Dear Dr. Sabin:

Please excuse the delay in getting back to you to celebrate your great recovery. Everyone at Analytical Biosystems was delighted to hear the good news. I took the liberty of reading portions of our previous correspondence to the people at our small company.

I was able to reconnect with you by virtue of the article in *Oncology Times*. Since I wasn't at the meeting, I don't know whether or not the article accurately reflected what actually happened. I do know, however, that back in the late 60's and through the 70's you frequently rose in the audience and requested the microphone to ask a question. Your questions were always well conceived, thought-provoking and frequently misunderstood. I used to enjoy hearing these discussions which sometimes became very heated. So often the real significance of the question was lost in the clamor that followed and an excellent question went unanswered.

Now that you are feeling a little better I have taken the liberty of sending you additional information on my current mission in life. I truly believe the standard of care the average cancer patient in the country can be significantly improved if pre-surgical consultation with a medical oncologist became standard of care for those patients suspected of having a solid malignancy. The disjointed nature of patient care which is addressed in the short article in *Coping Magazine* (attached) is sinful.

I have enclosed, under separate cover, a "Blue Book" which is a document prepared to assist in the sale of the company. The Blue Book fails to address some of the key issues that need to be addressed if we are going to start making improvements in the quantity and quality of life of cancer patients.

As I travel around this country and give lectures at medical schools, hospitals and scientific meetings, I frequently start off my presentation with a brief contrast of problems which you had to overcome in developing an effective polio virus vaccine and the problems we are having in making *in vitro* chemosensitivity standard of care for cancer patients.

One easy way of looking at these differences is the development of an effective polio vaccine was a win-win situation
for almost everyone. The competition was fierce between the various scientific groups that were trying to develop a killed vaccine or isolate an attenuated strain of virus. There was competition between the pharmaceutical companies over who would have the rights to manufacture the vaccine. Historians will be able to write many stories of some individuals who won and those who lost. The most important thing, in my opinion, is that the world won. My children and grandchildren do not know the dread of polio and to you they can be thankful.

On the other hand, the fight against cancer is a very different one. In this battle the tobacco industry, 40 years after the data conclusively demonstrated a link between smoking and cancer, is still spending millions a year in such useless research as developing a "safe cigarette." We have a situation where most of the pharmaceutical companies have de-emphasized research on cytotoxic chemotherapeutic agents and have a very interesting attitude toward our chemosensitivity assay. I can summarize the attitude of many of these executives in pharmaceutical companies who currently sell cytotoxic chemotherapeutic agents. "I would never have these drugs injected into me without having an assay done first, but I would never embrace the widespread use of this technology because we couldn't afford the 30-40% reduction in sales." Executives in these companies and medical oncologists around the country know that as a minimum 30-40% of the cytotoxic agents they give to their patients are of minimal or no value. More importantly, the administration of non-effective cytotoxic agents may function as inducers of multiple drug resistance. This results in a significant reduction in the chances the patient will respond to the next drug pulled out of the hat "according to protocol."

I don't want to leave you with the idea the medical oncologists or the manufacturers of cytotoxic agents are the bad guys. The bad guys are the guys who decided we needed "to over specialize." If we return to the 1950's and look at the diagnosis of polio and its treatment, few individuals were involved in the examination of the patient's symptoms and obtaining correct diagnosis. Unfortunately, the prognosis was not good. The real turnaround in this disease was prevention through the implementation of an effective vaccination program.

In the case of cancer however, we are faced with an extremely different clinical situation. As I mentioned in the Coping article, the patient sees a diagnostican who orders a battery of tests. If the tests reveal the presence of a "mass," the patient is sent to a surgeon to have it removed. The mass goes to pathology and if malignant the surgeon is informed and will search for additional cancer in the patient. The next individual to see the patient, a few days post surgery, is an oncologist (radiation and/or medical). Unfortunately the tissue which could have been used in vitro to determine appropriate therapy has been fixed and the oncologist must confidently treat the patient "according to protocol."
I have met very few oncologists who won't admit they need information on a prospective basis like their infectious disease colleagues receive. However, since many of them have had disappointing experiences with earlier in vitro chemosensitivity assays, their attitude is negative or skeptical at best.

I have enclosed copies of a few letters which were submitted recently on our behalf, in an attempt to raise funds for additional prospective clinical trials.

After you have had a chance to look over the additional material, I would greatly appreciate your thoughts on how to best get people's attention. We have three patents on technology developed at Brown University which can help save lives of cancer patients and can significantly reduce the cost of care for the patients. We can truly make a significant improvement in this horrible disease if we can only get the "the powers that be" in the medical field to stand up and pay attention.

I look forward to your response and pray your recovery has continued.

Best regards

[Signature]

KEB/cb

Enc.
ABC Image*

Image Processing and Management
for the Fluorescent Cytoprint™ Assay

Analytical Biosystems Corporation (ABC) has developed and placed on-line a proprietary computerized image management and analysis system, "ABC Image", in combination with its patented technology, the Fluorescent Cytoprint™ Assay (FCA). The FCA is the laboratory procedure that provides physicians with a patient profile predicting the effectiveness of chemotherapy drugs on an individual's cancer tumor. The addition of this computer graphics technology will greatly facilitate the evaluation of the in vitro drug treatment on each individual cell culture and represents a singular advancement in the evolution of chemosensitivity analysis. ABC Image was developed on a Quadra 950** because of its graphics capabilities in utilizing 32 bit color video image acquisition and optical disk storage media.

ABC Image is specifically designed to capture, archive, retrieve and enhance images of microscopic cultures on a real-time basis during the assay test period of 7 to 10 days. Each assay procedure may require up to 240 images. The ability to evaluate the effect of each different drug and drug dosage is substantially enhanced by being able to directly compare pre and post drug treatment images. In the past, comparisons were made between the post-drug treated cultures and the untreated controls to determine sensitivity or resistance.

The rapid presentation of multiple images on a single screen or print copy is provided by ABC Image, permitting direct visual comparison of individual cultures before and after treatment of drugs. These multiple images are juxtaposed to provide instantaneous comparison of different drug dosages and comparative drug treatment. This visual presentation highlights the unique patterns (cytoprints™) of each cell culture and even after treatment, the identification of these cultures is recognizable.

Of equal or even greater significance is that the ABC Image system provides the first practical means for quantitative evaluation of an FCA analysis. The degrees of cell kill are currently presented in broad categories of sensitive, intermediate and resistant based on experienced technical judgment. With development of enhanced statistical methods, the drug sensitivities may soon be measured in real percentage terms.

The initial use of ABC Image in the laboratory is for significantly improving the process of evaluation by the technologist. It can also provide physicians with visual representations of their patients specific sensitivity profile. As a supplement, copies of the images can be provided as an additional part of the reporting process.

It is anticipated this innovative system will allow for more efficient specimen processing, including smaller specimen requirements, reduced processing costs and automated quantitative evaluation of the chemosensitivity of human tumors. This system will also greatly facilitate the archiving of specific patient data, tumor sensitivity and clinical response follow-up.

ABC Image will also be used extensively in the development of new techniques in performing the FCA as well as development of new products including ABC's RMCE project that tests for the sensitivity in a tumor subjected to both chemotherapy and radiation. ABC Image in conjunction with the FCA can also provide important information to drug development companies who wish to evaluate compounds against existing compounds and various tumor types.

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