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BioMarketing Insight Newsletter

Creating Markets and Marketing Strategies

Dear Regina,

Welcome to BioMarketing Insight's monthly newsletter.

Last month I talked about how 3D printing has influenced and advanced regenerative medicine and beyond. If you missed last month's article, click here to view it. Genomics is hot again and there has been a lot of activity in this area. This month I'll discuss today's definition of Genomics and how we need to translate this knowledge into clinical practice.

Read on to learn more about this topic and other current news. On the right are quick links to the topics covered in this month's newsletter. The next newsletter will be published on April 15th; don't forget to file your taxes.

We encourage you to share this newsletter with your colleagues by using the social media icons at the top left, or by simply forwarding the newsletter via email.

Please email me, Regina Au, if you have any questions, comments, or suggestions.

Sincerely,
Regina Au
Principal, Strategic Marketing Consultant
BioMarketing Insight

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Save the Date: April 28th - 29th, 2014 - Medical Informatics World Conference

The healthcare industry goal, particularly for those classified as Accountable Care Organizations (ACOs), is to deliver quality health care and reduce healthcare cost. This goal is believed to be achieved through the coordinated efforts of all stakeholders: providers, payers, patients, and pharma by way of electronic medical records used to analyze and stratify patients into various risk management groups. Risk group information would be used to tailor specific treatment programs that both ensure quality care and control costs. This meeting will focus on innovative solutions that include biomedical sciences, health informatics, and IT.

I will chair the session on "Patients and Consumers Managing Their Own Data," on Monday, April 28th at 1:55 pm under the Coordinated Patient Care, Engagement and Empowerment Program track. The Program is designed to show healthcare providers how to engage patients and encourage them to be more proactive in their healthcare and will include remote healthcare monitoring for early detection, healthcare portals for patients to access their medical records and information via automated communication and feedback to for specific diseases, all customized for patient involvement.

Click here for more details.

For full information on the conference, click here.

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Today's Definition of Genomics and Its Translation into Medicine

The term "genomics" was created in 1987. "For the newly developing discipline of mapping/sequencing (including analysis of the information) we have adopted the term GENOMICS. We are indebted to T. H. Roderick of the Jackson Laboratory, Bar Harbor, Maine, for suggesting the term. The new discipline is born from a marriage of molecular and cell biology with classical genetics and is fostered by computational science." (Victor A. McKusick and Frank H. Ruddle). The infamous Genome Project resulted from these findings and was completed in April 2003. Since the completion of the Genome Project, many scientists, and companies has embraced the knowledge gained and used it as a springboard to advance to its current definition:

The "understanding of the molecular mechanisms of disease, including the complex interplay of genetic and environmental factors. Genomics is also stimulating the discovery of breakthrough health-care products by revealing thousands of new biological targets for the development of drugs and by

giving scientists innovative ways to design new drugs, vaccines, and DNA diagnostics. Genomic-based therapeutics may include 'traditional' small chemical drugs, protein drugs, and gene therapy."

The National Human Genome Research Institute (NHGRI) of the NIH was formed to help advance this concept of understanding diseases better and developing new tests and therapeutics for diseases. One thing that helped to advance this field was the goal of sequencing a person's genome for $1,000. With the cost of sequencing dramatically decreasing, its access to scientists is increasing, thus enabling the use of these tools in scientific research, and also attracting funding from NHGRI and VCs.

