From: [redacted] <[redacted]>
To: Jeffrey Epstein <jeevacation@gmail.com>
Subject: Fwd: Trip Report: Bioscience & Philanthropy Summit (Allen Institute)
Date: Mon, 25 Sep 2017 13:33:55 +0000

Begin forwarded message:

From: Bill Gates <[redacted]>
Date: September 25, 2017 at 12:01:55 AM EDT
To: [redacted] <[redacted]>
Cc: Larry Cohen <[redacted]>, Steven Sinofsky <[redacted]>
Subject: RE: Trip Report: Bioscience & Philanthropy Summit (Allen Institute)

I agree these are exciting topics and that there is real progress.

I am confused about what the goal of this event was.

Was it to have scientists learn from each other? The range of topics was so diverse and therefore shallow enough that I doubt it would fill that role compared to the focused conferences.

Was the goal to convince philanthropists to give more? The material was too complex for that and they didn't have the right people there.

It is complicated to have philanthropists feel like they should give in an area where Paul is already funding a lot of things and most don't do science but rather specific diseases or universities.

I agree the work is exciting and that you could understand it since you are broad and know these areas but I am still not sure what would be different if they didn't do the conference.

I don't why the photos didn't come through.

From: [redacted] [mailto:[redacted]]
Sent: Saturday, September 23, 2017 11:09 AM
To: Bill Gates <[redacted]>
Cc: Larry Cohen <[redacted]>; Steven Sinofsky <[redacted]>
Subject: Trip Report: Bioscience & Philanthropy Summit (Allen Institute)

Trip Report: Bioscience & Philanthropy Summit (Allen Institute)

[redacted] co-authored this report - thought you both might enjoy hearing more about what Paul was up to in the biosciences. Let us know if docx easier.

The Allen Institute held an inaugural two day "Bioscience and Philanthropy Summit" featuring a speaker program of leading research scientists across biology, genetics, engineering, immunology, computational biology, and memory. Over 20 lecture (and q&a) sessions were offered. The stated goal of the summit was to bring together cross-disciplinary work in the spirit of "big science" to better inform philanthropic sources of funding and to offer visions for what large scale research funding could bring.

The Allen Institute is the umbrella covering several institutes created by Paul G. Allen, the co-founder of Microsoft. The institutes include Allen Institute for Brain Science, the Allen Institute for Cell Science, the Allen Institute for Artificial Intelligence (AI2), and the Frontiers Group (focusing on "out of the box" science). Each of these institutes is funded in excess of $100M with about 15% of the total coming from outside sources. In addition to advocacy and grantmaking, hundreds of scientists work full time at the institutes and collaborate with researchers worldwide.

The Institutes favor industrial scale research, open science, and work hard to incentivize a team-based approach. There is a strong focus on creating open data sets for use broadly, referred to as **C.A.P.**, complete, accurate, & permanent. An example of this is the human brain atlas which is a huge dataset encompassing imaging, genetics, histology and more.

Attendees spanned a wide range of academic and industrial sciences, some as speakers and others as guests. In addition, there were many involved in various areas of practical application of science (doctors, corporate) as well as a cross-section of investors and philanthropists who fund science. The attendees were carefully researched and specifically invited. The speaker program was curated by the executives of the Allen Institute.

It would be an understatement to call this first summit a great success at a fantastic forum. Throughout the summit attendees were freely sharing a feeling of excitement and energy around the gathering. The evening gatherings were packed, energized, on topic, and went quite late. There was a freshness to the approach and a desire to continue sharing across this unique audience. It was special to be at something that you hope continues *and* to be invited back to!

Takeaways.

Given the wide range of topics covered, it would be difficult to settle on key takeaways but these represent some of the major points:

- ***21st century biology is like 20th century physics.*** This was a meme throughout all the talks and was used by Paul to frame the summit. The idea is that biology is now developing underlying models and understanding that will make for compounding discoveries the way that theories of physics (and chemistry) in the early 20th century drove the rapid rise in understanding of the physical world and subsequent innovations. And, while chemistry dominated the industrial life sciences in the 20th century, there will be greater convergence between biology and the physical sciences in coming decades: less pharma more physics and computation.
- **Sequencing dividend.** The dividend from sequencing and now CRISPR/Cas9 is paying off in ever-increasing ways across more and more domains. With the economics approaching commodity research levels, there's no aspect of bioscience that will go untouched by sequencing.
- **Stem cells.** Stem cells have been exciting for years and at the same time the major breakthroughs is understanding and use are yet to come. The deepening understanding of how they function and the underlying mechanisms are contributing to rapid increases in moving from research to reliable therapies.

