HUMAN LONGEVITY

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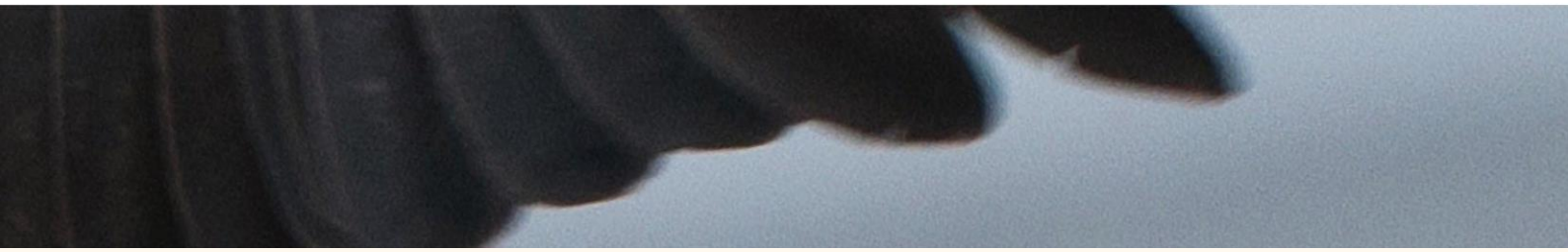


CONTENTS

ABSTRACT

At KIS Capital we try to keep ourselves at the forefront of technology and innovation, attempting to identify which industries may blossom, and which may be disrupted. In the middle of 2016, KIS Research published its in-depth report on Autonomous Vehicles. That paper proved to be well ahead of the curve, with autonomous cars and electric vehicles becoming an important investment theme over the last year. To follow up the success of that report, we have released this one, focusing on a new topic: human longevity. We see human longevity as a huge new investment theme. Whilst its impact on the healthcare system alone will be enormous, we expect its ripples to extend further, washing into the broader economy. Human longevity will create a more productive working age population, extend the retirement age, create new consumer spending patterns amongst the elderly, cause a revamp of the superannuation system, increase unfunded pension liabilities, change life and health insurance premiums, and even alter the way in which fiscal policy is managed, to name a few. In this report we will explore the burgeoning technologies that are seeking to extend healthy life well north of 100 years.

Be sure to use the contents page to skip around and find the sections that most interest you (NB: there is a section on life hacks that you can be doing today to increase your longevity). ***If this investment theme is of further interest to you, get in touch with us!***

COULD YOU REALLY LIVE FOREVER?

The quest for eternal life is by no means a new one. From religious scripture through to folktales and science-fiction, stories of immortality permeate our culture. It seems the notion of living forever has always been an alluring one. Indeed, one could scan the headlines of a newspaper from any year in the last hundred, and find at least one that professed to have found the elixir of life. So, are we finally on the verge of a true scientific breakthrough, or is the idea of significant life extension destined to remain within the realms of fiction? These are the questions we hope to answer, or at the very least, to examine.

Today's scientific advancements are more promising than ever. A convergence of the burgeoning fields of genomics and artificial intelligence proposes new boundaries for the limits of biological discovery. **Never before has such an elementary understanding of the human genome been within our grasp.** With the invention of the CRISPR-cas9 gene-editing technology we can now become the authors of our own evolution. If the genome is mankind's manual, then CRISPR-cas9 is the pen with which to write new chapters. New studies into stem cells suggest that they may hold the key to biological rejuvenation, proposing that one day your treatment may be a cell, rather than a pill.[1]

These advancements give us hope of reaching what biologist Aubrey de Grey describes as 'longevity escape velocity', the point at which life expectancy continues to increase at a rate faster than time passes by. But it's not just about extending life span, but also about extending healthspan; extending the period of healthy life that is free from chronic and debilitating disease. **How big is the market? According to Credit Suisse, the richest one percent of the world's population now owns more than half of its wealth. That is over $140 trillion in the hands of 75 million people, and they can't take it with them![2]**

SHIFTING THE PARADIGM

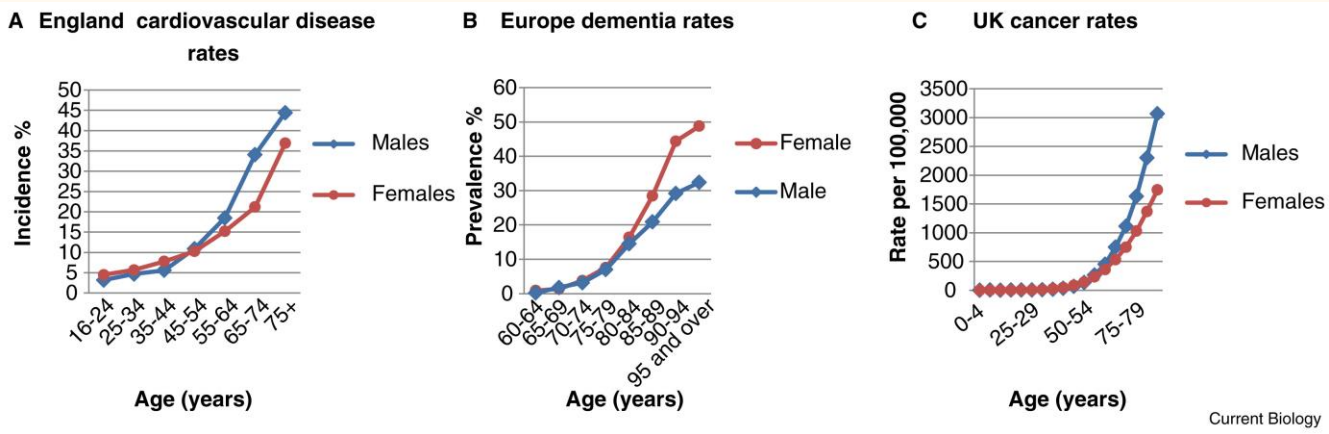
With Alexander Fleming's discovery of penicillin the Antibiotic Revolution was born. Since that day, Western medicine has followed a symptomatic approach; a person shows symptoms for an illness, they are diagnosed, and medicine is prescribed. It is reactionary by its very nature – we wait for an illness to materialise and we take pills to kill whatever it is that ails us.[3] For us denizens of the macroscopic world this model makes sense.[4] But with a newfound understanding of the process of ageing, it seems we are finally ready to break free from the shackles of this archaic paradigm. We are

[1] Mukherjee, S. 2015, *'Soon we'll cure diseases with a cell, not a pill'*, TED Talk
[2] Frank, R. 2017, 'Richest 1% now owns half the world's wealth', *CNBC*, 14 November
[3] Mukherjee, S. 2015, *'Soon we'll cure diseases with a cell, not a pill'*, TED Talk
[4] Dawkins, R. 2005, *'Why the universe seems so strange'*, TED Talk

finally at the onset of a paradigm shift that takes us from a symptomatic approach, towards a preventative one.

Age is the major risk factor in the development of the diseases that plague the developed world; cancer, cardiovascular disease and neurodegeneration.[5] As such, rather than attempting to treat and cure these diseases individually, perhaps a more holistic approach is required; one that targets ageing as a treatable illness, and in turn, helps to delay the onset of these diseases entirely. This isn't as outlandish as it might seem. **Scientist Andrzej Bartke extended the life of a mouse from two to five years by editing genes responsible for insulin production. That is the equivalent of living to be 170 in human years.**[6] Whilst humans are not mice, it is not unreasonable to believe that if a mouse could live to be five, a human could live to be 170. If more research was focused towards delaying the onset of ageing there could be real progress made.

Compare the quantum of research invested in cancer versus that in ageing: the total number of drugs trialled by the National Cancer Institute to cure cancer in mice exceeds 100,000. The total number of drugs trialled by the National Institute of Ageing to treat ageing in mice, numbers just thirty. Even with just thirty trials there has already been one success, rapamycin.[7] **Typically used to prevent organ transplant rejection, rapamycin has been shown to increase the immune response of elderly patients by around 20 percent.**[8] Other drugs have exhibited similar phenomena.



