



MAY - 7 2010

National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20892

To the Review Committee:

It is our pleasure to write a letter of support for the group working at the Advanced Biochemical Computing Center (ABCC) under the supervision of Dr. Robert Stephens. We are particularly grateful to Dr. Ming Yi who was the primary contact for our collaboration on a project aimed at identifying markers for and mechanism behind the reprogramming of the microenvironment in cancer.

For this project our lab established primary fibroblast cell lines from clinical samples obtained from patients who underwent surgery for endometrial cancer. From each patient we obtained both normal and cancer endometrial samples and compared these matched pairs for differences in mRNA, microRNA and protein expression. This project required a very high level of bioinformatics support, which was ably provided by Dr. Ming Yi. The first level of analysis of the mRNA expression microarrays involved multiple algorithms, including: Principal Components Analysis; Significant Analysis of Microarrays with varying normalization parameters; pathway enrichment using KEGG; Biocarta databases; GSEA; and SLEPR, a new method Dr. Yi developed for pathway analysis. Dr. Yi then analyzed the mRNAs that were differentially expressed in normal and cancer fibroblasts to determine which might be targets for the known human microRNAs; he then identified the microRNAs with statistically significant enrichment of their target genes that also had a reverse correlation between mRNA and microRNA expression. Lastly, Dr. Yi analyzed the proteomics data we generated from our samples and was able to identify the protein targets of certain enriched microRNAs. We were able to validate the major findings of these analyses by a variety of molecular biology methods. The contributions of the ABCC group to this project have been critical to its progression. At present, we are preparing two manuscripts on our findings, with both Dr. Yi and Dr. Stevens as coauthors. We plan to continue our collaborations to gain a more in depth understanding of relationships between protein and microRNA and between protein and mRNA.

During the collaboration, the ABCC group made themselves available for a number of face to face meetings with all parties involved, despite a distance of 30 miles between them and the other collaborators. In addition, they were very responsive to telephone and email communications. The group was prompt and thorough in working through our questions and concerns and routinely followed through until all options were exhausted. We have been extremely pleased with this collaboration and look forward to its continuation.

Sincerely,

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