

THE **DRA** Accelerating Disparity
Reducing Advances
PROJECT



**Report of the Early Detection of Cancer Using Blood
Testing Committee**

September 2006 Report 06-04

Report of the Early Detection of Cancer Using Blood Testing Committee

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Report of the Early Detection of Cancer Using Blood Testing Committee

INTRODUCTION

The Biomonitoring Futures Project Advisory Committee at its April 2006 meeting identified early detection of cancer using blood tests as a promising area of focus as a Disparities Reducing Advance for further evaluation. A committee reviewed the current state of this technology and anticipated advances (see Appendix A, the background paper and Appendix B, the results of interviews, at the end of this report). Committee members and others provided input via telephone interviews. Their comments and subsequent review of the draft are the basis of this report.

NEED

One half of men and one third of women will develop cancer during their lifetimes and it is the second leading cause of death in America. There are significant disparities in screening, diagnosis and effective treatment of cancer involving particular ethnic groups and the poor. Effective, easy to use screening tests detecting early cancer could make a big difference in beginning treatment early in the course of disease when therapy has a greater chance for a cure.

Are there specific cancers that are associated with the greatest health disparities? If so what are their underlying root causes? Is there an unmet need for screening and diagnostic testing that DRA should accelerate? What is the specific problem to be solved? The more important problem may be the next stage of the diagnostic process – getting timely access to mammograms, colonoscopy, etc. The committee was not tasked to do specific research on these questions.

CONCEPT BACKGROUND

Advances in biotechnology are leading to the discovery of underlying genetic and molecular processes that lead to the development of cancer. Based on this expanding knowledge researchers are identifying specific biomarkers of genetic risk and early cellular changes of cancer (and even precancer). Specific blood and other fluid and tissue tests are under development to detect these early biomarkers. Once perfected, proven effective and commercialized, they will be used to identify high risk populations for monitoring and to screen for early cancers. Even if the tests have high sensitivity and specificity it will take larger trials to identify their appropriate use in finding cancer and improving mortality in a way that

is cost effective for society. Although there are many promising early indicators that effective genetic, proteomic and cellular screening tests are possible, most experts expect that they will come on the market slowly with advances usually benefiting only a subsegment of the population with a particular cancer. It could easily take 10 years for major breakthroughs to occur and make it through clinical trials to become available to the public. (See Appendix A for more detail)

DIRECTION

Cancer biomarkers are a hot topic in biopharma R&D with numerous investigators looking at various technologies to identify hundreds of cancer subtypes. Progress is most pronounced in identifying specific biomarkers in existing cancers to guide therapeutic decisions, such as gene over expression as an indication for treatment with the drug, Herceptin. The development of a specific biomarker in association with development of a new drug is another area of significant activity. The biomarker would be used in clinical trials and once on the market, for personalized drug selection. Even though there is much work in identifying gene and protein patterns associated with cancer, much more research appears to be necessary to identify and validate specific profiles for identifying early cancers. This will be an ongoing process with increasing successes over the next 25 years.

OPPORTUNITIES

- Anything that can speed discovery of discriminating cancer screening biomarkers and their translation into useful clinical tests is a worthwhile endeavor. The challenge is what can the DRA Project do to have an impact at this point in time?
- Hundreds of labs are doing basic and applied research now. Although funding is significant, more money could always be used. But with the thousands of potential candidates, which ones should be singled out to leverage? The entire process usually takes 10-20 years to produce a successful test. When is the right time to get involved? Could the DRA Project's efforts make a significant difference in accelerating development or approval?
- What does it take to reduce disparities with a biomarker blood cancer for cancer screening? Clinics and patients are very comfortable with blood tests so that doesn't seem to be much of a barrier. Are there any cancers particularly related to disparities which would require a unique test for detection which aren't already under investigation? Is the real issue effective incorporation of the test in the daily practice of clinical medicine? This can be addressed for current deficiencies in screening, but what can be done now for a test of unknown qualities that might become available in 5, 10 or even 20 years?