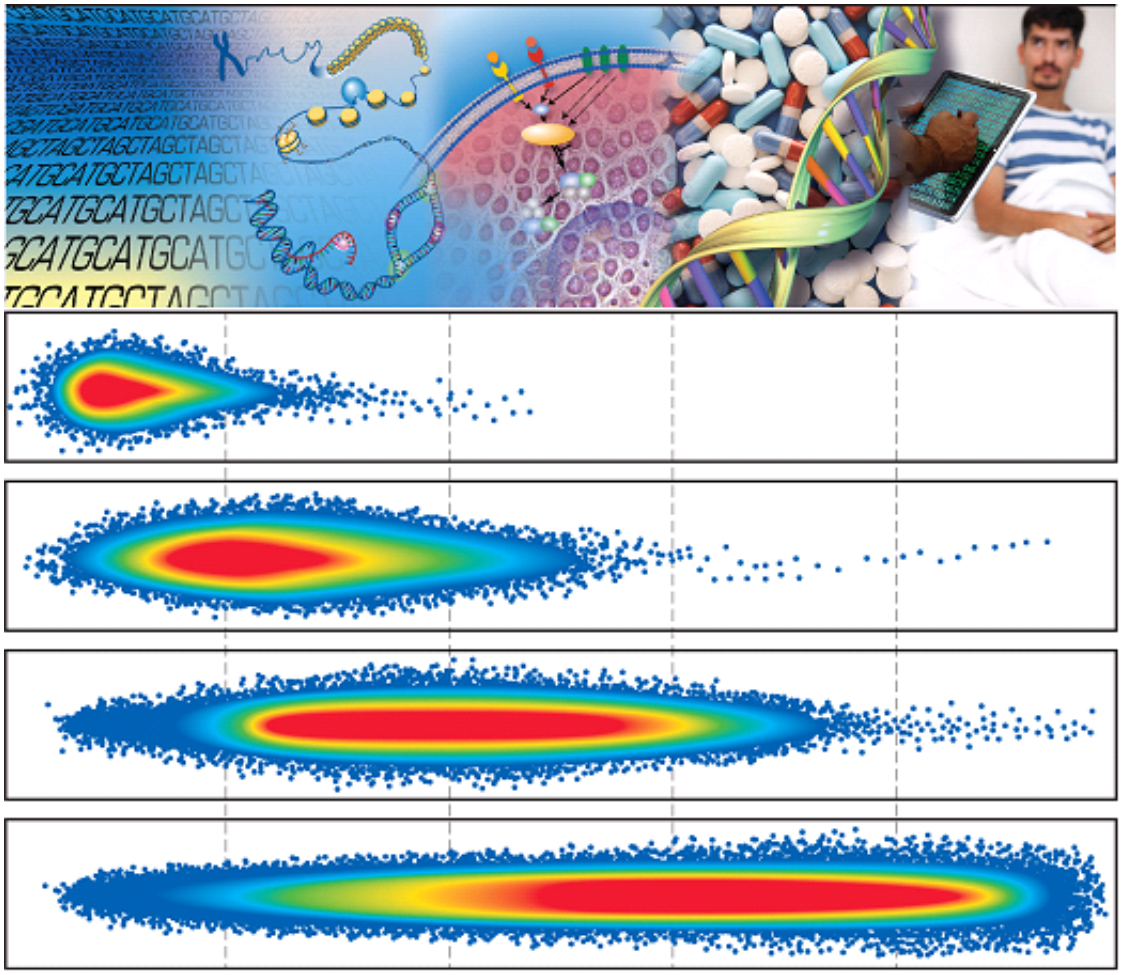
Below is a simplified schematic by Eric Green, and Mark Guyer from the NHGRI along with their prediction as to the progress of basic research being translated into effective medicines in the time frame from 1990 to beyond 2020, in their article "Charting a course for genomic medicine from base pairs to bedside." To read the full article click here.

The five domains of genomics research (left to right in the diagram below):

1. Understanding the structure of genomes
2. Understanding the biology of genomes
3. Understanding the biology of disease
4. Advancing the Science of Medicine
5. Improving the Effectiveness of Healthcare

The Y axis from top to bottom:

1. 1990 - 2003 Human Genome
2. 2004 - 2010
3. 2011 - 2020
4. Beyond 2020



Schematic representation of accomplishments across five domains of genomics research. The progression from base pairs to bedside is depicted in five sequential, overlapping domains (indicated along the top). Genomic accomplishments across the domains are portrayed by hypothetical, highly schematized density plots (each blue dot reflecting a single research accomplishment, with green, yellow, and red areas reflecting sequentially higher densities of accomplishments). Separate plots are shown for four time intervals: the HGP; the period covered by the 2003 NHGRI vision for the future of genomics research17; the period described here (2011-2020); and the open-ended future beyond 2020.

Source: E. Green & M. Guyer, NHGRI.

The most difficult steps in the five step process are to understand the biology of diseases; combining that with an understanding of the biology of the genome; and then translating that know-how to the clinic, or the next step of advancing science into medicine. Since we can now sequence the whole genome of any organism, creature, and human, how do we interpret this enormous amount of Big Data? By sequencing the human genome, we can find every mutation a person has, including those that indicate a particular disease, but which is the most relevant mutation or biomarker in developing a diagnostic test or treatment that will be successful? Understanding the biology both at the cellular and molecular level is the key. A good example of this would be Vertex and their drug Kaledyco for Cystic Fibrosis.

Jeffrey Leiden, MD, Chairman, President, and CEO of Vertex told the story of Kaledyco at the Whitehead Institute Rare Disease Forum held February 27th, 2014. Cystic Fibrosis (CF) was found to be caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. When scientists at Vertex were studying cystic fibrosis, they found that there were 1,900 mutations of the CFTR gene.

Mutations in the CFTR gene have also been found to affect other parts of the body, including the digestive or respiratory system and congenital bilateral absence of the vas deferens in males. Since it is not feasible to develop a drug for all 1,900 mutations, scientists looked at the phenotype of the

disease rather than just the mutations.

