Forbes/Wolfe Emerging Tech REPORT

Volume 14 / Number 2 / February 2015 www.forbeswolfe.com

The Insider

JOSH WOLFE, EDITOR

This month's issue pays tribute to American science, with pioneers in education, visual arts and biological discovery sharing their knowledge with us.

We lead with Larry Bock, founder of the USA Science & Engineering Festival, the largest celebration of STEM in the United States (*Full disclosure: Larry is Special Limited Partner at my venture firm Lux Capital*). A tremendously successful biotech entrepreneur, Larry is now tirelessly working to change the way America's youth view science and technology. The

Festival Atmosphere Sells Science To American Kids

Larry Bock is the founder and executive director of the USA Science and Engineering Festival—the nation's largest celebration of science and engineering (*Full disclosure: Larry is Special Limited Partner at my venture firm, Lux Capital*). Larry was a co-founder and executive chairman of Nanosys. Prior to Nanosys, he was a managing general partner of CW Group, a life sciences venture capital fund. Larry was also a general partner of Avalon Ventures, a seed stage venture capital firm. Larry has been the founder and initial chief executive officer of Metra Biosystems, **Neurocrine Biosciences** [NBIX], **Pharmacopeia, Argonaut Technologies** [AGNT] and **Caliper Technologies** [CALP]. Bock was also a co-founder of **ARIAD Pharmaceuticals** [ARIA], Athena Neurosciences, GenPharm International, **Vertex Pharmaceuticals** [VRTX], **Onyx Pharmaceuticals** [ONXX] and **Illumina** [ILMN]. He holds a B.A. in Liberal Arts from Bowdoin College and an M.B.A. from the Anderson School at the University of California, Los Angeles.

LARRY BOCK

What inspired you to start the USA Science and Engineering Festival?

I was traveling abroad and saw the science festival in Europe. The attendance I saw made it very compelling, and I wanted to import the concept to the States. For example, one festival in Cambridge, England, draws

continued on page 2

Creating Images At The Intersection Of Science And Art

VIKTOR KOEN

Viktor Koen is an award winning artist and educator. He holds a BFA from the Bezalel Academy of Arts & Design in Jerusalem, Israel and an MFA with honors from the School of Visual Arts in New York City. Koen serves on the faculty of the MFA Illustration program and the BFA Graphic Design

continued on page 4

Young Blood Fights Effects Of Aging In Old Bodies

DR. AMY WAGERS

Amy Wagers is the Forst Family Professor of Stem Cell and Regenerative Biology at Harvard University, Senior Investigator in the Section on Islet Cell and Regenerative Biology at the Joslin Diabetes Center, an HHMI Early Career Scientist, and a member of the Paul F. Glenn Laboratories for the Biologi-

continued on page 6

Festival Atmosphere Sells Science To American Kids

continued from page 1

about 50,000 people out of a surrounding population of around 400,000. If a similar event in a major U.S. city brought in one in eight people that would be a tremendous accomplishment.

What is the USA Science and Engineering Festival?

STEM stands for science, technology, engineering and mathematics, and our festival is the largest STEM outreach event. It's a celebration of science and engineering. Our mission is two-fold—first, we want to highlight the great role models we have in science, and create the next generation of role models. Second, we want to showcase the fun and entertaining sides of science and engineering and expose how science impacts every part of our lives, from music to health to sports.

We run the festival every other year, and it has doubled in size each time. We are now planning our fourth festival, coming up on April 15-17, 2016. We want to celebrate science and engineering the same way we celebrate professional athletes, pop-stars or Hollywood celebrities.

Many Americans can name far more reality TV stars than prominent scientists or engineers. Why do you think that is?

We don't celebrate them. When you ask most kids to name a famous scientist or engineer, you'll be lucky if you get Albert Einstein for an answer. You ask them to name a living scientist and they're usually dumbfounded. We want names like Elon Musk to be as household to kids as Albert Einstein.

Starting the festival must have been a massive job. How did you approach this undertaking?

I started the festival in a similar manner to most of my high-tech companies—by capturing the high ground and surrounding the festival with a set of thought leaders in science and engineering. My initial advisory board of 25 people included about 10 Nobel laureates and leading chief technology officers of major companies like **Lockheed Martin** [LMT], Genentech and **Amgen** [AMGN]. The credibility gained from the board helped launch the first festival in San Diego.

We started with a small team and we're still just a handful of people, but the catalytic effect of the festival process has been amazing. At our first festival, Lockheed Martin (our primary sponsor and exhibitor) had more than 100 people working the event. Now we have about 1,000 organizations involved and it continues to grow.