- Committee members identified ways to fund development of a promising biomarker concept. The National Science Foundation invests more money into devices than the National Institutes of Health, and has a fundamental obligation to get a societal payoff. The Department of Defense (particularly the Army Medical Research and Materiel Command at Fort Detrick, MD) does a lot of medical research for things that have application in military medicine. Private donors such as the Bill and Melinda Gates Foundation and Katie Couric can provide resources and influence for health problems that fit their interests. The big challenge is finding a proven concept biomarker candidate worthy of the DRA Project's efforts when there are so many possibilities – most in early stages development.
- When a test gets FDA approval there often is not enough clinical trial evidence of how it can be effectively used in clinical situations. What patients or individuals should receive the test and what must be done if the test is positive or inconclusive? Does the test lead to a reduction in cancer mortality? Will it lead to over treating nonaggressive cancers? How can a screening protocol be made cost-effective for society? Medicine in reality is very complex as illustrated by the dilemmas created with the prostate specific antigen (PSA) test for prostate cancer. DRA partners could participate in clinical trials to develop rational protocols for test use when a biomarker test is in advanced clinical trials.
- Committee members emphasized that biomedical R&D is part of the free market healthcare economic powerhouse that has the incentives for tremendous innovations, but is not focused on reducing disparities. Players take large financial risks and expect to get rewarded. The view is that if a test is good at saving lives and reducing overall treatment costs, the public should be willing to pay for the value received. Few developers will be interested in price reductions to reduce disparities. For instance, developers are unlikely to provide discounts to CHCs in exchange for participating in clinical trials. This means that a more effective approach is to demonstrate the worth of a test in terms of reducing morbidity, mortality and overall treatment costs so payors will see the value of authorizing adequate reimbursement for the blood test. The Agency for Healthcare Research and Quality (AHRQ) would be a good partner in achieving this for Medicare reimbursement, which is usually the benchmark other payors follow.
- What are the true disparities in cancer screening and diagnosis and what are the underlying root causes? Would a literature search on these questions better equip the DRA Project for identifying the greatest leverage in reducing disparities?

RECOMMENDATIONS

Genetic and proteomic blood tests for cancer screening and diagnosis are in early stages of development and will likely take 10 or more years to reach the marketplace. Similar tests for pre-cancer conditions are also possibilities during this time frame. Many research efforts are underway, but committee members could not identify obvious winning approaches or developers that would warrant DRA Project intervention on behalf of specific advances or tests at this time. However because of the promise of

these tests, there are activities that the DRA Project can undertake to increase their potential to reduce health disparities.

A three horizon strategy is recommended:

1. Horizon 1 (1-3 years) – Review Currently Available Approaches; Monitor and Shape Emerging Potentials

- As it is unclear which biomarker technologies for cancer screening will be successful, when they will become available or exactly how they will be used, direct action to advance specific candidates at this time is not practical.
- We recommend that progress be monitored as it is possible for certain cancer screening tests to advance faster than expected, possibly becoming available within the next few years. This monitoring progress should include not only blood tests (the focus of this committee), but for other novel approaches such as testing saliva, breath, urine, stool, skin, etc. (see the comparative analysis in Report #4 Biomonitoring Platform Analysis www.altfutures.com/bfp)
- We recommend that a study be undertaken to document the extent of real disparities of cancer screening and diagnosis, and which cancers are the biggest problems. What are the underlying root causes? What can be done now to eliminate the major disparities? Information should ideally be quantifiable. This knowledge would be valuable in deciding near term strategies and encouraging a research focus where there is the greatest need for reducing disparities.
- In preparing for effective use of future tests, those treating the underserved can make sure they are effectively conducting early cancer screening and overcoming any cultural barriers using current screening approaches. This will not only reduce disparities now, but it will also build the processes and expectations of their patient population to be well prepared to effectively utilize new cancer screening tests when they become available. This could be done through the use of the chronic care model, more general quality improvement processes, or efforts focused on cancer screening specifically.