Correlation between age and incidence of disease (Niccoli, T. and Partridge, L. 2012)

[5] Niccoli, T. and Partridge, L. 2012, 'Ageing as a risk factor for disease', *Current Biology*
[6] Smith, G. 2005, *The genomics age: how DNA technology is transforming the way we live and who we are*, AMACOM, New York,
[7] *The science of extending life*, 2017, audio podcast, a16z podcast, 17 April
[8] Keown, A. 2015, 'Novartis AG may already have first true anti-aging drug in its pipeline', BioSpace, 19 February

WHY DO WE AGE?

[Watch Elizabeth Blackburn's TED Talk on the Science of Cells That Never Get Old]

At first glance, ageing is a curious notion. From an evolutionary standpoint it seems counterintuitive. After all, if an organism survives for longer, should that not mean that it has more time to reproduce and pass on its genes? The Medawar theory of ageing provides for this, suggesting that ageing may be a by-product of otherwise 'good' genes that activates late in an organism's lifespan, and thus, is a net beneficiary to the organism's chance of reproduction.[9]

At a biological level, the process of ageing involves the over-shortening of telomeres as cells divide. This leads to an accumulation of mutations in the cells' DNA and ultimately cellular dysfunction. Telomeres are a segment of non-functioning DNA that protects the end of chromosomes during the process of division. During division, not all the DNA can be copied, so telomeres create a buffer that means no important strands of DNA are lost. **As Elizabeth Blackburn describes them, telomeres 'are like the protective caps at the end of your shoelace; they keep the shoelace (or the chromosome) from fraying.'[10]** As we age and our cells continue to divide, the length of our telomeres shorten. When telomeres over-shorten it leads to cellular senescence and the accumulation of genetic mutations. In a study that won her the Nobel Prize, Blackburn discovered an enzyme called telomerase. This enzyme was particularly active in a unicellular organism named tetrahymena. Tetrahymenas' telomeres do not shorten over time, making the organism effectively immortal. This was because the telomerase enzyme was constantly working to repair and increase the length of the organism's telomeres.

So why not just use telomerase to increase the length telomeres in human cells? Well unfortunately it's not that simple. Telomerase is active in some cells in the human body, but to varying degrees. Cells like hair follicles, stem cells and germ cells all have active telomerase. But telomerase is also active in cancer cells, which is the reason for their unfettered and unregulated growth. According to Blackburn, we live on the balance of a knife-edge; whilst it is true that increasing telomerase would decrease the risk of certain age-related diseases, it would also simultaneously increase the risks of certain cancers.[11]

Some researchers have not given up hope though. Listed player Geron Corp (NASDAQ: GERN) is a biopharmaceutical company whose telomerase inhibitor is currently undergoing clinical trials. Private company BioViva is looking to use gene therapy to alter the lengths of telomeres. The company's founder, Elizabeth Parrish, has gone so far as to inject herself with a modified version of a telomere extension therapy used to increase the lifespan of mice by forty percent.[12]

[9] Dawkins, R. 1976, *The selfish gene*, Oxford University Press, Oxford
[10] Blackburn, E. 2017, *'The science of cells that never get old'*, TED Talk
[11] Blackburn, E. 2017, *'The science of cells that never get old'*, TED Talk
[12] 13D Research 2017, *What I learned this week: January 19, 2017*

WHAT IS A GENOME?

[Watch Riccardo Sabatini's TED Talk on the Human Genome]

A genome is an organism's blueprint. It is the set of instructions passed on by a parent to their offspring, generation through generation, which determines all manner of an individual's physical and non-physical features. Genomes are written in the language of chemical compounds called bases. There are four bases – A, G, C and T – arranged in pairs to form the familiar double helix DNA structure. **In the human genome, there are approximately three billion of these base pairs. If transcribed letter-by-letter, the genome would span 262,000 pages and its volumes weigh over 450 kilograms!**[13] The vast majority of the human genome is common amongst all people; it is only in 500 pages that the uniqueness of a person is written.

Before discussing further, an important distinction must be made between genetics and genomics. Genetics is the study of hereditary traits that pass from parents to their offspring through genes, or sections of DNA. There are approximately 20,000 to 25,000 genes in the human genome. This is separate from the study on genomics, which is the branch of science concerned with the mapping, structure and function of genomes. Genomics takes a more holistic approach, analysing the variation in whole genomes, rather than just individual genes. Gene sequencing refers to the process of mapping a genome. This is an extremely complicated process, with the first human genome being sequenced just fourteen years ago. As such, the field of genomics is still in its infancy.

With each passing day, advancements in sequencing technology and computational biology are shedding greater light on the structure and functionality of the genome. By enriching our understanding of the genetic basis of certain diseases we can begin to open up new avenues of therapy, develop new techniques for early detection, and determine those individuals most at risk given their genetic profile. For certain diseases early detection may be the most important factor in increasing survival rates.

For instance, we know that one in eight women in the U.S. will develop breast cancer at some point in their life. However, for those women with the mutated BRCA1 gene, the probability of developing breast cancer increases to between 70 and 80 percent.[14] This is critical information, especially when viewed through the lens of early detection and survival rates. **The five year survival rate for women diagnosed with breast cancer at Stage II is 90 percent. For those diagnosed at Stage IV, the survival rate falls to just 15 percent.**[15] This correlation between early detection and survivability holds true for virtually all forms of cancer.

Biotech Track chair Robert McCauley predicts that by 2020, DNA sequencing will allow us to detect thirty different types of cancer in a single drop of blood.

[13] Sabatini, R. 2016, *'How to read the genome and build a human being'*, TED Talk
[14] Mukherjee, S. 2016, *The gene: an intimate history*, pp.1004-5
[15] Cancer Research UK 2015, *Why is early diagnosis important?*,

These cancers will be detectable at Stage 0, when the tumour is no larger than the head of a pin.[16] With a truer understanding of the human genome and the genetic variants responsible for diseases, we could vastly improve the detectability of all diseases, not just cancer. As alluring as this sounds, it does beg the question, why now?

THE LAYERS OF SEQUENCING

On a commercial level, genome sequencing can be separated into two layers; the sequencing layer, and the application layer. The sequencing layer refers to the physical hardware component: the machines that do the actual sequencing. **This segment is dominated by one player, Illumina (NASDAQ: ILMN), with an incredible 90 percent market share!**[17] The application layer refers to software used to process and interpret the enormous amounts of data that is generated. This layer uses computational techniques like machine learning to give clinical diagnoses.