The festival has since moved to Washington D.C. Why did you switch locations?

After the San Diego festival, which was one of the largest events in the history of Balboa Park, Lockheed Martin came to me and said, "That was fun, but why don't we do this on a national basis in Washington D.C.?" My first reaction was that Washington wasn't a science city, but in reality most of the professional science and engineering societies and trade associations are in D.C., most major government science efforts are there, and most major corporations have at least some satellite office in D.C. It's an ideal location.

What kind of response have you seen from government policy makers?

We have quite a bit of government support. The president has done a PSA for our event, and the Obama daughters have attended. Several major government officials have been to the festival: the Secretary of State, the Secretary of Transportation, the Secretary of Engineering, and the heads of the NIH, NSF and NASA.

We take no policy standpoints on issues such as climate change, and we're not politicizing things like evolution, so we get bipartisan support. We're just presenting the science behind the issues—sort of a science Switzerland. This way, everybody wants to play on our platform.

How do you manage the logistics of having 1,000 organizations involved?

Even though we are a non-profit, we run this like a business startup. From an infrastructure standpoint, we use a lot of automation tools like CRMs to help facilitate all aspects of the process. We do a lot of software integration between these different platforms so we're not spending all our time working on spreadsheets.

We spend a lot of time evangelizing the festival. Usually, once we've talked to an organization and educated them about the event, we can get them to participate. From that moment on, until the day they exhibit, it's a lot of automation of the process. And, once organizations participate in a festival, they always participate the next year, and often expand their exhibits.

How do people participate in the festival?

There are three ways in which people participate in our festival: as an exhibitor, as a performer in the final expo, or as a speaker in one of our X-STEM events. On the exhibitor side, we host a full spectrum of exhibits. These can range from a Dragon space capsule to surgical robots, to virtual reality environments. At the other end of the spectrum, we have exhibits for making structures with marshmallows and toothpicks.

Who were the science celebrities you featured?

Bill Nye the Science Guy participates regularly, and we've also had the Mythbusters, Mike Rowe from Dirty Jobs, and Grammy

The Insider

fourth festival will be held on April 16-17, 2016, and we strongly urge all of our readers to participate!

Next we speak with Viktor Koen, a faculty member at the School of Visual Arts who shares with us his fascination for science fiction, how he wanted to be an artist, what fascinates him so much about technology and how his award-winning work has been regularly featured in the *New York Times, Wall Street Journal*, and dozens of other media outlets across the U.S. and around the world.

Lastly we sit with Dr. Amy Wagers, whose astonishing work is blurring the lines between science and fiction. Building on the astonishing discovery that young blood has the power to rejuvenate aged tissues in mice and vice versa, Amy and her team at Harvard are working to isolate proteins that have the potential to reverse the physical decay of aging. As always here's to thinking big about thinking small...and to the emerging inventors and investors who seek to profit from the unexpected and the unseen.

Festival Atmosphere Sells Science To American Kids

continued from page 2

Award-winning groups. Last year we featured Paul DePodesta, the statistician portrayed in the movie *Moneyball*, and David Pogue, the technology writer at Yahoo. Other top listings include Amanda Boxtel, the first woman paraplegic to walk with an exoskeleton, and Travis Dade, one of the few quadruple amputees who uses bionic technology to get around.

What are the X-STEM events?

X-STEM is a TED-style symposium for kids. Last year, our X-STEM events involved about 50 speakers, including Craig Venter, who discovered the human genome; Anousheh Ansari, the first private female space astronaut; and the President's chief science advisor. About 4,000 students attended.

We have an X-STEM event on April 28 this year, in D.C. The event is free.

In addition to X-STEM, have you developed other outreach events?

We have another program we call the Nifty Fifty, where we bring speakers into schools. This year, we'll bring 250 leading scientists and engineers into about 350 schools—some speakers do it multiple times. Our goal is to grow that program to 50 scientists in each of the 50 states, each doing outreach in schools.

We have another program we call Lunch with a Laureate. We have 30 Nobel laureates going into schools. This runs continuously, in a different school every week.

What have you found to be the greatest challenge in recruiting scientists as speakers?

The first time we did this Nifty Fifty program, I brought some well-known, leading scientists and engineers into a school, and I almost went home in tears. I learned that while these scientists were great communicators to their peers, they were horrible communicators to the general public, and especially to young people.