2. Horizon 2 (4-6 years) – Position strategy and resources to leverage

- Once likely biomarker winners are discerned, the DRA Project can possibly work with developers to obtain funding from the public sector in return for developing ways to meet the needs of the underserved.
- DRA can influence the inclusion of ethnic minorities into clinical trials and encourage CHC participation in trials to determine appropriate use.
- DRA can build bridges between the Centers for Medicare and Medicaid Services (CMS) and developers, possibly with the help of AHRQ, to get tests accepted and adequately reimbursed.

All these efforts can accelerate the process, provide good will and influence availability for the underserved.

3. Horizon 3 (7-10 years) – Uncover possibilities and create options

- As mentioned, there is already great momentum in developing screening and diagnostic tests based on specific cancer biomarkers. Because of the uncertainty over which tests will likely succeed it is impossible to determine where DRA should apply leverage at this time. Monitoring progress is the best strategy – not only for blood tests (the focus of this committee), but for other novel approaches such as testing saliva, breath, urine, stool, skin, etc.

Appendix A

This background paper was developed to assist committee members in their deliberations. More related details on biomonitoring are at www.altfutures.com/bfp.

Disparities Reducing Advances Committee for Early Detection of Cancer Using Blood Testing

Prepared by Bill Rowley, MD – July 2006

INTRODUCTION

The Biomonitoring Futures Project Advisory Committee recently recommended blood tests for early detection of cancer as a promising area of focus as a Disparities Reducing Advance. Given that certain minorities and the poor frequently have delayed diagnosis of their cancers with resultant poorer prognosis, promoting the development of inexpensive, easily used screening tests could make a big difference in reducing disparities. For the DRA Project a working group will consider the merits of this technological advance and the opportunities for accelerating its capacity to reduce health disparities. To aid the committee considering this issue, this background paper gathers the latest information of the current state of various types of biomarkers for the identification of cancer, particularly for malignancies of the breast, colon and lung.

BACKGROUND

Cancer develops over a period of years before it becomes big enough to cause symptoms and be detected. Screening tests are available for easy to reach cancers such as breast and colon cancer, but these tests can miss a lot of early malignancies and are often inconvenient and expensive. Many harder to reach cancers such as ovarian, pancreatic and lung cancer are difficult to diagnose before they reach an advanced state with poor prognosis. Many researchers and biotech companies are looking for biomarkers for early cancer that can be detected in easily accessible bodily fluids such as blood, urine or saliva. If tests can be developed that are easy to use, have high sensitivity and specificity and are modest in cost, screening for patients at risk could detect asymptomatic cancers and even precancers. Straight forward therapy would then have a high likelihood of cure.

REAL WORLD CRITERIA

There are many important criteria to consider in deciding if a particular cancer test is valuable and practical.

- A screening biomarker needs to have high specificity (identifies the cancer, but is negative for non-cancerous conditions and in healthy people) so there are not many false positive tests that subject

normal subjects to expensive, unpleasant and risky diagnostic tests for clarification. Ideally the specificity should be 99% - a high barrier.

