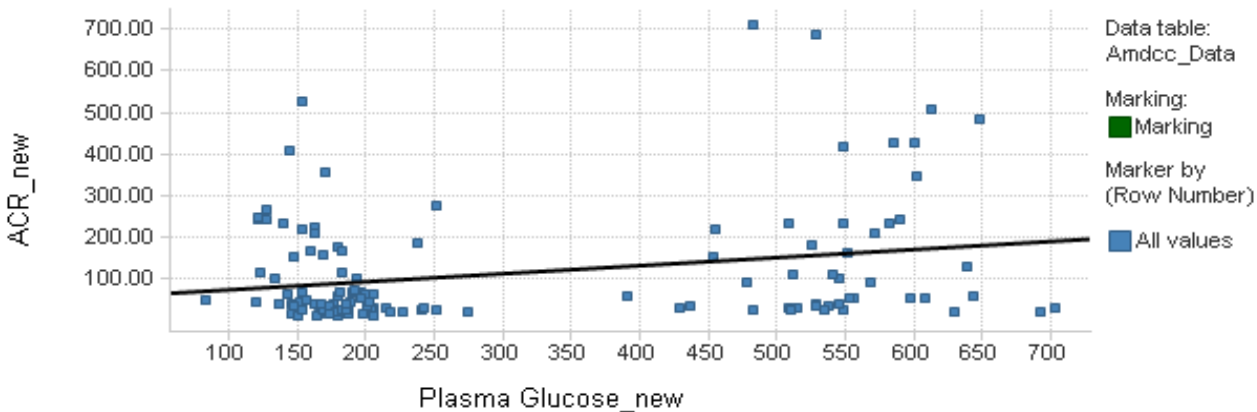
The data in Figure 2 was examined for female mice only. Although the degree of hyperglycemia was not as severe and there were not as many diabetic mice there remained a significant relationship between urine ACR and plasma glucose. However, much of the data may be affected by one outlier. A further analysis will determine if this outlier is a true outlier (>2-3 SD greater than the mean) and if the relationship holds without this data point. Upon examining the data it appears that there is not a strong relationship between urine ACR and plasma glucose in the females.

**Figure 3. Relationship between plasma glucose and urine ACR in males only**

**Data Relationships (Linear Regression)**

Y (numerical)	X (numerical)	p-value	FStat	RSq	R	Df
ACR_new	Plasma Glucose...	3.14E-003	9.07	0.07	0.26	126

**Data Relationships (Details)**



The data shown in Figure 3 demonstrates a very interesting relationship. There is much more variation in urine ACR in the males within the normoglycemic group than in females with normoglycemia (compare Figure 2 to Figure 3). In fact there is almost as much variation in urine ACR in the normoglycemic male mice (blood glucose <300 mg/dl) as in the male diabetic mice (blood glucose >300 mg/dl). This data was completely unexpected and will need further explanation.

Ongoing analysis is being performed with the measurements of nerve function and blood glucose. The initial parameter that will be evaluated is the sciatic motor nerve conduction velocity. Unfortunately the data as presented in the database does not show the blood glucose value for the same mice that had the nerve measurements. Thus, the initial analysis will group the mice by age and strain. Further consultations with Dr. McIndoe and Calcutt will determine how best to perform this analysis.

In summary, the data analysis by the students has led to some fascinating understandings between blood glucose and diabetic complications. In particular, there was an unexpected difference in the urine ACR in the normoglycemic male mice that was not seen in the female mice. The degree of variation in urine ACR in the male diabetic mice was also much greater than in the female mice. Further analysis of the various strains, type of diabetes and other parameters will be addressed.