

TRANSFORMING THE FUTURE OF HEALTHCARE AND AGING WITH ARTIFICIAL INTELLIGENCE AND **AI-POWERED AGING RESEARCH**

Insilico Medicine, Inc Emerging Technology Centers Johns Hopkins University B301, 1101 33rd Street Baltimore, MD, 21218



ALEX ZHAVORONKOV, PHD alex@insilicomedicine.com

ARTIFICIAL INTELLIGENCE MEETS LONGEVITY RESEARCH, DRUG DISCOVERY AND BIOMARKER DEVELOPMENT

BIOMARKER DEVELOPMENT

ARTIFICIAL INTELLIGENCE

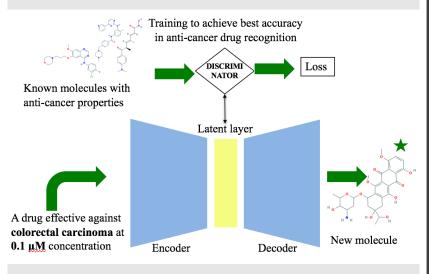
BIG OMICS DATA LONGEVITY RESEARCH

DRUG DISCOVERY



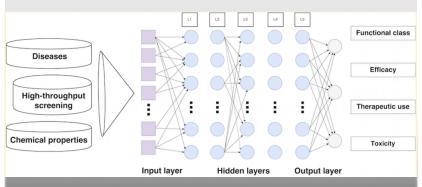
INSILCO MEDICINE 19 PEER-REVIEWED RESEARCH PAPERS IN 2016

First application of Adversarial Autoencoder (AAE) generating new molecular structures with desired properties



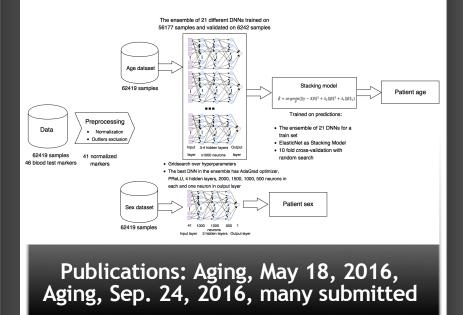
Published: Oncotartet, Dec. 22, 2016

Generative Adversarial Networks (GANs) "imagine" new cancer drugs on demand First transcriptomic and structural DNN ensemble predictors of therapeutic class, side effects and Phase I/II clinical trials outcomes



Publications: Molecular Pharmaceutics, May 20, 2016 (American Chemical Society Editors' Choice Award), Nature Communications, Nov 16, 2016, bioRxiv Dec 29, 2016

Pharma.Al A Set of Predictors of Toxicity and Efficacy First deep learned biomarkers of aging using DNN ensembles; multimodal one-shot learning disease markers; navigator of differentiation state; First nutraceuticals to be launched in 2017