I had to change my model in order to recruit leading scientists and engineers who were very effective at communicating to a young audience. That's not an easy thing. It's very difficult to explain your work in lay terms without jargon, and without dumbing it down.

Why do you think that science education is so important for children?

Look at the trends. First, American students are not going into science and engineering; second, we're not retaining the people that we're educating from abroad in those fields due to visa issues. Finally, the science and engineering opportunities are now greater abroad than in the States.

"Our mission is two-fold—first, we want to highlight the great role models we have in science, and create the next generation of role models. Second, we want to showcase the fun and entertaining sides of science."

The confluence of those trends has led to a perfect storm of Americans not going into these fields. I fundamentally believe if we don't turn this around in one generation, we will have outsourced innovation. When that happens, the game is over.

On that note, have you seen any changing trends since you first started the festival?

I see a much greater spotlight on STEM now than when we started seven years ago. I can't say that STEM teaching in the schools has improved, but there has been a great improvement in the number of afterschool programs, like First Robotics, or Project Lead the Way.

Beyond inspiring students at the festival, what impact have you seen from the festival?

One unexpected consequence has been for the exhibitors and the presenting scientists. Many of them have thanked me after the event, saying, "For the first time, my own kids understood that my work is important, after they saw a hundred kids standing in line to do the activity in my booth."

We also get a lot of comments from STEM teachers. We run special events to expose them to creative ways to demonstrate STEM ideas beyond the textbook. For many classroom and homeschooling teachers, this is where they get a lot of their curriculum ideas for the following year.

What are some near-term and long-term goals that you have for the festival, in terms of funding, attendance or other metrics?

My key long-term goal is to make this sustainable, to give it a life of its own. I think we're on the verge of that. Last year we raised our sponsorships and built the program, and it was the first year we ended up with a surplus.

One challenge is that we are nearing maximum capacity at our current venues. We had 325,000 people in the Washington Convention Center over a three-day period. We're looking at ways to expand into the streets around the Convention Center, but if we grow at the same rate again this year, we will far exceed the capacity of the Convention Center.

Do you have any plans to expand beyond D.C.?

At the moment, we go beyond D.C. through a number of satellite events that are anchored to us but are created and run by other organizations. Last year, there were 73 satellite events held in 23 states, plus an additional 25 events held in other countries. These might be analogous to TED-X events, produced by local organizations ranging from small entities to giant festivals.

What sort of businesses or organizations would you like to see grow in number at the next festival?

I would like to get more entrepreneurial, high-tech startups involved, because often that's where some of the most interesting work is being done.

This year I'm working on getting the NVCA (National Venture Capital Association) and similar organizations to support the festival, so we can showcase more of that type of work. The challenge there is that startup companies have limited resources to deploy. The flip side of that argument is that without better STEM education, they may not have anybody to employ in the future.

And how can people sign on to get involved?

The best way to get involved is to go to our web site (http://usasciencefestival.org). We're looking for speakers, we're looking for exhibitors, we're looking for sponsors and we're looking for volunteers. **ET**

Creating Images At The Intersection Of Science And Art

continued from page 1

Department at SVA. His images are regularly published in the *New York Times*, *Wall Street Journal* and *Nature*. His prints are widely exhibited in galleries and museums in the United States, Europe, Japan and Australia and are part of private and institutional collections. He is a TEDx Athens speaker and lectures for academic and professional institutions such as the Type Directors Club, the New York Public Library and the Graphic Artists Guild. Koen's work is regularly featured in books and publications worldwide. Distinctions include Communication Arts Award of Excellence, Graphis Gold Awards, First Prize Digital Hall of Fame and Folio Gold Awards.

When did you realize you wanted to be an artist?

It started on my first day in kindergarten when I lived in Greece. I drew a nice picture and my teacher told my mother I would be an artist. As I grew up, I knew I would try to make pictures for a living. That was not really a great business plan, but I stuck to it. At age 18, I traveled to Israel, and was accepted to the Bezalel Academy of Arts and Design. I did my Bachelor of Arts degree with a concentration in graphic design and communication, and I took every illustration elective. I then came to the School of Visual Arts in New York City for a Master of Fine Arts in Illustration, and have stayed here since.

Do you think that formal training is necessary to become an artist?

I am an absolute believer in education for the arts and that it should include both a technical and a philosophical framework. You could do it alone, but the environment of an academy provides the solid know-how for specific techniques and schools of thought to develop and grow your art, along with the interaction with professors and peers.

I believe in the chemistry between students that helps develop individual artists. Add in the professional practice and strategies that help our students go out and actually make a living…as I mentioned, art is not a fantastic business plan, but it's a doable one. A working, thriving artist that creates for a living still needs to put food on the table.

