AlphaBioCom
Precision Integrity Passion
10th Anniversary

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One Decade Down

We've completed our 10th year ... and our newsletter

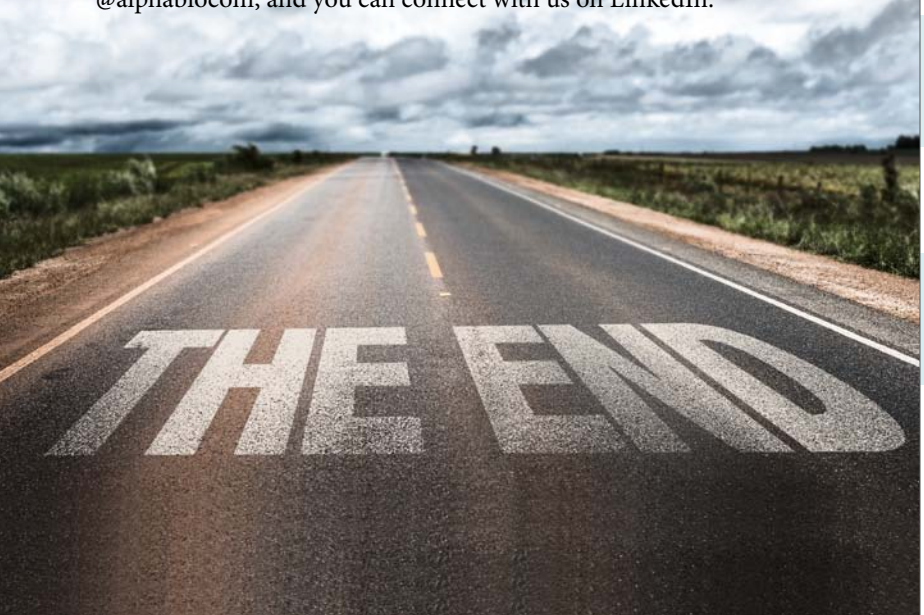
"Oh, the last ten years, it's been quite a trip."
– Kenny Rogers, "The Last Ten Years (Superman)"

That's right. We've reached the conclusion of our yearlong celebration of AlphaBioCom's 10th anniversary and our look at how our company, the business, and the world have changed in the past decade. To those of you who have been reading this newsletter on its (approximately) monthly basis, we thank you for joining us on this ride. For those of you who came in along the way, past editions are posted on our website at AlphaBioCom.com. Go catch up on those earlier issues. Go on … we'll wait.

Seriously, though, we want to take this opportunity to thank everyone who has read or received this newsletter, because you are the reason why we have made it this far, and you are the reason why we are thriving. We have said it before and we'll gladly tell you once again: Your trust, partnership, and friendship have meant the world to us.

And if you really enjoy this newsletter, we've got some good news. Though our 10th anniversary is coming to a close, we are going to continue putting out a newsletter to keep in touch with our clients and friends. Beginning somewhere around late March or early April, AlphaBioCom Monthly will morph into AlphaBioCom Quarterly (that's still just a working title) and appear in your inboxes four times a year.

For the final time, we invite you to check out the AlphaBioCom website (www.AlphaBioCom.com), and feel free to leave comments and suggestions about our newsletter and our organization. We can be found on Twitter at @alphabiocom, and you can connect with us on LinkedIn.



MEDICAL DEVICES

2005
- **May:** The US Food and Drug Administration (FDA) approves Wako LBA AFP-L3 [Wako Chemicals USA, Inc.], a lab test that helps determine the risk of developing liver cancer in patients with chronic liver disease.

2006
- **September:** FDA approves INTROL™ CF Panel I Control [Maine Molecular Quality Controls, Inc.], a DNA quality control material used to monitor the performance of genetic tests used in the simultaneous detection of 38 variations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene in human blood specimens.

2007
- **June:** FDA approves BinaxNOW® Malaria Test [Binax, Inc., a subsidiary of Inverness Medical Innovations, Inc.], the first rapid laboratory test that can detect plasmodium parasites using a whole blood sample drawn from a vein or a finger stick.

2008
- **January:** FDA approves xTAG® Respiratory Viral Panel (RVP) [Luminex Molecular Diagnostics Inc.], the first multiplex assay for detection of nucleic acids from 12 viruses, including Influenza A, Influenza A subtype H1, Influenza A subtype H3, Influenza B, Respiratory Syncytial Virus subtype A, Respiratory Syncytial Virus subtype B, and Parainfluenza 1.

