

2009 NCGR Pilot Project Sequencing Award

Title: Cutting through the fat: A quantitative survey of vascular wall gene expression changes following a high-fat diet.

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Obesity is associated with hypertension, dyslipidemia, and insulin resistance. a collection of conditions referred to as metabolic syndrome that affects about 45 million US residents. Vascular dysfunction (VDys) is major component of metabolic syndrome. Indeed, VDys is the keystone and initial event of numerous cardiovascular diseases. This proposal employs an animal model (Sprague-Dawley rat) of metabolic syndrome (60% fat diet, 8 weeks). The phenotype of which closely parallels human disease. A quantitative assessment of total gene expression within the vascular wall (aorta) of lean (normal chow) and obese rats will reveal potential mediators of vascular dysfunction in diet-induced obesity. Moreover, this data will facilitate the generation of new hypotheses and suggest new therapeutic drug targets. The relationship of epigenetic regulation to diet is well established and genes modulated by diet will be clustered in the genome if they are subject to epigenetic regulation. In addition to differences in transcript levels, splice site variation may also be induced during vascular dysfunction.

Aortic tissue from age-matched lean and obese rats is available from Dr. Benjimen Walker, Department of Cell Biology and Physiology, University of New Mexico School of Medicine. Reagents for total RNA isolation are available and the extraction can be performed in the Reiss lab at NM Tech.

The reference sequence for *Rattus norvegicus* strain Sprague-Dawley genome and the complete mitochondrial sequence is available as are the necessary bioinformatics resources for this project^{1,2}. There are approximately 20,000 genes in the rat genome and it is estimated that 4% are expressed in heart tissue. Assuming that a similar number are expressed in the aorta, then 800 transcripts are present per sample and a single lane will provide at least 10⁴ hits per transcript. Bar coding the RNA from lean and obese rats and running these in a single lane will still provide adequate coverage to detect rare transcripts and splice-site variation.

Both undergraduate and graduate students will be involved in transcriptomic analysis. Moreover, it is possible to include analysis of this data set into the Bioinformatics courses taught at NMT.

1. Rat gene and RefSeq Statistics, NCBI.

<http://www.ncbi.nlm.nih.gov/genome/guide/rat/10116stats.html>

2. Twigger, Simon et al. 2008. Year of the Rat: What everybody should know about the rat genome and its online resources. Nature Genetics 40, 523-527.

<http://www.nature.com/ng/journal/v40/n5/full/ng0508-523.html>