Can you talk a bit about your career trajectory and how you ended up where you are now?

I was attracted to science fiction long before being attracted to science. I created post-apocalyptic imagery, day in and day out, and for a while it went nowhere. I kept showing my evil little pictures, and my images improved and began to communicate ideas. Slowly but surely, I built a base of clientele that used my work to resolve problems for book or CD covers, magazines and newspapers.

Over the last decade, I started doing a lot of scientific illustration. I was not savvy in the sciences, but had ideas about how to illustrate. I needed to understand the basic premises of the texts I was reading and come up with ways that other non-scientists could follow. My challenge was to digest a scientific article and then produce an image that not only explains the gist of the science, but also creates an impactful piece of art. The image needs to communicate messages from the article and even give some extra knowledge about the breakthroughs that are developing.

Are you currently teaching, in addition to creating art?

I've been teaching in the graduate and undergraduate levels at the School of Visual Arts, my alma mater, for the last 10 years. I teach a professional illustration boot camp that exposes students to everything a new illustrator can do to attract clients and become established.

Can you describe your creative process for developing an illustration?

I am sent a first draft of the article, so I have a solid understanding of what we're trying to communicate. While I'm working on the image, the author and editor finalize the article. I start with a couple of ideas in a sketchbook, pencil sketches just for myself, and then photographic concoctions that I send out for changes and input. After approval, I finish it up and send a digital file to the publisher.

You started off making art influenced by science fiction. Who were some of your inspirations in that area?

I was exposed to the look mostly in New York, in our Gotham environment. I have also been inspired by people like H. R. Giger, and have had the great fortune to collaborate on a couple of projects. Sci-Fi movies are another great inspiration. I won't miss a chance to see how others visualize the future.

Much of your art focuses on the intersection between technology and society. How do you think technology is affecting us as a society?

The impact is radical and direct. A lot of my work communicates social criticism, both from the way I illustrate and from the way I teach. We've seen great advancements, mind-blowing things, but human nature remains the same.

Here's an example. I grew up as a person who did research by going to the public library to ask for a box of cutout photography. Today we do this with the push of a button on a search engine. To a certain degree, the ease with which this happens has increased the results. On the other hand, I find it inexcusable when people come unprepared for class, because it only takes 30 seconds to do the research.





continued from page 4

What do you think about the impact that technology has had on art?

It's like it always was. At some point, photography was a new thing, digital was a radical technology and then coding as artwork was brand new. I don't run after the changes, but I love to see what the synergies are between what I do and what new, advanced technologies can do.

It's not like every time a new technology arrives you clear the table. There is space for people that are in love with old techniques and for people with a passion for things to come, and the most interesting space is the interaction of these two segments. For example, I just finished a series of digital images that were done using vintage photography and printed using very old photographic process to translate the digital files.

I get very excited about the mix of old and new because it establishes the new in the minds of the skeptics. It brings opportunity and a fresh breath of air for people working traditionally to use new, ever-changing techniques. 3D printing is another amazing development. I can't wait to get my hands on it.

What tools do you use for your art right now?

I get excited about new technology, but I'm a conservative guy, and not an early adopter. I'll wait for things to be debugged and become established (although, as I said, I can't wait to get my hands on a 3D printer).

I use the good, old-fashioned digital technology, the **Adobe** [ADBE] suites, particularly Photoshop and Illustrator. I do a lot of identity and design imagery, and combine platforms and software to make it work. These technologies have so much depth, and I've been working within them for more than 20 years now, so I enjoy knowing how to model them exactly the way I want it.

Tell us more about your typography. Do you have the same creative process when you're creating an alphabet as when you illustrate a book cover?

It's actually very different, due to the time that it takes to develop an illustrated alphabet. These alphabets are almost like fine arts pieces. I've done commissioned alphabets for organizations like *Time* magazine, but usually the exhibited alphabets are more complex pieces that take six to nine months. It's almost like giving birth, creating an illustrative alphabet.

I start with a lot of photography as my raw materials, and collecting a library of images can take years. One alphabet requires 26 complex illustrations, and you can't exhaust the subject matter by letter number four—you have to maintain that fire all the way to the end.

Right now I'm working on "sci-phabet," the scientific alphabet. This will be exhibited in 2016 at the International Conference on Typography. These exhibits are the places where you find your exact demographic, and are a growing opportunity for illustrators.

Where do you find your photographic images?