2009
- **February:** FDA approves Reclaim™ Deep Brain Stimulation for Obsessive Compulsive Disorder (OCD) Therapy [Medtronic Neuromodulation], an implanted brain stimulator intended to suppress symptoms associated with OCD.

2010
- **July:** FDA approves the Implantable Miniature Telescope™ - P050034 [VisionCare Ophthalmic Technologies] to magnify objects and improve vision in patients with end-stage, age-related macular degeneration.

2011
- **October:** FDA approves APTIMA® HPV Assay [Gen-Probe Inc.], an assay to identify messenger RNA of two HPV viral oncogenes (E6 & E7) from 14 high-risk genital HPV types commonly associated with cervical cancer.

2012
- **February:** FDA approves The BreathTek UBT *H. pylori* Kit (BreathTek UBT Kit) and Pediatric Urea Hydrolysis Rate Calculation Application (pUHR-CA) [Otsuka America Pharmaceuticals, Inc.], Version 1.0, a noninvasive urea breath test to detect current *H. pylori* and to diagnose and monitor *H. pylori* infection.

2013
- **November:** FDA approves RNS® System [NeuroPace, Inc], a stimulator implanted in the skull with leads implanted in the brain, which helps reduce the frequency of seizures in epilepsy patients.

2014
- **June:** FDA approves artus CMV RGA MDx Kit [QIAGEN, Inc.], a laboratory test used to detect CMV viral DNA to assess virological response to treatment in immunocompromised solid-organ transplant patients at high risk for developing severe CMV infections.

2015
- **March:** FDA approves WATCHMAN LAA Closure Technology [Boston Scientific Corporation], a delivery catheter and device that is permanently implanted in the left atrial appendage (LAA) of the heart, where it prevents LAA blood clots from entering the bloodstream and potentially causing a stroke.

Embracing the Transformation

The scientific world is experiencing a veritable tsunami of change, and we need to ride the wave

Can we disrupt the scientific publication process and produce a better, faster, easier-to-access product?

Consider that, on average, a scientific publication:

- **Takes between 6–12 months** to develop and publish
- **Needs about 250 hours** of writing and editing
- **Uses around 2500 words,** 8–10 figures and tables, and 30–50 references
- **Requires 25 minutes to read,** at an average speed of 130 words per minute
- **Is only read by the authors and the editors;** 90% of all papers are never cited

Each year, more than 1.8 million scientific articles are published, appearing in about 28,000 journals. One study estimated that half of these articles are read only by those involved in the publication process—the authors, reviewers, and journal editors.

"I distinctly remember focusing not so much on the hyper-specific nature of these research topics, but how it must feel as an academic to spend so much time on a topic so far on the periphery of human interest," says Aaron Gordon, reporter at Pacific Standard. "Academia's incentive structure is such that it's better to publish something than nothing."

Is there a way to produce research of equally high quality that is easier and faster to access? To answer this question, we first need to look at why we have the peer-review process.

According to Kathleen Fitzpatrick, scholar of digital humanities and media studies, "the scientific publication process has changed little in the centuries since it began." Journals began publishing scientific research results in the mid-17th century, although the main mode of dissemination was scientific society meetings, where authors met to share their findings with other researchers. The process of peer review dates from the mid-18th century with the formation of committees to review papers for publication. Originally, peer review focused merely on helping editors select manuscripts, leaving the responsibility for quality in the hands of the authors. Over time, as the number of authors seeking publication increased, peer review became a safeguard against unsound or fraudulent research that could damage the reputation of the journal and its editors. The contemporary practice of assigning outside scholars, rather than journal editors, to review manuscripts began in the mid-20th century. "The long history [of peer review] makes it difficult to imagine scholarship without the process," says Fitzpatrick.

Today, we have a globally accepted standard format for the dissemination of science—a format that is universally accepted and rarely challenged. We see harmony and consistency in that format, despite it being ineffectual at what it is supposed to do. It takes too much time to prepare the information, to wait for publication, and to read the studies when they appear in print.

Our world moves at an incredible pace. We are exploring the boundaries of science as never before, but the process of sharing that information is still stuck in the Middle Ages. In any other industry, we would have been rendered obsolete by a wave of new technologies, swept up by 20-something entrepreneurs, and shut away to debate the use of an em dash vs an en dash in a dusty corner of a decaying typesetting print room. But not in the world of medical science publishing.

We need to change that

At AlphaBioCom, we are pioneering the deployment of new technologies—alongside our traditional scientific writing services—as options for clients to extend the reach of their data.

