From: mark fisher <[redacted]>
To: Jeffrey Epstein <jeevacation@gmail.com>
Subject: Current Medical Status
Date: Mon, 12 Sep 2011 03:22:09 +0000

Hi Jeffrey

I hope that all is well with you.

As you know, I have been treated for the past 21 months for cancer with aggressive chemotherapy, surgical resection and radiation. Thank G-d the results have been good. I still have recurring spots on my liver and recently on a rib. There is cancer in my system that has to be undermined.

In the search for a possible cure, I have gone to see Dr Daniel Von Hoff http://en.wikipedia.org/wiki/Daniel_Von_Hoff (please take a look). Dr Von Hoff is a preeminent cancer clinicians and researchers worldwide. Dr Von Hoff would like me to participate with him in a clinical trial at the Mayo Clinic Scottsdale where my entire genome will be sequenced in conjunction of the sequencing of a sample of the tumor tissue. The clinical plan of the study by Dr Mitesh Borad of the Mayo Clinic, Scottsdale is below.

The comparative informatics of the two genomes can identify which drugs can work and which may not. More importantly, because of Dr Von Hoffs' reputation and that of the team at the Mayo Clinic they will use this information to try to get drugs that have not yet been approved by the FDA to be available to me because of 1) my appropriate molecular profile and 2) the rare nature of the tumor type (2500-3000 US patients/ year), utilizing single patient INDs on a compassionate care basis.

This would help solve a problem I now am having with the chemo. My platelets are very depleted from a year and a half of chemo and I currently cannot receive the chemo-therapies that have been working because of the damage to my bone marrow and ultimately the platelets. I need new drugs that work differently to keep fighting the cancer. This massive sequencing can identify drugs that can work on me.

In terms of science, they are proposing leveraging the billions of dollars that have been invested in genome sequencing and super-computing to make non obvious drug selections, some of which will not be on the market for years. Aside from converting this basic science into actual clinical practice, they hope to reveal unknown molecular information about my tumor type that can be a turning point for other cancers as well. The clinical trial is self funded. It costs the patient $50,000.

Jeffery, I do not have the funds. Although I am embarrassed and it is hard for me to ask, you are the only person I know that can do this financially and may also be interested in helping me medically as well as contributing to these medical and scientific advancements.

If you can help me obtain this treatment, there are no words...
I thank you again for the kindness that you have already done for me and family.

Mark
(917-497-0911)

MAYO CLINIC WHOLE GENOME SEQUENCING STUDY
Dr. Mitesh Borad, [redacted].

The Human Genome Project accomplished the sequencing of the human genome in 2000. Two parallel publications in world renowned peer-reviewed scientific journals, Nature and Science, highlighted this accomplishment. The project was completed ahead of schedule and at a lower cost than anticipated. However, these numbers still translated into approximately a decade of effort and close to $3 billion in funding both government and private to achieve this feat. Since this time, the pursuit of genome sequencing towards applying these technologies to benefit the individual patient have been the thrust of hundreds of organizations and have captured the interest of academia and industry alike. The $1000 genome has been dubbed as the barrier to break so as to make this technology ubiquitous and to be able to accomplish this within a matter of days to weeks at the most to have clinical relevance. Oncology is an area where there has been heightened interest with regards to providing "precision" therapy. In patients with advanced cancer with disease that is resistant or refractory to standard therapies, investigational agents are often the only potential options. Traditionally an empiric approach where patients with "solid" tumors are enrolled on a Phase I trial has been employed in those situations where there is no data, clinical or laboratory, to support choice of Drug X versus Drug Y. Not surprisingly, this empirical approach has not led to major successes in most instances as there is no provision to understand, characterize and delineate an individual patient's cancer by way of characterizing their genome and making decisions based on such. With the advent of Next Generation whole genome sequencing (NextGen WGS) available whereby this technology can be applied to an individual patient in time frames ranging in the order of 2-3 months and at a cost that becomes achievable in some, if not all cases (Current estimates at $50,000 and dropping), we can conceive of characterizing individual cancer genomes and applying the knowledge gained towards eventual treatment decision making at a dramatically much more precise and logical level. Several recent examples of this have been highlighted with WGS of patients with acute myeloid leukemia, breast cancer and hairy cell leukemia. The hope is that this type of approach will become widespread and not something simply highlighted in scientific publications. Organizations such as TGen, Mayo Clinic, Broad Institute and Washington University are at the forefront of utilizing these technologies and are conducting the appropriate clinical investigations towards this end.

A study being conducted at Mayo Clinic and Translational Genomics Research Institute is looking to study the feasibility of this approach to individualized patient care. From a technical standpoint the process would involve the following : 1) Biopsy of the patient's tumor, 2) Collection of a patient's germline (i.e. non-cancerous) representative tissue (in most cases peripheral blood mononuclear cells [PBMCs], (3) Extraction of DNA (genetic material) from samples mentioned in 1) and 2), 4) Sequencing using massively parallel sequencing technology (either Illumina HiSeq 2000) or Life Technologies SOLid (this step is anticipated to take about 2 weeks and involves DNA library preparation and sequencing) [~ 3 billion base pair readout will be generated with coverage of 30X or higher (i.e. the equivalent of sequencing the entire genome of both the cancerous and normal cells 30 times, this would help sort of the true changes from the false positives with extremely high reliability (>99.99%))], 5) alignment of data from tumor and normal genomes and data analysis to identify changes between the two and to sort of the changes that may cause structural changes in proteins that can be putative drug targets [this will be carried out by the world renowned team led by Dr. John Carpten and Dr. Daniel Von Hoff from TGen] (data analysis entails evaluation of approximately 1 Terbyte of data and needs supercomputing resources that are available at TGen/ASU (Sahuaro supercomputer), 6) Final delivery of results to patient's treating physicians (including Dr. Daniel Von Hoff and Dr. Mitesh J. Borad, both experienced researchers in genome methodologies and their clinical application in cancer care. There are very few teams globally who have the scientific, clinical and translational capabilities and the TGen-Mayo group is amongst the few that are at the forefront in these efforts. The overall process from tissue acquisition to delivery of final data is anticipated to take ~3 months (a fraction of the decade it took for the Human Genome Project), well within a time frame for potential clinical application to the care of an individual patient.

Once the drug targets are identified, the specific agent/combination of agents will be determined and if not approved their development status will be determined (Phase I, IB, II, etc.). If the drugs are investigational agents, then contact will be made with appropriate pharma/biotech manufacturers and a single agent IND process will be pursued to try to obtain drug on an emergency/compassionate basis. Early successes have already been

observed and it is anticipated that this approach will become a standard approach to care of patients with cancer over the next few years.