I have great photography from science and technology museums. Whenever I need something specific, there's no place like New York City to take shots. I do a lot of cleaning and clipping, arranging and retouching, mixing and matching. Fitting parts into typography shapes is done by trial and error, because legibility of the type is very important. We take liberties, but the whole point is to recognize the alphabet.

You work with publishers, primarily. Have you ever partnered with tech companies?

I am a junkie for tech developments, but not everyone can visualize that direct connection between science and art. There is more of a collaboration on the back end rather than on the front end of a tech development. Few technology companies will directly assign something without involving a publication in between.

What is your advice for aspiring artists right now?

My first piece of advice is very simple. Wake up an hour earlier and invest an extra hour in the work. The biggest problem an emerging artist has is the lack of production, so create a framework that makes you produce. An artist needs to be completely self-motivated so when you have no assignments, instead of jumping out of the window in desperation, start creating new images. Develop a work ethic where you produce more today than you produced yesterday.

Second, get educated. Become savvy about the marketplace, and not just by using the Internet. One byproduct of technology may be that we forget our basic people skills, which are of utmost importance to networking.

Would you elaborate on the importance of networking for an emerging artist or illustrator?

The way you meet people, introduce yourself, and keep in touch is important. You need to create alliances and connections with like-minded people who share an interest in the development of art. Be available and collaborate and donate things.

Young people are often afraid to ask hard questions, and sometimes don't want to hear difficult answers. If you only want to hear good words, there's always space for your artwork on your mother's refrigerator, but that's not what it's all about. You need people who will tell you what they really think. You might not like it, but maybe they will bring a breakthrough, or resolve a dead end, and help you push through to the next level.

In addition to the commissioned work that you do, where can people see your art?

I exhibit extensively in galleries and museums. My new work is booked for June at the Benaki Museum in Athens. The series of fine art illustrations for this show has been four or five years in the making. I've been developing some poster campaigns and working on a book based on the new exhibition, which has been a very exciting process.

I currently have a big public art installation around the base of the Manhattan Bridge. This is a series of 4x4 blowups of images called *Tasks and Games*. I also collaborate in group shows, and exhibit in specialized conferences like the International Conference of Typography.

What do you see as the greatest challenge, or the greatest reward of working in illustration art?

It takes juggling: the professional career, the design career, the teaching, and the fine art. There is that duality, but I think the thrill of illustration is so great. No matter how many illustrations I will publish—and I've published thousands—I grin every time I see one of my pictures in print. **ET**

Young Blood Fights Effects Of Aging In Old Bodies

continued from page 1

cal Mechanisms of Aging at Harvard Medical School. Dr. Wagers received her Ph.D. in Immunology and Microbial Pathogenesis from Northwestern University, and completed postdoctoral training in stem cell biology at Stanford University. Dr. Wagers' research seeks to understand how changes in stem cell activity impact tissue homeostasis and repair throughout life. Work from her lab provides evidence for the existence of a conserved systemic regulatory axis that modulates tissue maintenance and regeneration across a wide variety of tissues that vary significantly in their intrinsic repair capacity, and her ongoing studies have begun to identify the molecules responsible for age-variant regulation of regenerative potential. Dr. Wagers has authored more than 100 primary research and review articles, and her work has been recognized by awards from the Burroughs Wellcome Fund, Beckman Foundation, WM Keck Foundation, Glenn Foundation and National Institutes of Health. In 2013, she received the New York Stem Cell Foundation's Robertson Prize for outstanding achievement in translational stem cell research.

Tell us a bit about your background.

I started my career as an immunologist looking at immune cells and wound repair. I was in the bone marrow donor registry, and I matched with a patient for a transplant. That sparked my interest in stem cells. I went on to Stanford for postdoc work, where I transitioned into stem cell biology.

I started my lab about 10 years ago, and have worked broadly on stem cell function in tissue repair and regeneration, and how that changes with age. I started using a parabiotic model to look at how stem cells migrate. In parabiosis you create a conjoined blood system between two animals to study the influence of certain circulating blood factors, and to track how they move in the body.

Are there certain cell types you've focused on in your studies?

I collaborated with Thomas Rando's group to look at the impact of circulating cells on skeletal muscle and aging. We used the parabiotic system to find blood factors that could affect muscle repair in older animals. Our experiments showed that old muscle could repair itself better after exposure to young blood. We all became very enthusiastic at that point. Those initial studies were done several years before the paper was published in 2005.

Over the past decade, you've tracked down a factor you suspect to play a role in aging. Tell us how that came about.