Embryonic.Al Aging.Al Geroprotectors.Al

BREAKTHROUGHS IN BIOMEDICINE 2012-2017



DIGITAL

MEDICINE

IMMUNO **ONCOLOGY**

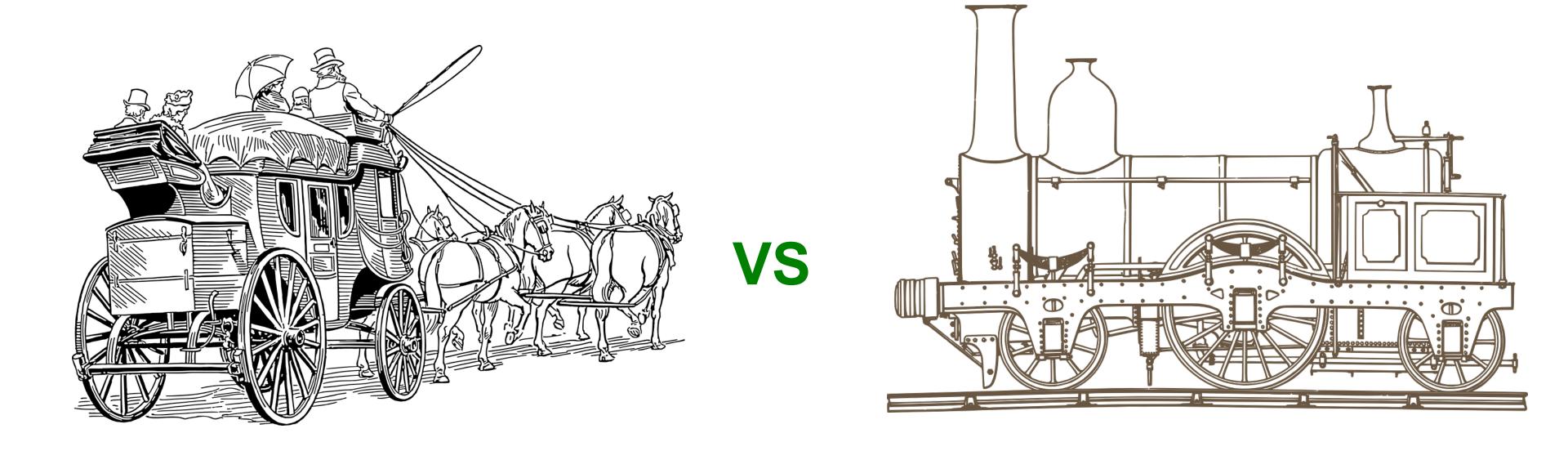
ARTIFICIAL INTELLIGENCE

CRISPR/

CAS9 GENE EDITING

AGING BIOMARKERS

ANTI-AGING THERAPIES



DATA IS THE NEW OIL

AI IS THE NEW COMBUSTION ENGINE

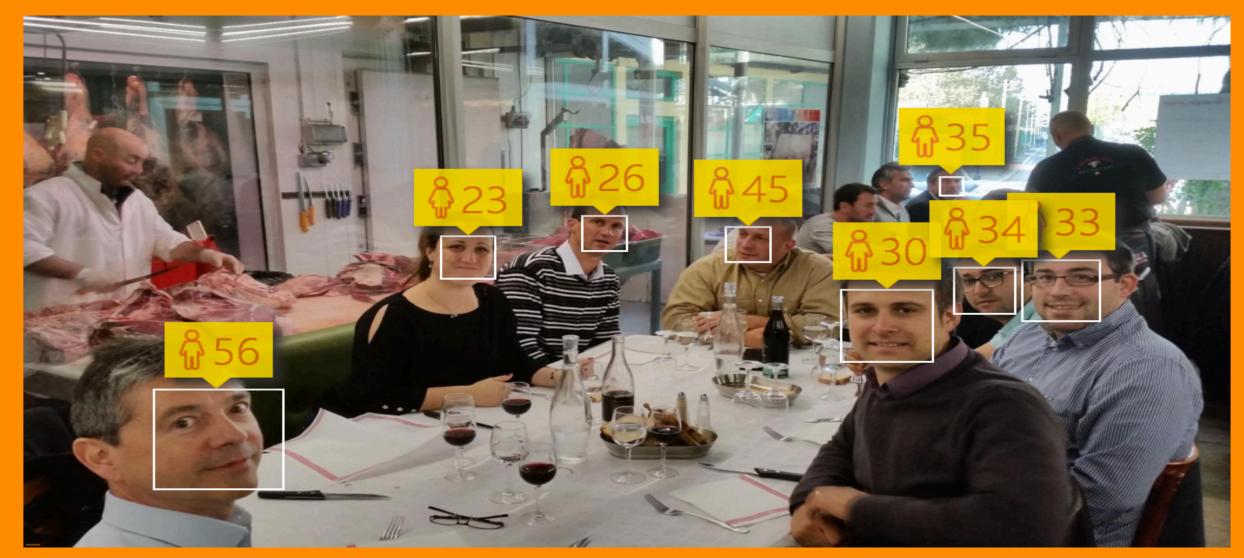
CAN DNNs PREDICT HUMAN AGE BETTER THAN HUMANS?