There was no animal model for CF, so scientists used the patient's lung cells and with the combination of genetics and cell biology, stratified patients according to phenotype. They then addressed the underlying cause of the disease and came up with a phenotype that included 9 mutations. These 9 mutations prevent the channels from opening and allow chloride ion and water to move in and out of the cells. As a result, cells that line the passageways of the lungs, pancreas, and other organs produce mucus that is abnormally thick and sticky. The abnormal mucus obstructs the airways and glands, leading to the characteristic signs and symptoms of cystic fibrosis. Vertex is also investigating mutations of the CFTR gene that affect protein folding which affect about 70% of the CF population.

Kaledyco is a transmembrane conductance regulator (CFTR) potentiator indicated for the treatment of cystic fibrosis (CF) in patients age 6 years and older who have one of the following mutations in the CFTR gene G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N,or S549R. These mutations represent 4% of the cystic fibrosis population. Vertex recently received approval for Kaledyco from the FDA for eight additional mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that cause cystic fibrosis.

Market Trends

Genomics is hot again and the focus of many companies. GE Ventures just recently invested $16.5 million Series E round with another investor in RainDance Technologies, a Billerica, Mass.-based company that is developing, and selling genomic tools for the early detection of cancer, as well as inherited and infectious diseases.

Rafael Torres,senior managing director of healthcare at GE Ventures in Menlo Park, CA said in an interview with *San Francisco Business Times* that with the cost of next-gen sequencing coming down "it creates a number of opportunities for research and the clinical diagnostics markets. There's a large growth in how researchers and clinicians eventually need to deal with understanding genetics and genomics." He sees RainDance Technologies as the company to create more efficient operations for them.

In translating this research into clinical practice, Torres says "That requires three things: precision - in the clinic, where you can change people's lives; efficiency - in the amount of time and processes that (users) put into these; and cost-feasibility - you're looking in very, very small samples and you need to keep costs under control."

Also getting into the action is Illumina, a San Diego-based life sciences research toolmaker whose leaders claim "it will create the world's first genomics incubator, aimed at accelerating the number of entrepreneurs, start-ups, and early-stage companies working on next-generation sequencing applications." Legendary Russian entrepreneur and investor Yuri Milner, who invested in the Y Combinator seed accelerator in Mountain View, CA, will give companies in Illumina, Inc,'s genomics incubator $100,000 in exchange for convertible notes. Milner was an early investor of Facebook Inc., Zynga Inc., and Twitter Inc. and in 2012 took a stake in 23andMe, Inc. a genetic testing company.

Craig Venter, Genome pioneer, along with stem cell pioneer Dr. Robert Hariri and X Prize Foundation CEO Dr. Peter Diamandis, raised $70 million Series A from investors to start Human Longevity, Inc. (HLI), to create the world's largest sequencing project, whose mission is to gather an extensive database covering the "complete" human genotype, microbiome, and phenotype. HLI plans to use the information to create cell-based treatments that can extend lives and improve the quality of life, particularly in diseases related to aging and cancer.

Venter plans an aggressive goal to sequence 40,000 genomes a year and then scaling it up to 100,000 genomes. He will then license this information to biopharma companies while simultaneously pursuing novel therapeutics and diagnostics.

"Using the combined power of our core areas of expertise--genomics, informatics, and stem cell therapies--we are tackling one of the greatest medical/scientific and societal challenges: aging and aging related diseases," said Venter in a statement. "HLI is going to change the way medicine is practiced, by helping to shift to a more preventive, genomic-based medicine model which we believe will lower healthcare costs. Our goal is not necessarily lengthening life, but extending a healthier, high performing, more productive life span."

The trend for a number of companies is to introduce gene sequencing into everyday diagnostic testing. Last fall, NextCODE Health launched with $15 million in Series A financing to use gene sequencing technology for routine diagnosis of disease. In November, GenapSys secured $37 million in Series B financing to develop next-generation genomic sequencing tech to gather detailed data for research and everyday testing of various diseases. NextGxDx Inc., a Nashville, Tenn.-based company developed an online genetic testing platform for healthcare professionals and hospitals, raised an undisclosed amount of Series B funding.

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Closing Thoughts

The genomic-based medicine model as described above is the future of how drugs/biologics (medicines) will be developed and will bring us closer to genotype/phenotype personalized medicine. Many companies are taking this approach now and their numbers will continue to grow, just as we saw numerous companies focusing on rare diseases once Genzyme proved it a successful business model. Superior therapies targeted to micro groups of patients will invite more drugs/biologics into the market without inviting a competitive landscape that resembles the antihypertensive market. Niche market genotype/phenotype therapies are the future and a one size fits all medicine is in the past.