- High sensitivity (test is positive if there is cancer) so the test does not miss a lot of cancers. Many current tests are in the 50 – 90% range; meaning a negative value must not give a false sense of security to the patient nor lull the physician into complacency.
- Easy to obtain biological specimen with blood, urine and saliva being ideal. Stool samples are a barrier for many and tissue and internal fluids are hard to obtain.
- Assay complexity. Although testing devices are becoming self-contained and easy to use at the point of care, sophisticated DNA and protein tests still require complex lab equipment with multiple steps that only large labs with skilled technicians can perform. Eventually (several years) most tests will become easy to perform.
- Cost is a huge issue because of the high R&D expenses to create the test, cost for clinical trials and regulatory approval, and efforts to turn it into a reliable and convenient device for commercial use. Once on the market investors expect a healthy return for their risk.
- Clinical benefit – does it make a difference? The gold standard is whether use of the test reduces mortality or reduces morbidity. If early detection can't clearly achieve one of these ends it has little value for screening and early diagnosis. Another factor of increasing importance is timeliness of results. Tests that can be performed at the point-of-care with results during the patient encounter are much more likely to be acted upon in a timely matter.
- The dilemma of new knowledge. A biomarker test may detect precancer or minimal cancer so early that it can not be located by existing diagnostic tests. For instance, a colonoscopy with removal of any polyps discovered could be done on everyone with a positive colon cancer screen, but what if nothing is found on a large number of studies? It will take years to sort out the best way to proceed and whether therapy based on a positive screen alone is ever warranted.
- Population cost-benefit issues are important for widespread use. Many tests find too few cases or have too little impact on survival to warrant the expense of use for large populations. Selection criteria for who should receive the test are important to improve the cost-benefit ratio.
- Show me the evidence! There are numerous examples of biomarker ideas that in small preliminary studies are extremely promising, but larger controlled clinical trials fail to demonstrate significant benefit. It is not easy to discern the likely successes because there is a “black hole” between initial public statements to lure investors and the results of published clinical trials. Often there is a flurry of hype and a couple years later no trace of the technology or the company can be found on Google.

- Acceptance within the health care community. It is difficult to get physician buy-in for new concepts, in spite of compelling clinical trial evidence. If providers and patients do not see a test as convenient, it will not gain acceptance. The other big hurdle is the decision by payors to cover the test. Compelling efficacy and cost-benefit data is importance to win their acceptance.
- Patient acceptance – cultural, ethnic, age, language barriers and perception of convenience can influence whether a test is used.

There is tremendous momentum in finding new cancer biomarkers with many universities and biotech companies doing R&D with grant and venture capital funding. When promising biomarkers reach the market, cancer advocates and researchers will assure that additional clinical trials determine the true value and indications for use. It is likely these new tests will be satisfactory for use in minority and underserved populations to reduce disparities. Additional evidence of long-term cost-savings may be required to make the case for Medicaid and other funding source coverage. It is hard to address specific issues until there is a better sense of which tests will be successful and about when they will likely reach the market. Those in clinical medicine and policy makers need to monitor progress, ignore the hype and wait for the evidence of effectiveness before deciding when it is appropriate to incorporate the new tests into patient care. Along the way issues may need to be addressed to accelerate the use of specific tests in reducing disparities.

ADVANCES IN PROTEIN AND GENE CANCER DETECTION TESTS

Researchers are aggressively looking for ways to assess proteins and genes in the blood to assess the risk for cancer, make early diagnoses before symptoms develop and help guide therapy. This is a very complex undertaking and most tests are still experimental. While the goal has been to find effective early screening tests for cancer, there usually are not enough abnormal proteins circulating in the blood to be detected until the tumor is large enough to be detected in other ways. Tests that look at genes to characterize cancers require analysis of biopsies of the cancer cells themselves. Effective screening tests may still be a few years off. Examples of current progress are as follows:

GENETICS

- **Gene variations that increase risk**, mostly consisting of scattered changes to single letters of the DNA code (called single nucleotide polymorphisms or SNPs), might be responsible for a disease or make a person more susceptible to getting a disease. Tests looking for specific mutations can identify higher risk individuals for close monitoring or preventive interventions. The BRCA genes significantly increase the risk for breast cancer and men with a genetic marker variant have a 60% greater chance of getting prostate cancer. Intensive research is ongoing attempting to find predictive genetic differences between those with specific cancer types compared to the population as a whole.