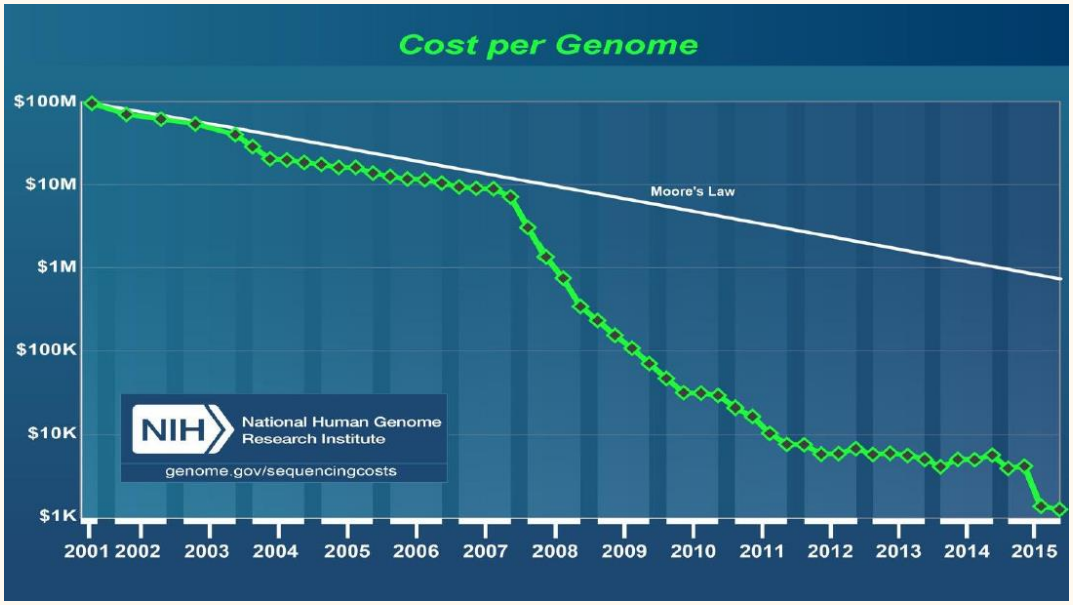
A useful analogy can be drawn here to the hardware and software layer in the computer industry. At the burgeoning of the personal computer, these two layers and the companies that produced them, shared a symbiotic relationship. The hardware layer was the platform on which the software was created, and the software layer provided much need functionality to the hardware layer. Without Microsoft's operating system and the utility it added to personal computers, IBM would struggle to saturate the market. Yet, if the market doesn't take up personal computers, Microsoft isn't incentivised to create its operating system in the first place. This is a sort chicken and egg scenario of incentives; one that the gene sequencing industry is yet to overcome. So, is there any reason to suggest this is about to change?

GETTING YOUR GENOME SEQUENCED FOR THE PRICE OF A PIZZA DELIVERY

The first human genome was sequenced as part of the Human Genome Project back in 2003 and cost over US$3 billion. Since then, breakthroughs in sequencing technology have allowed significant progress to be made, both in reducing costs, and in the time taken to sequence a genome. Earlier this year Illumina (NASDAQ: ILMN) unveiled their new sequencer, the NovaSeq, which is set to reduce the cost of sequencing an entire human genome to as little as US$100.[18] This is a truly astonishing rate of decrease.

[16] 13D Research 2017, *What I learned this week: August 10, 2017*
[17] Zhang, S. 2016, 'Illumina, the google of genetic testing, has plans for world domination', *Wired*, 26 February
[18] Buhr, S. 2017, 'Illumina wants to sequence your whole genome for $100', *TechCrunch*, 10 January

According to TechCrunch, the machines are set to cost around US$900,000, with the Chan Zuckerberg BioHub, the Broad Institute of MIT and Harvard, and Human Longevity Inc. all signing up to order a machine.[19] **The chair of Biotech, Track Raymond McCauley, argues that this rate of decline is set to continue, with sequencing costs declining to the cost of 'one pizza delivery' by 2018, and to as low as one cent by 2022!**[20]



The decreasing cost of sequencing a genome (National Human Genome Research Institute, 2016)

The time taken to sequence a genome has also decreased drastically. The initial Human Genome Project spanned a total of thirteen years. Processes like DNA alignment, which used to take several days, can now be done in as little as five minutes. **Illumina's NovaSeq sequencer can reportedly sequence an entire human genome in less than one hour!**[21]

Both of these advancements are critical to bringing whole genome sequencing into mainstream medical practice, but there is still one more issue; without any useful diagnoses or analysis of my genome, why should I bother getting it sequenced?

DATA AND THE APPLICATION LAYER

Since the birth of genetics with Mendel and his peas, significant progress has been made in deciphering the human genome. But our brains have their limitations. Millions of years of evolution have shaped us to interact with the macroscopic world, and thus it is

[19] Buhr, S. 2017, 'Illumina wants to sequence your whole genome for $100', *TechCrunch*, 10 January
[20] 13D Research 2017, *What I learned this week: August 10, 2017*
[21] Buhr, S. 2017, 'Illumina wants to sequence your whole genome for $100', *TechCrunch*, 10 January

that world that we understand best. **As Richard Dawkins describes, 'we are evolved denizens of Middle World, and that limits what we are capable of imagining.'**[22]

The traditional approach to genetic analysis was one of point-mutation: studying a single gene mutation that is responsible for a certain disease. Whilst this analysis is sufficient in monogenic diseases like Huntington's, the majority of diseases have more subtle causal roots. This requires a more systemic or holistic approach. **There are over three billion base pairs in the human genome that combine to create 20,000 to 25,000 genes. For some perspective, the entirety of Google's internet services span just two billion lines of code** (Click here for a cool visualisation of the level of coding that has gone into different technologies).[23] Any attempt to understand the various interactions of these genes and their phenotypes presents the challenge of immense data analysis. The computational complexity of this task far exceeds the capability of traditional computing techniques. This has led to the new field of computational biology; a midpoint between traditional single-point analysis and generalised machine learning.

This is why the decreasing cost of genome sequencing is so important. The complexity of genomic data warrants an extremely large sample size for any meaningful interpretation of cause and effect. For certain diseases, "big data" may be a dataset in the millions. **This means that each new genome added to the dataset, along with that individual's phenotypes, enriches analysis not only of future genomes sequenced, but of those held on record also.**

What is machine learning?

Most simply, machine learning involves the exposure of an algorithm to an annotated dataset that it can make predictions against and learn from. The larger the dataset that is fed to the algorithm, the better it can become at its intended purpose. Data is the essential factor in this equation. Big data simply refers to the quantum of data required for an algorithm to learn a specific topic. As described by Christopher Nguyen, co-founder of Adatao, ***'big data is to machine learning as life experience is to human learning'****. As a general rule, the more complex the task, the larger the dataset required.*

As discussed in the previous paragraph, the cost of genome sequencing is reaching an inflection point at which the widespread use of sequencers can take place. **It seems the quantum of data essential for machine learning analysis will soon be within our grasp.**

[22] Dawkins, R. 2005, *'Why the universe seems so strange'*, TED Talk
[23] Desjardins, J. 2017, 'How many millions of lines of code does it take?', *Visual Capitalist*, 8 February

GENE THERAPY: AUTHORING OUR EVOLUTION

> *"Early hopes are always frustrated by the many incremental steps necessary to produce 'success'. Gene therapy will succeed with time.* ***And it is important that it does succeed, because no other area of medicine holds as much promise for providing cures for the many devastating diseases that now ravage humankind.****"*
>
> French Anderson, Gene Therapy: The Best of Times, The Worst of Times

> *"Probably no DNA science is at once as hopeful, controversial, hyped, and even as potentially dangerous as the discipline known as gene therapy."*
>
> Gina Smith, The Genomics Age

If genomes are the manuals of organisms, and with the help of machine learning we can begin to read those manuals, could we also learn to write new chapters? Virtually all diseases that afflict mankind have at least some basis in genes. If we could somehow rewrite or delete the related genetic code, could we in turn erase or cure those diseases? This is the controversial world of gene therapy.

Gene therapy involves the therapeutic delivery of modified DNA into a patient's cells, commonly using some form of viral vector. A virus survives by invading foreign cells and inserting its own viral DNA into that cell. These foreign interlopers are cell specific too, meaning that a certain type of virus will only infect a certain type of cell, be it a brain or lung or blood cell. These two traits make them the perfect vector for gene therapy, allowing for edits to the genome of a targeted cell type.

Since its origins in the late 60s and early 70s, gene therapy has had a tumultuous history, one marked by extraordinary peaks and devastating troughs. In 1990, Ashanti DeSilva, then suffering from the "bubble boy" disease SCIDS, was treated with modified DNA to became the first person cured by gene therapy. Just nine years later, DNA introduced into Jesse Gelsinger in an attempt to cure his chronic liver disease resulted in his death, marking a low point for the field.[24]

Gene therapy falls under two categories; germline (those edits to DNA that will be passed on through generations) and somatic (those edits that won't be passed on). **A germline edit, say the removal of a specific gene in an embryo related to cardiovascular disease, would not only result in that individual being immune to the disease, but also the immunity of their offspring, and their offspring's**

[24] Mukherjee, S. 2016, *The gene: an intimate history*, Bodley Head, London, UK, pp. 940-86

offspring, and so forth. This would make mankind truly the author of his evolution, whether or not those writings be constructive or dysgenic.