Finding the factor responsible for aging is like finding a needle in a haystack. Tons of substances exist in the blood: proteins, non-proteins, small molecules and lipids. Sifting through them all requires a number of different approaches. It's incredibly satisfying to finally identify at least one of the active substances in the blood. All of our studies linked improved activity in older animals, after parabiosis, to a protein called GDF11. This protein is abundant in the blood of young mice and is lost in the blood of old mice.

Can you talk about the different experiments that have taken place since 2005 and what we've learned from each of them?

The original study focused on skeletal muscle repair and the role of a particular protein called Notch. From there, Tom's lab went on to ask a new question: if old mouse muscle gets better after exposure to young blood, what happens to young mouse muscle after exposure to old blood? A follow-up paper, published by Andrew Brack, showed that young muscle repairs poorly after it's exposed to old blood, and identified a factor partly responsible.

We went on to ask whether that same result occurs in other tissues as well as muscle. We collaborated with Robin Franklin, at the University of Cambridge, to look at spinal chord remyelination. Nerve processes are wrapped in myelin and that's important for the conduit of the nerve signal. There's a population of regenerative cells that make new oligodendrocytes, which are the cells that wrap around the axons. In diseases like multiple sclerosis, that myelin wrapping is destroyed. We modeled myelin destruction by injecting a toxin into the spinal cord, to cause very small, demyelinated lesions. Then those oligodendrocyte progenitors made new oligodendrocytes to rewrap the axon. When you're young, that happens really well, just like in the muscle system when a stem cell responds to injury, making new replacement cells for damaged cells. When you're old, that process doesn't happen well. We found parallels between repairs in muscle cells and in the spinal cord. An old mouse exposed to young blood by this parabiotic system could repair damage more efficiently. The young partner did just as well at repairing damage, whether joined to another young partner or to an old partner.

Did you test other tissues as well as muscle and spinal cord?

We looked in the heart, brain (especially olfactory cells) and skeletal muscles and found that one protein, called GDF11, is involved in the restoration and function of all these tissues—even in the mature, non-dividing cells like skeletal muscle fibers and cardiomyocytes. After parabiosis, GDF11 levels in old animals went up, and it was possible that the boosted levels of GDF11 explained why the old guys were doing better. For example, we looked at activity in a population of immune cells called macrophages, which clear up the mess left after spinal cord damage. In old animals, this cleanup process was deficient. Joining to a young partner brought in a better 'clean up crew.'

We also began working with Rich Lee on a series of studies published last year, in which we showed that old hearts become younger if exposed to young blood. As animals age, hearts enlarge and become more fibrotic, and we can reverse that by joining to a young partner. Most interesting is that each of these tissues differs biologically. They serve different purposes in the body and respond to different physiological cues, yet they're all listening to this common factor. That suggests that the aging process is coordinated across body organs.

Let's go back to the study on the heart cells. Why is heart tissue significant?

Before the heart, we focused on regenerative tissues that have a capacity to repair themselves, and that capacity goes away with age. It was possible that this whole blood effect related only to tissues that turn over at some rate.

However, the heart is a non-regenerative organ. If blood-borne factors affect a non-proliferating tissue, this system could actually remodel an existing tissue, not just build a new one. The results were visually amazing—the change in size of the treated hearts was significant. That was an important step in understanding how fundamental this pathway is to the aging process. Then we focused on differ-

continued from page 6

ent levels of regulation, different regions of the brain, and different mechanisms. We started asking what might suppress activity that might build up with age, and what's lost with age that we could resupply.

Why is the parabiotic model most useful for studying blood proteins?

The parabiotic model establishes the role of blood-borne factors. We use that model because proteins in the blood have a certain half-life. Many of them are unstable, and only present for a short period of time. With the parabiotic model you have constant exposure at the proper physiological level.

We looked at protein quantity as well as patterns of protein expression and gene expression. We learned that certain categories of protein were likely to be important, and that helped us focus in probable key proteins. So, if we find something that's lost with age, such as GDF11, we can add it back to old animals. If it's something that's accumulating with age, we can put it in the young animals. Many of our studies now are focusing on that protein, although we have data that suggests other proteins may be involved.

Do you foresee the use of transfusions to accomplish the results that you've found with parabiosis?

Through transfusion, proteins may not remain consistent. That's problematic because making this protein is difficult and inefficient, and its activity in recombinant form may not be as carefully regulated as in the normal protein.