We will be using professional social media tools to expedite the transfer of information, embracing new and upcoming digital apps that enable easy access to published data, encouraging the use of a one page executive summary to accompany a journal submission, looking into online journals and open access facilities, and adopting any other useful technology that comes along.

Dr. Max McKeown has pointed out that one can learn to shape and surf a wave of change like Apple and Uber have done, or be stranded and smashed like BlackBerry and Blockbuster.

As we enter our second decade of services, AlphaBioCom hopes to help you shape and surf the wave of change that will soon happen to our exciting, if old, industry.

A look at some of the slides in "Don't Be Left Behind — Learn to Evolve with the Changing Healthcare Environment," presented by AlphaBioCom's Stephen Douthwaite at the CBI Publication Planning 2015 Conference.

The Promise of Pharmacogenetic Testing

Despite government-imposed restrictions, advances help us move closer to personalized medicine

One of the most important biomedical advances of the past 15 years is the 2003 completion of the Human Genome Project. This landmark accomplishment involved the complete sequencing of the human genome, enabling researchers to find specific locations of many human genes. Along with coding for physical characteristics (eg, dimples and eye color), genes can also determine whether individuals are at increased risk of developing various diseases (eg, diabetes, hyperlipidemia, hypertension). Additionally, researchers have begun to discover the relationship between genetic sequencing and drug response; the field analyzing differences in how genes affect drug response is known as pharmacogenomics and pharmacogenetics. Although these terms have been used interchangeably, pharmacogenomics tends to refer to the overall study of genetic variations in drug response, whereas pharmacogenetics refers to the study of differences in clinical response(s) to a particular drug. Package inserts for medications now incorporate pharmacogenomic information such as drug-drug interactions, hypersensitivity reactions, drug resistance, and even drug indications based on specific genes.

Mutations within genes may involve one nucleotide being inserted, deleted, or replaced within the encoded gene. These mutations cause the creation of a mutated protein, such as a dysfunctional receptor or enzyme. The cytochrome P450 (CYP) enzymes play a significant role in drug metabolism, since about 75% of drugs are metabolized through CYP enzymes such as CYP2C9 and CYP2C19. Although some patients have CYP genes coding for enzymes that metabolize certain drugs at a normal rate, mutations in CYP genes code for enzymes that metabolize drugs at either a faster or slower rate, resulting in patients achieving drug concentrations above or below the normal therapeutic drug range. Some mutations may even result in patients experiencing drug toxicity.

An example of a drug metabolized differently by some patients is warfarin, an oral anticoagulant used to treat and manage thromboembolic events as well as to prevent thromboembolic complications associated with cardiovascular (CV) conditions such as atrial fibrillation. Warfarin is composed of two isomers (R-warfarin and S-warfarin); the S-isomer is 5 times more potent than the R-isomer and is primarily metabolized via the polymorphic CYP2C9 enzyme. Once metabolized, warfarin binds to vitamin K epoxide reductase (VKOR), antagonizing the production of vitamin K-dependent clotting factors, resulting in anticoagulation. Patients on warfarin need regular monitoring of their International Normalized Ratio (INR) to make sure it stays within acceptable range, usually between 2 and 3. Because the CYP2C9 and VKORC1 (VKOR complex 1) genes contain multiple alleles, the US Food and Drug Administration has updated the total daily dose range of warfarin based on an individual's CYP2C9 and VKORC1 genotype. In June, the Center for Medicare and Medicaid Services (CMS) restricted pharmacogenomic testing for CYP2C9 and VKORC1 due to insufficient evidence of clinical relevance and utility. CMS covers both pharmacogenomic tests for candidates for warfarin only under these conditions: (1) they have not been previously tested for CYP2C9 or VKORC1 alleles; (2) they have received fewer than 5 days of warfarin in their anticoagulation regimen for the ordered tests; and (3) they are enrolled in a prospective, randomized, controlled clinical study (CMS 2015).

Another example of a drug whose metabolism is gene-dependent is clopidogrel, an antiplatelet agent used to treat ischemic events in patients with acute coronary syndrome (ACS), percutaneous coronary intervention (PCI), and myocardial infarction. Unlike warfarin, which is metabolized via CYP2C9, clopidogrel is converted via CYP2C19 into its active metabolite. Once activated, clopidogrel irreversibly binds to ADP receptors on platelets, inhibiting platelet activation and aggregation. Concerning pharmacogenomics applications, studies have shown that mutations in the CYP2C19*2 gene, for example, result in decreased function of the CYP enzyme, leading to lower active metabolite levels and an increased risk of CV events. Mutations in the CYP2C19*17 gene, however, result in higher active metabolite levels and a decreased risk of CV events. Based on the lack of prospective randomized clinical trials evaluating pharmacogenetic testing of clopidogrel, the American College of Cardiology and American Heart Association issued a statement in 2010 that "the evidence base is insufficient to recommend either routine genetic or platelet function testing" (Shahin 2013). However, CMS will cover CYP2C19 gene testing if medically necessary for patients with ACS undergoing PCI who are starting or restarting clopidogrel.