The commercial world of gene therapy is an active one. Here are some of the field's leading companies:

- **Amgen (NASDAQ: AMGN)**, one of the world's largest biotech companies, recently invested over $55 million in Arrowhead Pharmaceuticals to partner in the development of a gene therapy that silences genes related to heart disease.[25]

- **Sangamo Therapeutics (NASDAQ: SGMO)** focuses on the development of gene therapies and medicines for genetic diseases. Candidates include haemophilia, HIV/AIDS, blood disorders and Alzheimer's.

- **Alnylam Pharmaceuticals (NASDAQ: ALNY)**, one of the world's leaders in RNAi therapeutics, recently reported the first ever positive Phase 3 results for an RNAi therapeutic, meeting both its primary efficacy endpoint as well as all secondary endpoints.[26]

- **Ionis Pharmaceuticals (NASDAQ: IONS)** has completed enrolment for its Huntington's therapy which targets the protein produced by the mutant gene. Ionis is a leading biopharmaceutical company specialising in RNA-targeted drug discovery and development.[27]

- **Biogen Inc's (NASDAQ: BIIB)** cell and gene therapy division recently collaborated with **Applied Genetic Technologies Corp (NASDAQ: AGTC)** to target a retinal disease associated with the RS1 gene.[28]

- **Intrexon (NYSE: XON)** is a synthetic biology company that provides a range of off-the-shelf gene editing technologies. Intrexon recently acquired GenVec, a company which owns a portfolio of proprietary adenovirus vectors for gene delivery.[29]

[25] Grover, N. 2016, 'Amgen, Arrowhead team up on gene-therapies for heart disease', Reuters, 29 September
[26] N/A, 2017, 'Alnylam and Sanofi report positive topline results from APOLLO phase 3 study of patisiran in hereditary ATTR (hATTR) amyloidosis patients with polyneuropathy', Business Wire, 20 September
[27] Henriques, C. 2017, 'Ionis completes patient enrolment in phase 1/2a trial of Ionis-HTTRx for Huntington's disease', *Huntington's Disease News*, 27 June
[28] N/A, 2017, 'AGTC announces topline safety data for x-linked retinoschisis phase ½ study', *Globe News Wire*, 8 June
[29] N/A, 2017, 'Intrexon to acquire GenVec to expand industry-leading gene delivery platform', *PR Newswire*, 24 January

CRISPR-cas9 – FINDING THE RIGHT PEN

"We can now 'read' human genomes, and we can 'write' human genomes in a manner inconceivable just three or four years ago."

Siddhartha Mukherjee, The Gene

In 2012, Jennifer Doudna and Emmanuelle Charpentier published a study on a microbial defence system that has proven to be a watershed moment for the field of gene therapy. The landmark study centred on a type of defence mechanism used by bacteria against viruses. The bacteria were using the pieces of viral DNA, inserted by the viruses themselves, as a sort of 'genetic vaccination card', transcribing that viral DNA into new RNA molecules. [30]

What is RNA?

RNA is a copy of non-coding DNA that acts as an intermediary between the cell and the genetic information encoded within its nucleus. An enzyme within the cell's nucleus transcribes pieces of DNA into new strands of RNA. These stands of RNA then leave the nucleus and interact in a variety of ways to help the cell create proteins.

The RNA molecule, with its viral coding, combines with a protein called cas9. This protein is the part of the technology that does the actual gene editing, working as a 'molecular scalpel' to cut the targeted DNA.[31] The viral RNA guides the cas9 protein along the genome, acting as a sort of primer, sampling candidates as it goes along, eventually finding its match in the viral DNA. Once found, the cas9 protein can work its magic, cutting and destroying the virus.

This CRISPR-cas9 microbial defence system has another useful trait; it can be reconditioned to deliver extremely accurate edits to other organism's genomes, even including our own. Since its discovery, CRISPR-cas9 has become the technology of choice for gene-editors due to its unprecedented accuracy, speed and ease of use. **The technology is so accurate that it allows for edits down to a single nucleotide. As Mukherjee describes, 'this technology might be likened to a copyediting device that scans sixty-six volumes of the Encyclopaedia Britannica and finds, erases, and changes one word, leaving all other words untouched.'**[32]

Significant progress has been made in attempting to make somatic gene therapy in a clinical setting a reality. **Recently, CRISPR-cas9 has been used to regulate the growth of cancer cells by targeting a certain protein, remove HIV from living organisms, and modify mosquitoes which could potentially lead to the eradication of the Zika virus and malaria.**[33] To overcome some of the current limitations, research has focused on diseases where the tissue can be temporarily removed from the body. Blood disorders like sickle-cell anaemia or thalassemia are particularly amenable to this process due to the ease of removing and returning blood

[30] *Humanity 2.0*, 2017, audio podcast, Waking Up with Sam Harris, 28 November
[31] *Humanity 2.0*, 2017, audio podcast, Waking Up with Sam Harris, 28 November
[32] Mukherjee, S. 2016, *The gene: an intimate history*, Bodley Head, London, UK, pp. 1106
[33] 13D Research 2017, *What I learned this week: August 10, 2017*

to the body.[34] CRISPR Therapeutics (NASDAQ: CRSP), a company founded by CRISPR-cas9 co-inventor Emmanuelle Charpentier, is set to enter the first clinical trial of its cure for thalassemia in early 2018.[35] **CRISPR Therapeutics has also formed a joint venture with Bayer AG, one of the world's largest pharmaceutical and life sciences companies, to discover, develop and commercialise new therapeutics in an attempt to cure blood disorders, blindness, and congenital heart disease.**[36]

The CRISPR-cas9 technology itself is constantly being updated to improve its efficacy, with new iterations arriving almost every week. Recently, scientists at the Salk Institute have altered the technology to modify the expression of disease-causing genes, rather than actually editing their underlying sequence. This process should help to reduce the risk of off-target mutations and side effects related to cellular repair. The scientists used this technique on mice suffering from acute kidney disease, repairing the function of damaged genes to restore normal kidney function and reverse the progress of the disease entirely.[37]

Some of the leading companies utilising the CRISPR-cas9 technology:

- **CRISPR Therapeutics (NASDAQ: CRSP)**, a company founded by Emmanuelle Charpentier who was one of the co-inventors of the CRISPR-cas9 technology. CRISPR Therapeutics have several gene therapy treatments in the pipeline, particularly focusing around blood disorders.

- **Intellia Therapeutics (NASDAQ: NTLA)**, co-founded by the other co-inventor of CRISPR-cas9 Jennifer Doudna, have a range of in-vivo and ex-vivo programs aimed at curing disease.

- **Editas Medicine (NASDAQ: EDIT)** is a discovery phase pharmaceutical company. Its diverse pipeline includes programs targeting cancer, sickle cell, muscular dystrophy, and eye diseases.