My preferred mechanism for targeting the pathway would be to learn why the protein goes away with age and how to tell the body to make more. If it's going away because the cells are dying, can we restore those cells? If the cells are just making less, can we tell them to make more? If some activity is degrading the cells, can we block that activity? This strategy is closer to the normal biology of the protein, with fewer concerns about side effects.

There's been discussion about clinical trials to study young blood transfusions in humans. What are your thoughts on that?

It's going to be several years before we see applications of this in human clinical trials because we still need to decide the best way to target this pathway. Tracking is important to identify why something did or didn't work, whether the right active substance was used, and whether the dose was actually therapeutic.

"Finding the factor responsible for aging is like finding a needle in a haystack. Tons of substances exist in the blood…It's incredibly satisfying to finally identify at least one of the active substances in the blood."

Without tracking the active substance in transfusions, they could fail to work—not because the fundamental idea is wrong, but because perhaps the donor happened to have low levels of the active protein. Mice are inbred, so they're genetically identical. The differences don't matter when you put blood from one young mouse into an old mouse, but humans have varied genetics. The variations include differences in the levels of proteins like GDF11, making it difficult to get a clean answer from the study. You'd have to be cautious about interpreting a negative result in that study.

A successful clinical trial with GDF11 would have to go through a lengthy regulatory process, even though blood and plasma are already FDA approved, correct?

People should not expect this to happen quickly. The FDA exists for a very important reason: to protect both researchers and patients. Some people feel the FDA moves too slowly and some feel it moves too quickly. We have to be somewhat patient to go through the process. At the end, having gone through all of those steps, the outcome is better and the therapy is better. To me, that's worth the wait.

I understand the attraction to blood transfers. They are FDA approved, and people are comfortable with the idea. But, when you consider the practicalities of acquisition and delivery, it doesn't scale up enough for all the people who will need it.

Do you have any clinical trials planned right now?

Before starting a trial, we have to choose the right pathway and think about the best human condition to treat. Aging is not a disease—that's not what we would want to treat. We have to think about what disease has an increased prevalence in older individuals, the availability of patients, and the character of the clinical outcomes.

Based on what you've studied so far, is there anything we can implement in terms of human therapies?

We still need time to do important investigative work. We understood the importance of this pathway only two years ago. This protein has not been extensively studied, particularly in older individuals.

All the published studies are in mice. We're now doing follow-up studies on humans looking at regulation of this protein and its role in different diseases. I'm very excited and optimistic, but it's incredibly important to do this in a careful, methodical, responsible way.

Have you observed any negative consequences in any of your experiments?

So far, no. However, we want to reveal them in the laboratory experiments and not in the trial. One question is whether this is a pro-regenerative molecule. Might it increase the progression of cancer formation?

We haven't seen anything in our experiments, but we haven't done long-term dosing, or used sensitized models where we know the animals are prone to develop tumors. Everything we've done is in normal animals. People have vastly different genetics and some will be predisposed to these sorts of things.

What are you working on right now, and what are your upcoming goals?

Beyond studying the role of this protein, GDF11, we're trying to understand what it means to say a cell is rejuvenated. Can we really turn back the clock, or do we create a sort-term pseudo-youth, until the cell starts aging again? Aging is a biological process that we do not truly understand yet. **ET**

The Emerging Tech Portfolio

Company[symbol]	Coverage Initiated	Current Price	52-week range	Mkt Cap ($mil)
INTELLECTUAL PROPERTY INCUMBENTS Leading researchers in the physical sciences, with big potential for spin-offs and revolutionary breakthroughs				
GE [GE]	8/07	$25.21	$23.41-$27.53	$253,160.00
Hewlett-Packard [HPQ]	3/02	38.39	28.75-41.10	70,160.00
IBM [IBM]	3/02	163.65	149.52-199.21	162,180.00
LIFE SCIENCES Companies that are working at the cutting edge of medical technology				
Nanosphere [NSPH]	11/07	0.29	0.22-2.62	34.43
ELECTRONICS Companies that have corralled the key intellectual property that will be the foundation for next generation electronics				
Nanosys [private]	3/02	n/a	n/a	n/a
ENERGY Companies that are developing high-efficiency, low-cost alternative energy technologies				
First Solar [FSLR]	8/07	49.02	39.18-74.84	4,910.00
ENABLING TECHNOLOGIES Tools and instrumentation that enable critical science and technology discoveries				
Veeco [VECO]	3/02	29.87	27.80-44.39	1,200.00
FEI Company [FEIC]	1/03	80.52	72.74-111.57	3,370.00
INVESTMENT VEHICLES Funds that have investments in promising emerging technology companies				
Harris & Harris Group [TINY]	5/02	3.29	2.51-3.94	99.67
PowerShares WilderHill Clean Energy [PBW]	8/07	5.43	4.75-8.02	138.19

