Current Candidate Biomarkers for Potential Commercialization - Section 3.4.4 of the COE application to the Ohio Board of Regents

Major national peer-reviewed research funding garnered by UT investigators in the health sciences has resulted in the identification of many novel predictive and diagnostic biomarkers (Table 5). These candidate biomarkers have a high potential clinical and commercial impact. The nature of the biomarkers is diverse and includes proteins in the blood stream or urine, molecular signatures obtained from tissue biopsies, mutations in certain genes (gene polymorphisms) and arrangements of the DNA sequence within particular regions of a chromosome. The potential clinical utility of the biomarkers includes: (i) identification of individuals at high risk for certain diseases, (ii) early detection of diseases that cannot be treated effectively because they are typically too advanced at the time of diagnosis, (iii) prediction of response to different treatments in order to determine the most appropriate treatment opt ion for a patient and (iv) the ability to monitor disease response and disease recurrence during or after treatment.

Table 5 provides a summary of eleven examples of candidate biomarkers already discovered by UT investigators. These biomarkers are in immediate need of further validation and development, and provide excellent opportunities for commercialization. Each represents a critical step in the development of personalized health care.

Table 5 Candidate Biomarkers Discoveries by UT Investigators

Biomarker and Source	Disease	Application	Investigator	Funding Source	Stage of Biomarker Validation
Bone marrow specimens; Adipocyte marker proteins: PPARg2, FABP4, UCP1-3, and osteoblast marker proteins: Runx2, Dlx5, Col1, alkaline phosphatase and osteocalcin	Bone loss due to anti-diabetic drugs; Age related osteoporosis	Assessment of bone quality and fracture risk; Assessment of bone regenerative potential in individuals with a risk of compromis ed fracture healing, such as the elderly or diabetic patients on TZD therapy.	Beata Lecka-Czernik, Ph.D. Department of Orthopaedic Surgery	NIH/NIA	Human bone marrow samples will be collected from patients undergoing orthopaedic surgeries at the UTMC and analyzed by real time PCR for expression of gene markers - pending IRB protocol approval

Biomarker and Source	Disease	Applica- tion	Investiga- tor	Funding Source	Stage of Biomarker Validation
Breast cancer tissue that is tamoxifen resistant; Responsive to glyceollin I	Breast Cancer	Monitoring disease and therapeutic options	Paul Erhardt, Ph.D., Center for Drug Design & Development	Ongoing US Dept Agriculture	In vivo studies underway
Raf kinase inhibitor protein (RKIP); a protein inside cells that is decreased or lost in aggressive tumors measured in tumor biopsies	Breast Cancer and Prostate cancer	To predict the course of the disease	Kam Yeung, Ph.D. Department of Biochemistry and Cancer Biology	NIH/NCI	human tissue
Endogenous cardiotonic steroids and Na/K-ATPase; measured in blood and in red blood cells	Cardiovascular disease	To predict adverse cardiovascu lar events in patients with renal artery stenosis (RAS)-induced hypertension	Zi-jian Xie, Ph.D. Department of Physiology and Pharmacology	NIH	pending
CEACAM1; a protein in liver; changes in the protein levels and also CEACAM1 gene mutations	Diabetes and other Obesity related diseases	To predict risk and onset of insulin resistance and obesity which precede overt disease	Sonia Najjar, Ph.D., Department of Physiology & Pharmacology	NIH, US Dept of Agriculture, American Diabetes Association	found to be reduced in the liver of obese individuals
WDNM1-like; a protein in the blood produced by white adipocytes, hepatocytes, macroph- ages	Inflammation and Obesity	To determine risk of obesity related diseases	Cynthia Smas, D.Sc., Department of Biochemistry and Cancer Biology	Discovery was the offshoot of a previously funded NIH NIDDK grant.	In vitro studies of regulation, function and correlation with inflammatory status are ongoing.

Biomarker and Source	Disease	Applica- tion	Investiga- to	Funding Source	Stage of Biomarker Validation
Antibodies, sensitized "memory" B cells (mB), and functional populations of donor-specific T cells in recipients; mRNA and protein expression for the signature markers measured in blood cells	Kidney transplant rejection	Selection of matching kidney donors and recipients; Monitoring transplanted recipients; Improving long-term survival for kidney transplants; Avoiding transplanting allografts to previously sensitized recipients	Stanislaw Stepkowski, DVM, Ph.D.,D.Sc., Department of Medical Microbiology and Immunology	NIH/Paired donation program	Human peripheral blood lymphocytes (PBL) from donors and recipients prior- and post-transplantation. Biopsies from transplanted kidneys.
Gene expression signature; mRNA profile of MYC, p21, and E2F1 expression in fine needle aspirate biopsy of suspected lung cancer to increase accuracy of lung cancer diagnostic tests	Lung cancer	To improve accuracy of lung cancer diagnosis from cytologic samples obtained at fine needle aspirate	James Willey, M.D., Department of Medicine	NIH/NCI CA1 0359 4	Two case control studies have been completed and support that the test improves diagnostic accuracy compared to existing cytomorpholo gic tests. Another larger study is planned*
Gene expression signatures; mRNA profile of antioxidant genes (GPX1, GPX3, GSTP1, GSTM3, GSTT, mGST, Catalase, Superoxide dismutase) and DNA repair genes (ERCC4, ERCC5, XRCC1) from normal airway epithelial cells	Lung cancer	To determine risk for lung cancer; To personalize approach to early detection of lung cancer	James Willey, M.D., Department of Medicine	NIH/NCI CA95806 ES00571 9-04 George Isaac Cancer Research Fund	Confirmed in two case- control studies. Prospective nested cohort study about to begin.*

Biomarker and Source	Disease	Applica- tion	Investiga- tor	Funding Source	Stage of Biomarker Validation
miRNA biosignatures of oxidative stress; the complement of small RNA molecules in blood cells	Neurotoxicity due to drug abuse and chronic stress; neurodegenera- tive disease including Parkinson's disease and ischemia and stroke	Detection of the disease states and assessment of their severity	Bryan Yamamoto, Ph.D., Department of Neuro- sciences	NIH DA07606	tissue and plasma measures
Folate receptor types –α and –γ; soluble forms in the blood	Ovarian cancer, Breast cancer, Lymphoma	To detect ovarian and breast cancers well before clinical manifestation of the diseases; To monitor the recurrence of lymphoma following surgical treatment	Manohar Ratnam, Ph.D., Department of Chemistry and Cancer Biology	NIH R01 CA1 4069 0, NIH R01 CA08018 NIH R01 CA10396 NIH R01 CA09567 3, Eli Lilly and Co. Totaling $3M in direct costs.	human tissue
Prostate cancer tissue that is hormone independent; PAM enzyme is over- expressed	Prostate Cancer	Monitoring disease and therapeutic options	Paul Erhardt, Ph.D., Center for Drug Design & Development	Prior US Army, Submitted RO1	In vivo studies completed

*Invention disclosure completed patents submitted IP licensed to Gene Express