[34] *Humanity 2.0*, 2017, audio podcast, Waking Up with Sam Harris, 28 November
[35] Molteni, M. 2017, 'CRISPR Therapeutics plans its first clinical trial for genetic disease', *Wired*, 11 December
[36] Bayer Press, 2016, Bayer and CRISPR Therapeutics joint venture, named Casebia Therapeutics, establishes operations in Cambridge, MA, *Bayer AG*, 19 August
[37] Cell Press, 2017, 'CRISPR-Cas9 technique targeting epigenetics reverses disease in mice', *ScienceDaily*, 7 December

STEM CELLS: THE ULTIMATE RESERVOIR OF REGENERATION

[Watch Robert Hariri's TED Talk on Stem Cells]

> *"A stem cell is somewhat akin to a grandfather that continues to produce children, grandchildren, and great-grandchildren, generation upon generation, without ever losing his own reproductive fecundity.* ***It is the ultimate reservoir of regeneration for a tissue or an organ.****"*
>
> Siddhartha Mukherjee, The Gene

One of the more remarkable examples of biological engineering is the phenomenon of scarless foetal surgery. Foetuses can often develop complications within the womb, ranging from cosmetic through to life-threatening. One of the most common congenital disorders is the development of a cleft lip and palate. According to the CDC, one in every 940 babies born in the United States will develop some form of cleft lip and palate.[38] Babies with this disorder can experience trouble feeding, speaking clearly, and are more prone to developing ear infections. If the particular case is serious enough, in utero surgical intervention may be required. The foetus is removed from the mother, operated on, and returned to the womb. The fascinating part of this, is that the markers of such an intervention can no longer been seen at birth.[39] **The foetus has completely regenerated the tissue, without even a scar left to trace the incident. An entirely scarless surgery.**[40]

The same phenomena is seen in the pre-implantation genetic diagnosis conducted during IVF, where cells are removed from the embryo for genetic testing. At this stage, the embryo consists of only a handful of cells and yet, miraculously, it can completely rejuvenate itself. **As Mukherjee writes, "for a moment in our history, we are actually quite like salamanders or, rather, like salamanders' tails – capable of complete regeneration even after being cut by a forth."**[41] One of the leading explanations for this phenomenon is the abundance in the foetus of regenerative cells called stem cells, or, more specifically, embryonic stem cells. Many scientists believe that these cells could be applied in a clinical setting, potentially sustaining healthy life and vitality well into a person's 90s.[42]

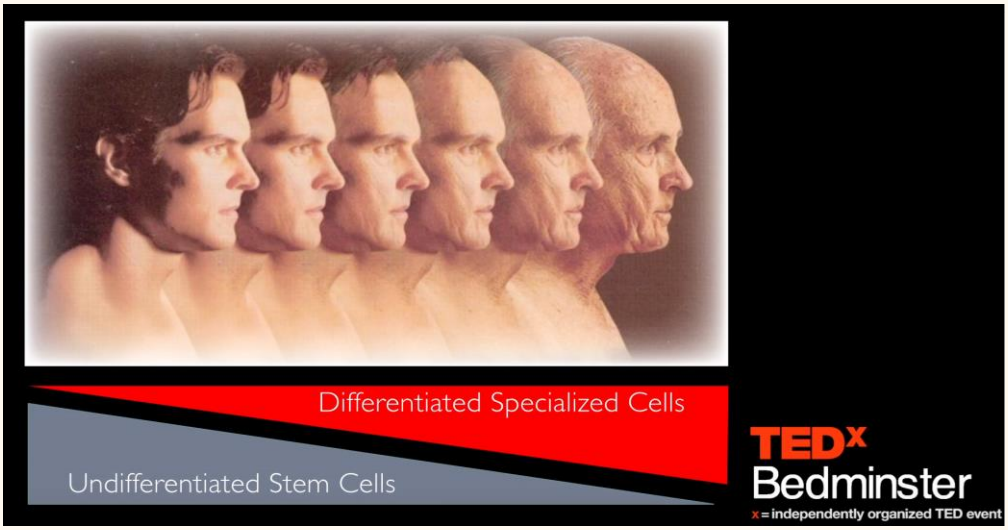
[38] Birth Defects, 2016, *Data and statistics*, CDC
[39] Larson, B.J. et al, 2010. 'Scarless fetal wound healing: a basic science review', *Plastic and Reconstructive Surgery*
[40] Hariri, R. 2011, *'Stem cells: where are we and where are we going?'*, TEDMED Talk
[41] Mukherjee, S. 2016, *The gene: an intimate history*, Bodley Head, London, UK, pp. 1029
[42] Hariri, R. 2011, *'Stem cells: where are we and where are we going?'*, TEDMED Talk

STEM CELL THERAPY: FIGHTING FIRE WITH FIRE

There are estimated to be over one million different types of chemical reactions that take place within the human body. Using the entirety of medicinal chemistry, we can target only 250 of these, or less than two basis points of the total universe of reactions. These figures make pharmacology seem like a rudimentary, blunt tool. So if stem cells are truly the regenerative engine of our bodies, could our medicine be a cell, rather than a pill?[43] But what are stem cells anyway?

Stem cells are undifferentiated cells that reside in the various cavities of the body, possessing a unique quality; stem cells can give rise to or differentiate into other functional cell types. They are your body's paramedics, converging on the site of a wound and differentiating into whatever cell type is required to heal that injury. All stem cells are pluripotent, meaning they can differentiate into more than one cell type, however their level of pluripotency – i.e. how many cell types they can differentiate into – falls on a continuum. **Embryonic stem cells are perhaps the most intriguing type of stem cell type due to their complete pluripotency, or their ability to differentiate into any cell type.**

Stem cells hold some other interesting traits. They are quiescent, meaning they remain inactive in the body until they are required for cell division. They have the ability to self-renew indefinitely whilst at the same time giving rise to normal functioning cells. They can be easily cultured outside of the body in petri dishes. And they share one more interesting trait; one that has led many researchers to believe they share a far more causal relationship with ageing than first thought – **stem cells counts in the body share an inverse relationship with an individual's age.**[44]



Undifferentiated stem cell counts mimic the process of ageing (Hariri, TEDx Bedminster 2014)

[43] Mukherjee, S. 2015, *'Soon we'll cure diseases with a cell, not a pill'*, TED Talk
[44] Hariri, R. 2014, *'The fountain of youth is closer than we think'*, TEDx Bedminster

Dr Robert Hariri, a co-founder of Human Longevity Inc., takes this notion a step further, suggesting that as we age and our stem cells continue to go through the process of self-renewal, those stem cells begin to lose their potency. They start to specialise, which allows them to become more efficient at a specific role, but at the sacrifice of losing some of the adaptability that is necessary to maintain youthfulness. Hariri speculates that this results in a reduction in the variety of proteins produced in the body, leading to the phenotypes we associate with ageing; wrinkled skin, grey hair, weakened immune system, et cetera.[45]

Perhaps then simply replacing the store of unspecialised stem cells within the body could be enough to reverse the symptoms of ageing. By injecting these stem cells into a damaged area, the natural process of regeneration could take place. **This has led companies like Osiris Healthcare (OTCMKTS: OSIR) to use placental stem cells to create grafts for burn and skin wounds.** Dr Hariri suggests that the placenta is in fact the best place to harvest stem cells, due to the placenta's immunologic nature – it is an independent organ to the maternal system yet it is retained for nine months without rejection. According to Hariri, this means that placental stem cells could be delivered to patients without having to match between recipient and donor.[46]

Here are some of the key players in the world of stem cell therapy:

- **Mesoblast (ASX: MSB)** are positioning themselves to have the first industrially manufactured allogenic (no need to match donors) cell-based product approved in the US. Their pipeline of products fall across a variety of diseases from chronic heart failure to graft versus host disease.

- **Athersys (NASDAQ: ATHX)** are developing MultiStem, an off-the-shelf stem cell product platform with applications across neurological, cardiovascular, and inflammatory and immune diseases.

- **Cynata Therapeutics (ASX: CYP)** is a life sciences technology business that has developed the Cymerus Platform, allowing the scalable and versatile manufacture of mesenchymal stem cells.

- **LifebankUSA** is a private company that allows the storage of placenta and cord blood after a child's birth. **Cell Care** is an equivalent in Australia.

[45] Hariri, R. 2014, *'The fountain of youth is closer than we think'*, TEDx Bedminster
[46] Hariri, R. 2011, *'Stem cells: where are we and where are we going?'*, TEDMED Talk

- **Thermo Fisher Scientific (NYSE: TMO)**, a leading manufacturer of scientific instruments, has a division that provides kits and tools for stem cell culture and engineering.

- **Osiris Healthcare (OTCMKTS: OSIR)** uses placental stem cells for the development of grafts and bandages.