Stock prices as of FEBRUARY 21, 2015

Word on the Street

GE: General Electric shares gained almost 5% last month as the conglomerate reported strong Q4 2014 results, with earnings rising to $5.15B (from $3.21B). Despite concerns that plunging crude oil prices would hurt the industrial giant, the 6% drop in oil and gas revenue in that sector was offset by strong performance in jet engines, power equipment and locomotives. Commenting on strong domestic demand, CEO Jeff Immelt said that the American market was "the best we've seen since the financial crisis."

HPQ: Hewlett-Packard retreated slightly from a new 52-week high, slipping less than 1% on the month. The computing giant announced that it was acquiring Voltage Security, an encryption and data-protection specialist, in order to bolster its security division, HP Atalla. Additionally, the company offered more clarity regarding leadership structure for its coming split into two independent, publicly traded companies.

IBM: Big Blue shares finished the month up 7.6% as Forbes published a report that the company was prepared to cut its workforce by 26%, affecting more than 100,000 employees. An IBM spokesman dismissed the rumor as "ridiculous" and "baseless" and clarified that layoffs would be taking place, but only a small fraction of that number. Separately, it was reported that Warren Buffett's **Berkshire Hathaway** [BRK.A] increased its stake in the IT giant by 6.5M shares. Berkshire Hathaway is IBM's largest shareholder, owning almost 77M shares. CEO Virginia Rometty is working to turn around the struggling giant, as IBM has been the worst performing stock on the Dow Jones Industrial Average for the past two years.

NSPH: In a volatile month of trading that featured a number of swings greater than 20%, Nanosphere stock finished up 4.8%. The company reported fourth quarter earnings below analyst expectations. On January 22, the company received a warning letter from the FDA due to deficiencies in the company's quality controls found at an inspection. Additionally, on January 26, both the CFO and Board Chairman announced their resignations. Nanosphere stock is down 90% over the past 12 months. While Nanosphere's technology remains unique and compelling, we will be removing the company from the portfolio, as it no longer appears to be a viable operating entity.

FSLR: First Solar broke its losing streak, gaining more than 18% on the month. **Apple** [AAPL] announced that it was investing almost $850M in the company's California Flats Solar Project in Monterey County. The 2,900-acre project will provide Apple with 130MW in a 25-year purchase agreement.

VECO: Veeco Instruments dropped 4.5%, touching on a new 52-week low. Despite beating analyst estimates for last quarter's earnings, the company issued lower earnings guidance for Q1 2015. Separately, analysts from **Stifel Nicolaus** [SF] lowered their price target on the stock from $45 to $40.

FEIC: FEI Company shares finished flat despite a strong start to the month as Q4 results missed estimates. The company announced that a strong dollar dampened revenues and will likely continue to impact profits in 2015.

TINY: Harris & Harris Group gained 4.6% on the month.

PBW: The PowerShares WilderHill Clean Energy portfolio gained almost 13% on the month due to a rebound in oil prices.

Forbes/Wolfe Emerging Tech Report
is published monthly by Forbes Media LLC and Angstrom Publishing LLC, 499 Washingtn Blvd., Jersey City 07310
Editor: Josh Wolfe Contributing Editor: Jeff Weinstein

Forbes Media LLC
Vice President/Editor, Newsletters: Matthew Schifrin
Senior Editors: John Dobosz, Tina Russo
Subscription Director: Diane Schmid

To subscribe call 1-877-733-7876 from within the U.S. or 952-646-5381 from outside the U.S.;
or visit Forbes.com Investment Newsletters
(www.forbesnewsletters.com) on the Web.

NOTE: The Forbes/Wolfe Emerging Tech Report is neither a market-timing service nor a model portfolio. Companies listed in the Emerging Tech Portfolio are early leaders in nanotechnology and, as such, should interest investors seeking to orient their portfolios toward this revolutionary technology. It does not guarantee that securities mentioned in this newsletter will produce profits or that they will equal past performance. Although all content is derived from data believed to be reliable, accuracy cannot be guaranteed. Josh Wolfe and members of the staff of the Forbes/Wolfe Emerging Tech Report may hold positions in some or all of the stocks listed. Josh Wolfe and members of Angstrom Publishing LLC may provide consulting services to some of the companies mentioned in this publication.

For editorial information, e-mail: nanotech@forbes.com