Pharmacogenetics and pharmacogenomics offer much potential for moving toward personalized medicine

Although future studies will be needed to determine the clinical relevance of these pharmacogenomic tests, pharmacogenetics and pharmacogenomics offer much potential for moving toward personalized medicine. As trials on pharmacogenetic testing are published, clinicians will be able to use greater precision when managing patients on multiple medications, likely resulting in reduced adverse drug events, hospitalizations, and readmission rates; decreased healthcare spending; and an improved quality of life for all patients. Personalized medicine will continue to advance and patients will benefit from more effective treatment.

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A Final Word ... or Two

What does the future hold for us?

Ed Shifflett, Partner

Is 2015 really over? It seems like just yesterday that we kicked off the celebration of AlphaBioCom's 10th year in business. I won't rehash what I wrote in the first newsletter. Instead, let's think about the future. You've seen us highlight the various changes in culture and medicine over the past 10 years. So, what will change for us both personally and professionally in the next decade?

- **More than half the population** will use self-driving cars
- **For any chronic medical condition,** you will have a small chip inserted (like a pet microchip) that will constantly provide information directly through an app on your smartphone (which will also be drastically redesigned) feeding into your physician's office to monitor your health
- **Print medical journal publications** will be completely replaced
- **Physicians will receive customized peer review updates** via short podcasts or simple voice-only messages like an audiobook on a wrist bracelet—available only to physicians—that uses a virtual screen
- **For the sleep-deprived**, a prescription medication will be developed that can put us to sleep in 5 minutes, allows us to get deep recovery sleep for 20 minutes, and then wears off, allowing us to wake naturally and completely refreshed
- **Your watch will answer calls** via a pop-up hologram, giving you visual conferencing with audio

Of course, if you don't believe that any of the above will be developed, you could always ask the Magic Eight Ball and see what answers you get. Recall that just eight years ago, no one expected to be reliant on their iPhones. And remember, the first tablet was only released five years ago.

It's been an amazing 10 years personally and professionally. We all wish nothing but the best for you in the future. Thank you for being a part of our past and we look forward to having you along for the ride in the future.

The promise of the upcoming decade

Stephen Douthwaite, Partner

In the last 10 years, we have witnessed amazing technological innovations and some tremendous leaps forward in knowledge and understanding. Within medical science, we have seen virtual cures for hepatitis C, amazing advances in the early detection and diagnosis of pancreatic cancer, and vaccines that prevent cancer. AlphaBioCom is proud to have worked on many of these and other inspiring and amazing medical breakthroughs. This year alone, we worked on 10% of all 2015 FDA-approved products. Currently, we are supporting the introduction of major improvements in cardiovascular treatments, groundbreaking new therapies for life-threatening infections, new modalities for hematological cancers, and an array of other life-improving and -enhancing treatments.

The next 10 years promise even greater excitement and discovery. In the broad study of science, physicists may soon know the origins of our universe, and many predict we will soon be able to accurately describe dark matter and dark energy. In our corner of medical science, it will be an unprecedented era of technological advancement. Genetically focused therapy, personalized medicine, and the deep pools of opportunity that lie in the heart of immunological programming and engineering mean that we are at the crest of a revolution in medical science. We should expect to see the approval and introduction of treatments that save the lives of millions of patients suffering from pancreatic cancer, Parkinson's disease, Alzheimer's disease, and incurable pediatric diseases. And maybe even old age!

As the science of medicine expands and changes, the need to ensure effective scientific exchange does not. Caregivers, physicians, healthcare providers, patients, and families all need balanced, reliable, and accurate medical information. AlphaBioCom's mission to be the world's best content developer of scientific information will remain strong and true. Our founding pillars of **Precision, Integrity,** and **Passion** will be the basis upon which we continue to operate, seeking new technologies with which to communicate and pioneering new approaches for the delivery of the information.

It looks like it's going to be a wonderfully exciting 10 years. Come and join us in our quest to create educational innovations and improve the practice of medicine.

Take a seat in our time machine, strap in, and enjoy the ride. 2025 … here we come!

AlphaBioCom

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