- **Fujifilm (JP: 4901)** has invested in stem cell research through its subsidiary Cellular Dynamics. The company recently partnered with the Harvard Stem Cell Institute to manufacture stem cells for use by Harvard researchers.[47]

MICROBIOME: THE WONDERFUL WORLD INSIDE YOUR GUT

There are just under 40 trillion microbes that live within each and every one of us. This outnumbers even the number of human cells within our bodies. In total, these microbes weigh an estimated 200 grams.[48] Given the enormity of these figures, it makes sense that researchers are starting to think microbes may contribute significantly more to our healthiness than first meets the eye.

With many of these microorganisms we share a symbiotic relationship, offering them a safe and nutrient-rich environment in exchange for their help in a variety of tasks like breaking down food or developing the immune system. For some microbes, however, the relationship is a parasitic one, causing a variety of illnesses and diseases for their host, some of which can now be treated with the use of antibiotics. Unfortunately, antibiotics are an imprecise tool; one that doesn't differentiate between helpful and harmful microbes.

With the advent of genome sequencing we can now begin to understand the relationship between human health and the microbes that call our bodies home. The accumulation of the genes of the vast community of microbes living within you is called your microbiome. **The microbiome's genes outnumber your own genes by a factor of 100.**[49] Over time, and with the use of antibiotics, the composition of your microbiome can degrade in quality. Researchers like Dr Robert Hariri believe that the health of your microbiome is an essential part of the overall health of your body. Being able to measure and correct the composition of your microbiome through dieting may be indispensable to increasing healthspans. This is why private companies like uBiome

[47] Buchanan, J. 2017, 'Cellular Dynamics adds to stem cell work with Harvard Institute', *Xconomy*, 25 April
[48] Fuchs, S. et al. 2016,, 'Revised estimates for the number of human and bacteria cells in the body', *PLoS Biology*, doi: 10.1371/journal.pbio.1002533
[49] Learn Genetics, *The human microbiome*, University of Utah

and Human Longevity Inc. have started offering their customers genomic sequencing of their microbiomes, hoping to provide their customers with actionable information in the treatment of illnesses like inflammatory bowel disease and Crohn's disease.

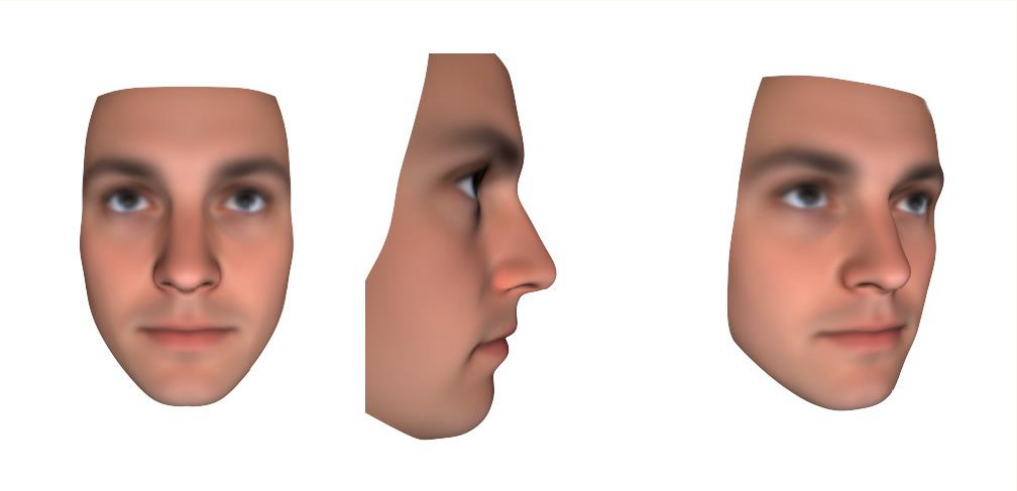
MINORITY REPORT: YOUR BAYESIAN FUTURE

> *"The genome will thus be read not in absolutes, but in likelihoods – like a report card that does not list past experiences but future propensities.* ***It will become a manual of previvorship.****"*
>
> Siddhartha Mukherjee, The Gene

In October of last year, KIS Capital CIO Josh Best got a taste of what the future may hold for us when he attended the Health Nucleus branch of Human Longevity. Health Nucleus is a clinical research centre that provides an assortment of medical testing, ranging from the sequencing of genomes and gut microbiomes, to full body MRI scans. The data collected from these tests is then collated and analysed by a team of medical professionals, and the customer is provided with an actionable summary report. The testing lasted just one full day, with the genome sequencing alone generating over 85 gigabytes of data!

The summary report features a selection of risk models, presenting you with a rather Bayesian outlook on your future. It compares your genetic profile to that of the sample population and suggests your susceptibility to certain afflictions versus the median person. The report covers a wide variety of illnesses and diseases including cardiovascular disease, cancers, and mental health disorders. It also offers an analysis of the individual's pharmacogenomics. This is the individual's amenability to different drugs therapies, illuminating what side effects they might be more likely to experience as well as suggested dose levels for certain drugs.[50] The report makes predictions on body weight, height, eye colour, hair colour and even facial structure (see below), all with impressive accuracy. **Importantly, as each year passes since the original testing took place, the customer is sent a refreshed report which includes a comparison against the new, expanded dataset. As previously discussed, the more people who partake in the Health Nucleus program, the greater the dataset and potential for analysis becomes.**

[50] 13D Research 2017, *What I learned this week: August 10, 2017*



Computer generate image of CIO Josh Best based purely on his sequenced genome

Health Nucleus is clearly still in its infancy, with plenty of room for the translation of generated data into clinical therapies to improve. But it does offer insight into what the future could look like. **As both the cost and the time to sequence genomes continues to decrease, genomic analysis could be done from the comfort of your own home.** Perhaps the morning visit to the bathroom replaces your visit to the local GP. The most innocuous and mundane parts of your morning routine becoming a daily health check-up. With the brushing of your teeth and a visit to the toilet, a sample of your DNA and biome could be sent to the cloud to be sequenced and analysed; a summary of the results available in mere minutes to be digested along with morning breakfast. With each report, you are prescribed the perfect diet, cocktail of supplements and pills, and optimal workout routines for that day. **As your genome changes with each passing day, so too does the report you receive, constantly updating and adapting its recommendations to fit your new state of health and outlook.** It will not be a crystal ball that predicts your future, but rather a weather forecast that draws on past experiences to make estimates of future probabilities.

REGENERATIVE MEDICINE: WHERE SCIENCE FICTION MEETS REALITY

According to the World Health Organisation, organ transplants could prevent or significantly delay up to 35 percent of all deaths in the United States.[51] That is over 900,000 people each year that could potentially be saved! Unfortunately, organ donors are in short supply. There are over 120,000 people currently sitting on the U.S. transplant waiting list alone, with a new person added every ten minutes. On

[51] New Organ, *What's New*, Methuselah Foundation

average, twenty-two people die each day while awaiting an organ transplant, and one donor can save as many as eight lives.[52]

Of those on the transplant list, 83 percent are awaiting a kidney, with the shortage exacerbated by the fact that a transplanted kidney generally only lasts twelve or so years. This isn't the only issue; transplants are expensive, costing as much as US$260,000. This is before accounting for the cost of immunosuppressant drugs, which can be as much as US$10,000 per annum.[53] These drugs also take a severe toll on the individual's vitality, smothering the immune system in an attempt to stop the kidney from being rejected. In short, the tribulations of receiving a transplant are extensive and exhaustive for the patient. But what if doctors had an unlimited supply of cheap, manufactured organs?

The field of regenerative medicine is seeking to make this a reality. Regenerative medicine is the area of medicine concerned with the ability to repair or replace a patient's damaged tissue or organs. This covers everything from 3D tissue printing through to lab-grown bladders.