- **Gene patterns associated with increased risk** – “Genomic fingerprints” look at variations in dozens to hundreds of genes to find predictive patterns associated with characteristics of specific diseases for identifying high risk patients or to detect early disease. Patterns differentiating disease subsets could also help determine the most effective therapeutic option. For example, a cluster of 22 genes has been identified that are expressed differently in lung cancer patients whose cancers rapidly recur after treatment compared to those with normal genes.
- **Abnormal genes in established disease** – Diagnostic biomarker tests for specific abnormal genes can be used to identify subtypes of cancer and help guide therapeutic decisions. There are tests available that detect mutations in specific cancer genes that make them susceptible to new targeted therapies. To assess the genes in cancer cells these tests must be done on tumor tissue samples.
 - An example of a single gene test is Genzyme’s EGFR Mutation Assay. It looks for the presence of epidermal growth factor receptor (EGFR) mutations in non-small cell lung cancer patients that correlate with a successful clinical response to Tarceva® (erlotinib) or IRESSA® (gefitinib). The test costs about \$975.
 - Examples of gene pattern tests that look at a profile of 21 or 70 genes are *Oncotype DX™* and *MammaPrint®*. These microarray cancer diagnostics analyze the DNA expression profile of an individual’s breast cancer to predict likelihood of recurrence and whether chemotherapy in addition to tamoxifen would be beneficial. Both tests cost over \$3,000.
- **DNA Methylation** – DNA methylation results when a carbon atom surrounded by three hydrogen atoms attaches to cytosine within the DNA sequence, silencing the gene without changing its actual sequence. Abnormal methylation occurs early in disease, especially in cancer where several alterations are necessary for cells to evolve into cancerous ones. So far about 50 genes have been identified where methylation plays a role in cancer development. Researchers are looking for methylation patterns in biopsy specimens, serum, saliva, sputum, urine and stool to detect precancerous changes and established cancer before symptoms develop. Someday these biomarkers could be used for risk assessment, screening, confirming diagnosis, staging disease and determining the most likely beneficial therapies based upon specific cancer mutations. These biomarkers could also determine that a patient is unlikely to have cancer avoiding invasive procedures, and if a cancer is likely to be slow growing so that radical surgery isn’t necessary. Workers are particularly interested in bladder, breast, colon, lung, ovarian, and prostate cancers. Current testing equipment used in research is very sensitive in detecting just a few cancer cells in a specimen. An example is:
 - Serum Methylated DNA Test for Colorectal Cancer - methylated DNA on the Septin 9 gene that encodes for a protein involved in cell division is thought to play a role in cancer. A study of 501 samples found that 57% of colorectal cancers have this abnormality detected by a blood test.

Different cancer stages were identified with similar sensitivity. The test was 95% specific, making it a good screening tool for asymptomatic colorectal cancer.

In another study a second marker, ALX4, a gene encoding for a transcription factor suggesting a role in gene regulation, was combined with the Septin 9 biomarker in 49 patients with and 22 patients without colon polyps. The detection rate for polyps larger than 1 cm was 67% and the specificity was 91% in asymptomatic patients over 50 years old.

It is exciting that a blood test might detect all stages of colon cancer and also detect polyps with intraepithelial neoplasia (IEN) 80% of the time. Only preliminary testing has been done so further trials are required. The company is looking for additional biomarkers that used in combination would give higher specificity to reduce false positives in screening and a sensitivity greater than 67% to find more asymptomatic cancers.

PROTEIN BASED BIOMARKERS

- **Single protein markers** – Prostate specific antigen (PSA) is a widely used but controversial screening test for prostate cancer. Other protein markers such as carcinoembryonic antigen (CEA) for colon cancer and CA 125 for ovarian cancer are not specific enough for screening, but are somewhat helpful in monitoring the management of extensive disease. Researchers continue to look for the ideal, highly predictive biomarker for serious diseases.
- Platelets contain proteins that regulate angiogenesis (development of new blood vessels). Therefore platelets selectively take up and preserve angiogenesis regulatory proteins secreted very early by developing cancer cells. A blood test monitoring for an increase of these regulatory proteins in platelets could provide an early indication that a cancer is developing or that a metastasis is occurring. Clinical trials are testing the predictive value of this methodology.
- **Protein profiling** – This methodology analyzes hundreds of proteins from blood or tissues with mass spectrometry and protein microarrays to identify significant changes occurring when cells progress from normal to disease. Cancer cells overproduce many proteins so a pattern of peaks and troughs, each representing the blood level of a specific protein, will hopefully detect a cancer with a high degree of accuracy. Large numbers of blood protein levels are compared between cancer patients and normal controls using sophisticated pattern recognition algorithms to discover unique “fingerprints” associated with specific early cancers. These must then be tested in large groups of cancer and non-cancer patients to determine predictive value.
 - OvaCheck® is a test for early detection of epithelial ovarian cancer. An initial study published in *Lancet* in 2002 had a predictive value of 94%, but later efforts to confirm the methodologies and reproduce the results ran into difficulties because of complexity of the concept and minute amounts of proteins being analyzed. The FDA has declared OvaCheck to be a new medical