• **Microbiome**. Many researchers seem to point at the microbiome as either a present or future direction for their investigation. It isn't understood how often the biome is a causal or correlated factor relative to findings but the presence cannot be denied and thus the interest continues.
• **Cross-over science.** Increasing collaboration has led to knowledge sharing across traditional disciplines: immunologic approaches are being applied to neuroscience, vaccine techniques are finding relevance for preventing chronic (vascular) disease, lessons from bleached ocean coral are driving a deeper understanding of climate science, etc.

Talk Highlights.

Over the two days there were a variety of lectures, interviews, rapid fire sessions, innovative snapshots and deep dives. During this event, scientists were asked to use the last few minutes of their respective presentations to propose similar large scale projects and spending outlines, which ranged from millions to billions of dollars. The most interesting, without the price tags:

Reversing Aging to Improve Brain Function, Tony Wyss-Coray, Stanford

While there is no known fountain of youth (only known to Melanie), *parabiosis* or the effect of sharing components of "young" blood with aged tissues appears to return levels of youthfulness in function. Starting from what we know, which is as you age cells themselves age and many diseases (or just aging) are the product of this aging. Experiments have shown that in mice the introduction of youthful cord plasma significantly improves the learning capability of mice (lots of cool tests with mice and mazes, where the young mice zip through the old mice just sit there until they are treated with plasma). There is interesting work on the cellular communication pathways enabling this parabiosis, specifically how it is related to the microbiome and whether the youthful cells also influence the microbiome or the rejuvenation capability. Across a large population cohort ranging in age from 20-106 years, about a dozen proteins have been identified that change in character and are being proposed to act as biomarkers for the aging process. These markers influence neural stems cells, synaptic activity and attenuate inflammation.

Reverse-Engineering the Brain—Mysteries of Human Memory, Susumu Tonegawa, MIT (Nobel Laureate)

This talk was amazing. Tonegawa won the 1987 Nobel Prize for his discovery of how the body creates diversity of antibodies. He's since applied his research to working to understand how memory works.

For decades there have been research theories on how the brain creates and retrieves memories. Only recently with cellular imaging and DNA research has it been possible to assign plausibility to the *engram* model, wherein certain neurons encode information from an "episode" and undergo some cellular changes to store the episode which is than "activated" at some later date. This discovery has led to the idea of creating "false" memories in mice (sort of a *Total Recall* for mice). In one experiment the ability for a mouse to remember an event (the presence of a blue light). The engrams are recorded chemically in transgenic mice and then implanted in a transgenic mouse. This mouse, with the blue box memory, is then shown a red light while simultaneously shocking their little feet thus training the mouse on red light and shocked feet while "remembering" a blue light. The mouse is then shown a blue light and suddenly stops moving for fear of a shock even though it never actually experienced a blue light and shock, but it had a fake memory of such. *CRAZY!* This talk raised some very interesting questions about the evolutionary nature of false memory and whether some aspects of "genius" or "vision" are actually the ability to create *a priori* false memories. The "reality distortion field" seems closely related to this.

Immune Cells that Re-wire the Brain—Beth Stevens, Boston Children's/Harvard Medical School
At the neuron level it is well-known that synapses are created when we are young, then slowly the number of synapses decline. Synapse loss is the strongest correlate of cognitive decline in Alzheimer's (a disease that cannot be diagnosed or treated). This research is beginning to show that cells of the neuro-immune system, known as microglia, are responsible for the re-wiring of synapses as the brain develops (and then ages). This research has the first imaging at the cellular level showing these microglia actually "gobbling" up synapses. The question for future research is how to further understand the function of the cells and process which could lead to a treatment for cognitive decline.