Anthony Atala and his team at the Wake Forest Institute for Regenerative Medicine are at the forefront of this field. They use a process called bioprinting to create artificial organs. In bioprinting, cells are grown in-vitro from a tissue sample. For those cells that aren't amenable to the process of culturing, stem cells are used instead. **The cells grow quickly, expanding from the size of a postage stamp to the size of a football field in just six weeks.[54]** Once enough cells have been cultured, they are printed onto a biomaterial scaffold, in much the same way as you would a traditional 3D printer. Apart from their potentially never-ending supply, these lab-grown organs hold another critical advantages over donor organs; given they are made from the patient's own cells they won't be rejected by the body, and there is no need for immunosuppressant drugs.

Here are some of the leading players in the world of regenerative medicine:

- **Organovo Holdings (NASDAQ: ONVO)** utilise a process of bioprinting similar to the Wake Forest Institute, seeking to create functional human livers and kidneys.

- **Tissue Regeneration Systems** is a private company with a proprietary bio-scaffold and coating technique. **DePuy Synthes Products**, owned by Johnson & Johnson, recently acquired 3D printing technology from the company, intending to use the tech to create their own implants.[55]

[52] New Organ, *What's New*, Methuselah Foundation
[53] New Organ, *What's New*, Methuselah Foundation
[54] Wake Forest Institute for Regenerative Medicine, *'The ABCs of organ engineering'*, Wake Forest
[55] N/A, 2017, 'DePuy Synthes acquires tissue Tissue Regeneration System's 3D printing technologies to treat bone defects', *PR Newswire*, 20 April

- **Bio3D Technologies** is a Singaporean start-up that provides bioprinting machines for as little as US$2,400.

LIFE HACKS: WHAT YOU CAN BE DOING TODAY

STRESS AND MEDITATION

In situations of chronic stress the body releases a steroid hormone called cortisol. In fight or flight scenarios, this served our ancestors well, helping the body to access glucose reserves and providing it with the extra energy needed to survive. However, if cortisol levels stay elevated for an extended period of time the effects can be very detrimental. **Studies have shown a correlation between increased levels of cortisol in the body and a reduction in telomerase, and as such, shorter telomeres in cells.**[56] As humanity has progressed we have found ourselves less and less often in situations necessitating fight or flight. Yet, chronic stress still persists in society. After all, we are the subjective interpreters of what is and isn't stressful. Elizabeth Blackburn, the discoverer of telomerase, conducted a study of caregivers, finding that those who were caregiving for a longer time tended to have shorter telomeres than their counterparts with shorter tenures.[57] **Most interestingly, those who identified as being in a stressful state were found to have shorter telomeres than those in similar circumstances who did not. Put another way, the caregivers who found their job more stressful had actually aged more than those doing the same job, but under a rosier disposition.** The inference here is that our temperament can directly affect the progress with which our cells age. Meditation has long been known to reduce stress and cortisol levels amongst those who practice it.[58] So could meditating really help to increase lifespan, especially amongst those who are chronically stressed? **Well that same study of caregivers found that those caregivers who meditated for just twelve minutes a day had longer telomeres than their counterparts.**[59]

NUTRITION

In his book How Not to Die, nutritionist Michael Greger suggests that the global pandemic of chronic disease can be ascribed, in part, to the shift towards animal-sourced and processed foods. Studies of lapsed vegetarians have found that they experience a 146 percent increase in the odds of heart disease, a 152 percent increase in the odds of stroke, and a 231 percent increase in the odds of weight gain after they

[56] Choi, J. et al. 2008, 'Reduced telomerase activity in human T lymphocytes exposed to cortisol', *Brain Behaviour and Immunity*, vol. 22, issue 4
[57] Blackburn, E. 2017, *'The science of cells that never get old'*, TED Talk
[58] Chentanez, V. et al. 1991, 'Effect of Buddhist meditation on serum cortisol and total protein levels, blood pressure, pulse rate, lung volume and reaction time', *Physiology and Behaviour*, vol. 50, issue 3, pp. 543-548
[59] Blackburn, E. 2017, *'The science of cells that never get old'*, TED Talk

started eating meat. After twelve years, this newfound meat-eating diet was associated with a 3.6-year decrease in life expectancy.[60] Thus, a shift towards a more balanced diet in the consumption of whole grains, beans, fruits and vegetables should help to reduce the onset of chronic disease. The consumption of added-sugars is of particular concern, increasing the risk of several diseases including heart disease.[61]

Several studies have found that caloric restriction can delay the onset of ageing across a variety of species including mice, dogs and monkeys.[62,63] Caloric restriction is a dietary regimen that reduces the calorie intake of an individual without sacrificing essential nutrients or experiencing malnutrition. Serge Faguet, a collaborator of Peter Diamandis, suggests achieving this effect through intermittent fasting for two or three days each week.[64] There are multiple competing hypotheses for why caloric restriction seems to extend life. **One prominent theory is that nutrient starvation induces a state of autophagy, whereby your body starts to consume cells starting with any damaged cells, allowing the body to essentially detox itself.**[65] Regardless of why this phenomenon occurs, if calorie restriction works in other primates, it probably works in humans too.

SLEEP

Sleep is essential to your health and wellbeing. Use data to see whether you are spending enough sleep time in REM sleep, the restorative sleep phase.[66] Whilst a smartphone app can do the trick, it can also be a tad intrusive. Try getting an Oura smart ring for easier sleep tracking. If sleep is something you struggle with, trying visiting a sleep lab, where they can test for disorders like sleep apnea. Listed player ResMed (ASX: RMD) provides a range of products to treat sleep apnea and other respiratory diseases.

EXERCISE

Numerous studies have shown that exercise can decrease the risk of a variety of diseases and even partially reverse the effects of ageing on physiological functions.[67] Serge Faguet suggests a focus on short, intense workouts like interval training that can help to increase your metabolic rate.

[60] Greger, M. 2015, *How not to die: discover the foods scientifically proven to prevent and reverse disease*, Flatiron Books, U.S.
[61] Corliss, J. 2014, 'Eating too much added sugar increases the risk of dying with heart disease', *Harvard Health Publishing*, 6 February
[62] Masoro, E. 2005, 'Overview of caloric restriction and ageing', *Mechanisms of Ageing and Development*, vol. 126, issue 9, pp. 913-922
[63] Anderson, R. et al. 2009, 'Caloric restriction delays disease onset and mortality in Rhesus monkeys', *Science*, vol. 325, issue. 5937
[64] Faguet, S. *'I'm 32 and spent $200k on biohacking. Became calmer, thinner, extroverted, healthier & happier'*, Hackernoon, web blog
[65] Ibid.
[66] Ibid.
[67] Gayda, M. et al. 2012, 'Exercise and longevity', *Maturitas*, vol. 73, issue 4, pp. 312-317

RAPAMYCIN

Rapamycin is a bacterial agent created by Novartis AG (VTX: NOVN) that is used to prevent organ transplant rejection. In mice, it has been shown to slowdown the onset of cancers as well as increase lifespans by circa 25 percent.[68] **According to BioSpace, elderly human subjects on rapamycin showed an astonishing 20 percent improvement in their immune response after being given an influenza vaccine.**[69] Scientists believe that Rapamycin induces a state of autophagy, which is responsible for the increased longevity of subjects.[70]

METFORMIN

Metformin is a drug used for the treatment of type 2 diabetes. **A study conducted by Bannister et al (2014) found that diabetics taking Metformin lived 15 percent longer than non-diabetics not taking the drug.**[71] Familial longevity has been known to be correlated with enhanced insulin sensitivity.[72] Researchers suggest that it is Metformin's ability to increase insulin sensitivity in patients that increases their life expectancy.[73] This begs the question: should "healthy" people be taking Metformin too?