device requiring successful clinical trials before approval. It remains to be seen whether the technology will succeed in passing this hurdle. Similar research is being undertaken by several biotech firms looking for predictive biomarker patterns for breast, lung, pancreatic and other types of cancer and a wide variety of other serious diseases. Researchers are seeing if protein profiling can distinguish between aggressive and indolent prostate cancers for selecting the right course of therapy.

- Li Zhong et al. of the University of Kentucky developed a protein diagnostic assay for early identification of non-small cell lung cancer. They screened 212 phage-expressed proteins and identified 5 which distinguish lung cancer associated proteins from controls using blood samples. Using this assay on 40 cancer samples drawn 1 to 5 years before detection, 6 prevalence cancers and 56 noncancer samples, the test predicted cancer with specificity of 87.5% and a sensitivity of predicting cancer 1-5 years before radiographic detection of 80%. If the results are substantiated on a larger controlled study this could screen those at high risk and those with a positive result would get a lung CT scan. If the scan was negative, the patient would be carefully followed for subsequent confirmatory evidence of cancer before treatment; because it is possible premalignant lesions can cause a positive test. So far benign pulmonary nodules and other lung diseases have not been shown to cause a false positive test. There are still several issues to resolve before the concept can be applied for clinical screening. (1) Larger controlled studies must confirm these preliminary results of high specificity and sensitivity. (2) It must be shown that cancers in other parts of the body do not produce a positive test. (3) A study showing the test can distinguish benign from malignant nodules on lung CT scans would be very helpful in determining which patients to biopsy. (4) Lastly it must be shown that the test increases the survival rate with earlier diagnosis and that the cost-benefit analysis justifies its expense for at risk population screening. Although this is an exciting preliminary report it is still several years away from approval and known clinical utility if further studies confirm effectiveness.
- **Metabolites** – a new area of investigation is using advances in biotechnology to detect and interpret the small molecules (metabolites) present in the body, particularly unique molecules that can distinguish the onset of a disease like cancer from normal body functions.

SOME COMPANIES WORKING ON CANCER BIOMARKER TESTS

- **20/20 GeneSystems** is developing antibody profiling of protein patterns in cancer. <http://www.2020gene.com>
- **Canary Fund** – promoting capabilities for the early detection of cancer. <http://www.canaryfund.org>

- **Correlogic Systems, Inc.**, creators of “Hidden Patterns” diagnostic testing methodology and the OvaCheck® ovarian cancer screening test. <http://correlogic.com>
- **Ciphergen Biosystems, Inc.** uses its SELDI ProteinChip technology to develop biomarkers for early detection and management of ovarian, prostate, pancreatic, breast, liver, lung and nasopharyngeal cancers, along with neurological, cardiovascular and infectious diseases. It is also working on measuring platelet accumulation of angiogenesis regulatory proteins secreted by very early tumors.
- **Epigenomics AG** is a German molecular diagnostics company focused on detecting and interpreting DNA methylation patterns. <http://epigenomics.com>
- **Genomic Health, Inc.**, maker of Oncotype DX™. <http://genomichealth.com>
- **OncoMethylome Sciences**, developers of DNA methylation biomarker tests. <http://www.oncomethylome.com>