The cautionary note to all this good news is that as we get closer to "personalized medicine," we are targeting subsets and subsets within subsets of patients, and market shares will shrink proportionately. Vertex's Kaledyco claims a mere 4% of the already small CF population. Can you meet the business goals of your company in that scenario?

Furthermore, unless you can truly justify to the insurance companies both short-term and long-term cost saving to the healthcare system, insurance won't be interested. Short term saving appeal to insurance providers because ironically, most people change insurance on a short term basis and therefore insurance companies will not benefit from only long term cost saving.

Forget about charging astronomical prices for your product as a way to recoup your investment which companies have historically done because insurance is pushing back. Recently, Gilead's Solvadi for Hep C was priced at $1,000 per pill or $84,000 for one 12 week treatment and some patients may require more than one treatment. A panel of California medical experts with the California Technology Assessment Forum, an insurance industry-affiliated group that assesses the costs and effectiveness of new medical treatments, voted Solvadi as a "low value" treatment. A final report is due out next month. The assessment was based on pricing of other medications similar to chronic diseases like HIV, patient access to the medication and overall cost to the healthcare system for Hep C patients both short-term and long-term.

Translation? Solvadi may not be reimbursed until the company lowers it price or be reserved for only the sickest patients.

So how do you get a leg up? Conduct the marketing due diligence that will not only confirm a place for

your product, but also ensure that you comprehend the marketplace dynamics that motivate key stakeholders (i.e. patients, physicians and other healthcare professionals, payers, regulatory). Be advised that stakeholders will not adopt your product unless it is demonstrably superior to what is currently available. In fact, if stakeholders believe that a superior therapy is on the horizon that alone can limit enthusiasm for yours. An example would be the face-off between the Merck and Vertex Hepatitis C drugs. Vertex's Incivek was better than Merck's Victrelis and Incivek obtained greater market share. However, there were a number of drugs in development that didn't require interferon and when they were predicted to be on the market soon, some physicians held off using Incivek until Gilead's Solvadi or J&J's Olysio was approved.

What marketing strategy you will use to obtain commercial adoption of your product? The inquiring minds of Angels and VCs want to know, so make sure to include an overview in your pitch for funding.

Developing a product? I can help you navigate through the commercial landmines as discussed above. To email me, click here or give me a call at 781-935-1462. Look forward to speaking with you.

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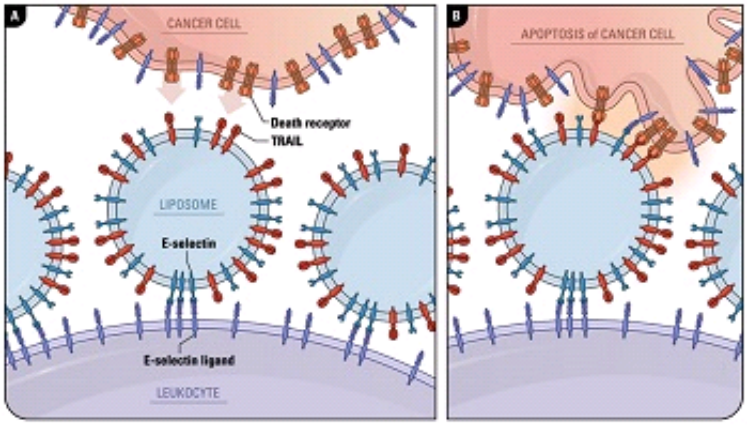
New Technology - "Armed with Cancer Drugs, White Blood Cells Become Cancer-killing Sticky Bombs"

Research Engineers at Cornell University have developed a "sticky bomb" or two proteins that attach itself to white blood cells to deliver cancer-killing drugs were found to be highly effectively throughout the body. "The tumor necrosis factor related apoptosis-inducing ligand (TRAIL) is a protein that induces cell death in cancer cells when it comes in contact with their surfaces...(the engineers) used an adhesive protein called E-selectin."



White blood cells hold the compound with TRAIL proteins that kill cancer cells upon contact.
Source:FierceDrugDelivery -Courtesy of Cornell

Their findings were published in the January 6, 2014 in the journal Proceedings of the National Academy of Sciences, calling these armed leukocytes "unnatural killer cells."

"The mechanism is surprising and unexpected in that this repurposing of white blood cells in flowing blood is more effective than directly targeting the cancer cells with liposomes or soluble protein," the authors said, as reported by the university's *Cornell Chronicle*.

To read the full article in *FierceDrugDelivery,* click here

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About BioMarketing Insight

BioMarketing Insight helps companies de-risk their product development process by conducting the business due diligence to ensure that it is the right product for the right market and the market opportunity for the product meets the business goals of the company. We are the translators between the scientists/engineers and the business people.

We understand the marketplace dynamics in helping companies navigate through the commercial landmines and will develop marketing strategies to drive product adoption.

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