STATINS

Statins is a drug prescribed by doctors to help lower cholesterol levels in patients. Statins is virtually an anti-ageing drug, prescribed far wider than its narrow approval specification. **Statins has been shown to reduce the risk of cardiovascular disease by over 20 percent.**[74] The drug has also allegedly been found to slow the progression of melanomas.[75]

LONGITUDINAL DATA

Whether it be genome or microbiome sequencing, or more traditional testing like MRIs and blood tests, it is important to collect data at multiple points in time to see how the body changes. This can be very useful for clinicians. Try Human Longevity Inc. for a thorough range of testing including sequencing; it's not cheap, but it may be worth it if you take collecting longitudinal data seriously. Over time this testing should become

[68] 13D Research 2017, *What I learned this week: January 19, 2017*
[69] Keown, A. 2015, 'Novartis AG may already have first true anti-aging drug in its pipeline', *BioSpace*, 19 February
[70] Niccoli, T. and Partridge, L. 2012, 'Ageing as a risk factor for disease', *Current Biology*, vol. 22, issue 17, doi: 10.1016/j.cub.2012.07.024
[71] Bannister, C.A. et al. 2014, 'Can people with type 2 diabetes live longer than those without? A comparison of mortality in people initiated with metformin or sulphonyl urea monotherapy and matched, non-diabetic controls', *Diabetes Obesity and Metabolism*, doi: 10.1111/dom.12354
[72] Cessie, S. et al. 2010, 'Familial longevity is marked by enhanced insulin sensitivity', *Aging Cell*, vol. 10, issue 1, pp. 114-121, DOI: 10.1111/j.1474-9726.2010.00650.x
[73] Niccoli, T. and Partridge, L. 2012, 'Ageing as a risk factor for disease', *Current Biology*, vol. 22, issue 17, doi: 10.1016/j.cub.2012.07.024
[74] WebMD, *'Side effects of cholesterol-lowering statin drugs'*
[75] *Humanity 2.0*, 2017, audio podcast, Waking Up with Sam Harris, 28 November

more affordable as the instruments and tools becomes both cheaper, and more efficient.

LOOKING OUTSIDE OF HEALTHCARE

The technologies explored in this report have broader ramifications for the various sectors of the economy outside of therapeutics. For one, the wide availability of genomic data will give businesses an unprecedented understanding of their customers and employees. It will allow companies to tailor products to customers with complete specificity, from dynamic life insurance pricing to drug preferences and ideal dosage levels with pharmacogenomics. According to 13D, the U.S. life insurer MassMutual recently partnered with Human Longevity Inc. to sequence the genomes of both its customers and its staff.[76] With the global spend for prescription drugs to reach $1.5 trillion by 2021, the market for pharmacogenomics is obviously enormous.[77] Education is another interest use case for genome sequencing. In a fascinating New York Times article, Jay Belsky explores the idea of using genome sequencing to position students to extract the most from the education system. Here's an excerpt from the piece:

> *"Evidence suggests that some children are — in one frequently used metaphor — like delicate orchids; they quickly wither if exposed to stress and deprivation, but blossom if given a lot of care and support. Others are more like dandelions; they prove resilient to the negative effects of adversity, but at the same time do not particularly benefit from positive experiences. In this sense, resilience, long thought to be an exclusively beneficial characteristic, is actually a double-edged sword."* [78]

Could the classrooms of the future be arranged into orchids and dandelions based on genetic profiling? Applications of the CRISPR technology are extremely promising too. Gene-editing could reinvent the agricultural system, creating more robust and nutritious crops or even engineering higher-yielding farm animals.[79] Harvard and MIT's Broad Institute, along with DuPont Pioneer, recently agreed to jointly provide non-exclusive intellectual property licenses to be used in agricultural research and development. The partnership aims to explore new ways to increase crop yields, improve drought resistance, and reduce the reliance on pesticides.[80] **ARK Research estimates that even if CRISPR penetrated only 20 percent of the space, it could increase the global value of agricultural production by more than $110 billion by 2025.**[81] The technology behind regenerative medicine could be used to remove the

[76] 13D Research 2017, *What I learned this week: May 25, 2017*
[77] Mukherjee, S. 2016, 'Global drug spending could hit a record $1.5 trillion by 2021 – and that's a good thing', *Fortune*, 6 December
[78] Belsky, J. 2014, 'The downside of resilience', *New York Times*, 28 November
[79] 13D Research 2017, *What I learned this week: August 10, 2017*
[80] Rozen, I. 2017, 'Removing a major CRISPR licensing roadblock in agriculture', *Broad Institute*, 18 October
[81] ARK Invest, 2017, *'ARK disrupt issue 97: electric vehicles, artificial intelligence, bitcoin, and CRISPR'*, 23 October

need for farmed animals entirely, creating inexpensive lab grown meat that can be grown anywhere in the world.

For the broader economic system, increasing healthspans has clear benefits. Let's take the average GDP per adult capita in the United Sates. In 2016 this figure was circa US$74,000 per adult. **If you were to increase the healthspan of the average American by just ten years, and subsequently their working life by the same amount, that's an extra US$740,000 added to the system per person over their life, all else being equal of course.** There would likely be some job cannibalisation to be sure, but these are the most capable members of society; they are at the point in their life where they have accumulated the maximum amount of knowledge and skills for their occupation. Furthermore, this would also mean pushing out the health costs that come with age-related debilitating diseases an extra ten years!

Here are some of the companies we may not have mentioned so far:

- **Illumina (NASDAQ: ILMN)** is the leading provider of genome sequencers with a circa 90 percent market share. They recently released their new sequencer, the NovaSeq, which is up to 70 percent faster than previous iterations.

- **Agilent Technologies (NYSE: A)** is one of the leading developers of hardware and software used in the process of DNA analysis and expression. Agilent's products range from DNA microarrays through to cell analysers.

- **Qiagen (NASDAQ: QGEN)** is a supplier of DNA readers and sequence data analysis software. The company has new microbiome and RNA products on the horizon.

- **Thermo Fisher Scientific's (NYSE: TMO)** life sciences division provides a range of instruments and tools across virtually all topics discussed in this report.

- **Pacific Biosciences of California (NASDAQ: PACB)** manufactures high accuracy, long-read sequencers. The company recently announced an agreement with genomic services leader **Novogene** to double their capacity.[82]

- **Roche Holdings AG (VTX: ROG)** has a next generation sequencing division that, amongst other things, provides liquid biopsy assays for DNA extraction.

[82] PacBio, 2017, *'PacBio announces new agreement with Novogene to purchase ten sequel systems'*, 2 August

- **NeoGenomics (NASDAQ: NEO)** is a company that specialises in genetic testing for different types of cancers.

TO CONCLUDE

The point of this report has been to provide you with a thought-provoking and somewhat educational piece about the future of medicine and how it may relate to the investment world. For the sake of easy digestion, there have been some drastic oversimplifications. For one, genomes do not remain static throughout life; in fact, they change rather quickly.[83] Interpreting genomes is not as simple as just reading the genetic code; the three dimensional structure of the genome is also important for gene expression. Most of the time, genes are not responsible for just a single phenotype, and there may be trade-offs. For instance, the gene for creativity and schizophrenia may be so intrinsically linked that any attempt to silence the phenotype of schizophrenia would also result in a smothering of that individual's creative potential.[84] As Richard Dawkins notes in his book The Extended Phenotype, the metaphor of genomes as blueprints is 'dreadfully misleading'. A blueprint is a one-for-one replica of a product to which one can, with relative simplicity, easily interpret and make alterations to that will be mirrored in the end product. Instead, the genome is more like a recipe.[85] As Mukherjee points out, 'if you quadruple the amount of butter in a cake, the eventual effect is more complicated than just a quadruply buttered cake.'[86] Regardless of these oversimplifications, the themes explored throughout this report reflect the general path on which these sciences are headed, no matter how much windier that path may be in reality.

[83] *When will genomics live up to the hype?*, 2017, audio podcast, a16z Podcast, 22 February
[84] Mukherjee, S. 2016, *The gene: an intimate history*, Bodley Head, London, UK, pp. 1011-14
[85] Dawkins, R. 1982, *The extended phenotype*, Oxford University Press, UK, pp. 175
[86] Mukherjee, S. 2016, *The gene: an intimate history*, Bodley Head, London, UK, pp. 1025

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