SUMMARY

- Blood-based molecular and genetic screening tests for cancer appear to be exciting means for early detection of cancer. However they are in various stages of development and it is unclear, in spite of the hype, when they will reach the market.
- The important issue will be clinical usefulness in everyday medicine – will the test effectively detect cancer and reduce mortality?
- Molecular and genetic screening tests will likely be very expensive. Looking at a total disease perspective, they should more than pay for themselves in savings in treatment costs, morbidity and mortality. This economic case must be made for wide acceptance by payors.
- From a disparity reducing perspective are there things which should be done to leverage the field now or in the next few years that the DRA Project should consider:
 - Helping community health centers anticipate the usability of specific tests or systems?
 - Helping CHCs track these developments to anticipate when they are likely to emerge in the marketplace so actions can then be addressed to improve access to the underserved?
 - Developing criteria to assess the clinical usefulness and appropriate use of these tests when they become available?
 - Helping CHCs develop processes and strategies to insure that patients get screened, followed up and treated when these diagnostic tests become available?
 - Help develop strategies for dealing with precancerous changes?
- Alternatively, is a wait and see approach of careful monitoring of research advances without action at this time a better option? Intervention could then be considered when clear winners and their dates of availability are determined.

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Appendix B

Committee for Early Detection of Cancer Using Blood Testing Results of Interviews

When will significant new cancer biomarkers reach the market? What are the challenges?

- It will likely take 10 years for new technologies to be developed, validated and approved
- Cancer is more difficult than hypertension, asthma, etc. because there are so many types with different characteristics. See faster return in genetic screening for hypertension, asthma, osteoarthritis, etc. that cause a lot of long-term disability
- See more promise in predictive tests, i.e. BRCA for breast cancer, which are expensive and tell which therapy to use
- Stool DNA is expensive, but useful because a positive test says there is cancer, not just blood
- Expect to see hand held genetic testing for about \$100 in 10 years and by then hopefully will have identified predictive gene patterns for risk of major chronic diseases
- Detecting cancer cells in urine, sputum, etc. could also be available within 10 years. Have ways of finding a very few cells and making a diagnosis on them
- Big challenges
 - Money for research and development – big pharma investing and partnering only when concept proven
 - Getting reimbursement – CMS agreeing to cover is key
- Other challenges are high predictive value, large trials to prove benefit, development of easy to use reliable test device/process and physician acceptance
- Cancer prevention studies and databases started adding blood samples a few years ago so there are large libraries to test specific cancers against promising biomarker tests – this will speed up the process somewhat
- Unfortunately the underserved will not get a new advance early – it has to be successful in the marketplace for the price to come down. Also it needs to be reimbursed by Medicaid, etc.
- Good predictive value important – given an abnormal finding it costs \$9-10,000 to work up a suspicious cancer
- Test must be proven to make a difference in life expectancy to be useful. PSA for prostate cancer points up the dilemmas of screening blood test
- See sophisticated tests being done in sophisticated labs rather than at the point of care – not worth investing in office based protein and gene biomarker tests at this time
- There is a lot of interest in biomarkers that go in hand with development and clinical trials of a specific drug which would be required for drug selection once it reaches the market. Pharma and investors see a return for this.

Roles for DRA Project?

- Can't tell what the promising technologies will be or for which cancers now so it doesn't make much sense to invest time and money now to reduce disparities
- Better to monitor the field for now until identify a specific biomarker and researcher that has proven the concept for late stage trials
- Potential funders and leverage (for a very promising biomarker technology):

- NSF
- Military – TATRIC
- ACS – for big cancers
- Private donors with special interest such as Katie Couric for pancreatic CA; Bill Gates focused on Africa
- RWJF
- AHRQ to get CMS reimbursement
- Increasing awareness of the valuable role of early screening
- Dialog with CDC and NCI about what is happening in diagnostics research
- Know the problem you are trying to solve. Screening tests are not difficult to administer, the problem is access to the next stage – colonoscopy, mammogram, additional workup
- The idea of getting CHCs involved in clinical trials in effort to get produce discount on the tests probably won't work – companies expect to get paid for value.
- If have great idea that want to translate into device useful for the poor in society will need to get public sector funding