Computer Modeling of Biology for a Longer Healthy Lifespan—Cracking the Morphogenetic Code, Michael Levin, Tufts
Do you remember that scene in *Starship Troopers* when wounds are repaired by some sort of cell regeneration apparatus? Well that's what this research is about, but it starts with trying to figure out how and when cells decide to change shape. Physiology trumps genetics. We all start from one cell but there is an unknown mechanism that causes cells to change from one cell type to another. If this mechanism could be understood then it should be possible to regenerate cells as though they were generated the first time, replacing tissue, organs, and limbs. The role of electrical currents, bioelectricity, in morphogenetics is not well-understood but clearly has a role and can have greater impact on form and function than altering genetic code. To demonstrate this idea, flatworms were used because much is already known of their geno- and phenotypic profiles. Flatworms can be cut into many pieces across any plane and subsequently regrow back to healthy, normal worms. It is thought that bioelectric signal "memory" causes the cells at the edge of the cut to grow back as the appropriate cell type. What if those signals could be "programmed"? To show this, the signals are measured and then played back in a modified manner – after the worm has been sectioned. The result is a worm that grows back as a two headed organism rather than one with a head and a tail. The CRAZY thing about this worm is that it looks like a mutant but is genetically identical to a normal worm because only the bioelectrics were changed – no genes. This has been replicated in frogs now enabling frogs to grow back legs (which absolutely doesn't happen in nature). The implications for creating organisms that look like mutations *but aren't* mutations is pretty intense. The role of computer modeling is to develop tools through machine learning that could help to combine DNA and bioelectrics to create specific cells "on demand" almost a Visio for organisms or "algorithm for life".

A Molecular Tricorder for Reading Biology, David Issadore, University of Pennsylvania
The peace dividend from mobile phones is paying off significantly in this research. The minimization of commoditization of incredibly small sensors (and the ability to build and iterate on sensors) are key parts of this research. Exosomes float around in our blood and importantly appear to be involved in communicating from cell-to-cell when something extraordinary happens. They are known to increase in volume around tumors or injury, but sensing them and diagnosing conditions from them has proven elusive. If one could identify the specifics of exosomes there would be an opportunity for much earlier diagnosis of fatal conditions (such as awful cancers). Similarly, in the event of an injury it would be very helpful to be able to rapidly diagnose the severity of an injury, such as a concussion. This research develops "chip diagnostics" which are silicon surface areas programmed to detect certain biomarkers. It does this by using protein signatures which can be matched via machine learning. The amazing thing about these chips is that they are actually thousands of sensors operating in parallel as they try to pick out the presence or absence of a protein based on a signature that cannot

be matched exactly (the blood flow is too fast and too voluminous for the complexity of the protein). It is known that exosomes in mice appear at the time of traumatic brain injury and have different exosomes depending on severity of the TBI. This research has developed a mobile device that can be used to determine TBI in mice and the next step is to build up a model for humans. The longer term goal of this research – among others – would be to identify a disease such as pancreatic cancer when it is early stage enough for treatment knowing that at the earliest stages the tumors cause exosomes to be emitted.

Designer Proteins for Curing Disease, David Baker, Univeristy of Washington

The history of drug design in the 20th century has been to develop therapeutics by finding naturally occurring proteins and synthesizing them for drug use and perhaps modifying them slightly to improve treatment or reduce toxicity. Beyond that the ability to create entirely new proteins is limited by the lack of understanding of protein folding—the 3D aspect of proteins combined with the amino acid sequence that makes them unique. This research starts with an idea for a protein, creates a gene that makes that protein and then implants that gene to cause it to be produced (**Steven: *"what could possibly go wrong*!?"**). Some examples of his work include influenza binders and RSV protein nanocages – with dozens more examples in other industrial sciences.

Food for Thought.

- **Micrologia monitoring.** Building from the fact that astrocytes are electrically silent but incredibly active, scientist Bhaljit Khank from UCLA is growing wearable mini microscopes to track their activity.
- **Hippocampal prosthetics.** Ted Berger from USC has identified a unique neural circuit and implanting new memory codes into a hippocampal prosthesis.
- **Tools for visualization of *In Vivo* architecture.** Biophysicist Elizabeth Villa from UCSD showcased her novel technology, cryo-electron tomography that allows imaging of truly *in vivo* and fully living tissues within their natural environment.
- **Beating cancer.** Irv Weissman from Stanford revisited the theory behind stem cell usage and proposed new applications and sources other than mobilized blood.

Scientists ~~can be~~ are fun.

Below we can see Nobel Prize winner Susumu Tonegawa using emoji to explain implanting false memories in mice. Beth Stevens of Harvard Medical School using Pac-Man to describe using immune cells to rewire the brain. And David Issadore of Univ of Pennsylvania with his lab mouse wearing a helmet as he studies the physiology of injury.