Share 2.3M Y Tweet

The magic behind How-Old.net Privacy & Cookies | Terms of Use

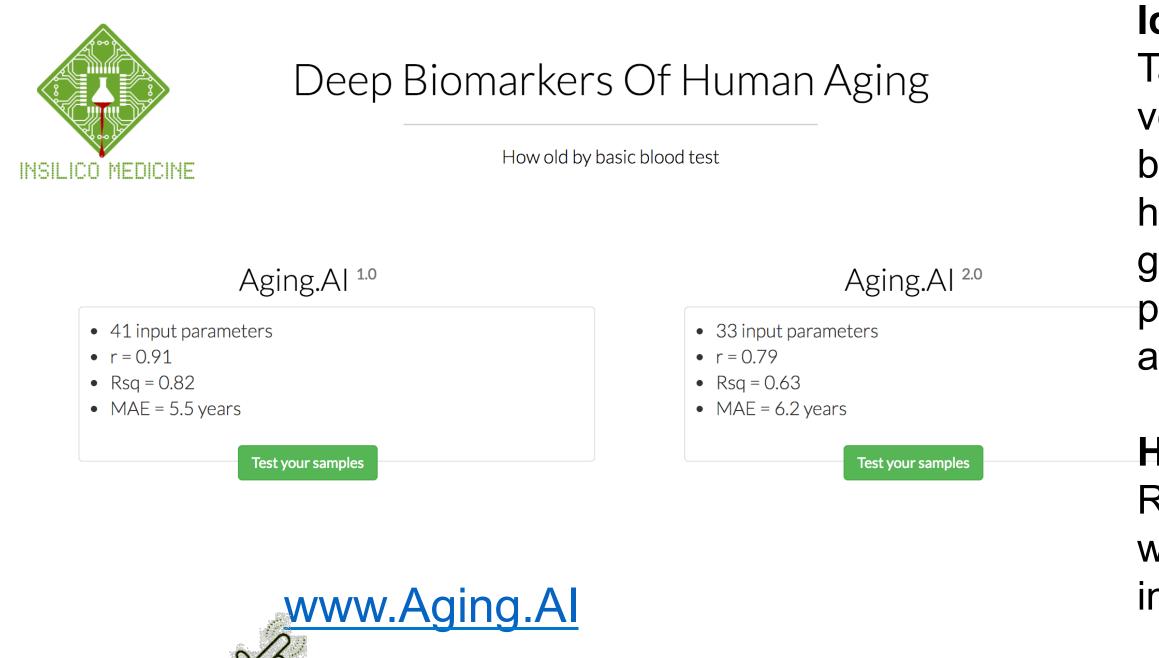




Sorry if we didn't quite get it right - we are still improving this feature.



DEEP BLOOD BIOCHEMISTRY PREDICTOR OF HUMAN CHRONOLOGICAL AGE



Idea:

Take a very large number of very common features from basic blood draws of reasonably healthy people linked to age and gender and build a deep predictor of chronological age and gender

Hidden agenda:

Reduce animal experimentation when testing anti-aging interventions

WHY AGING RESEARCH IS ESSENTIAL FOR **DRUG DISCOVERY, BIOMARKER DEVELOPMENT?**

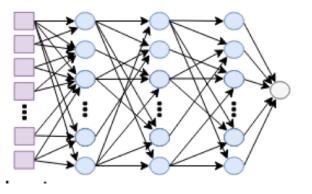


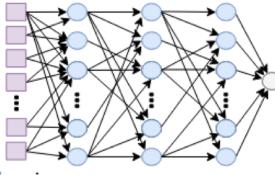
- Sex
- Eyes
- Eye color
- Skin color
- Hair color
- Race
- Height • Weight
- Age

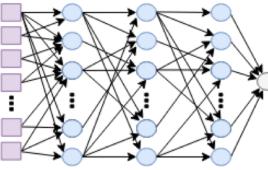
In this crowd very few people have cancer, but everyone has:

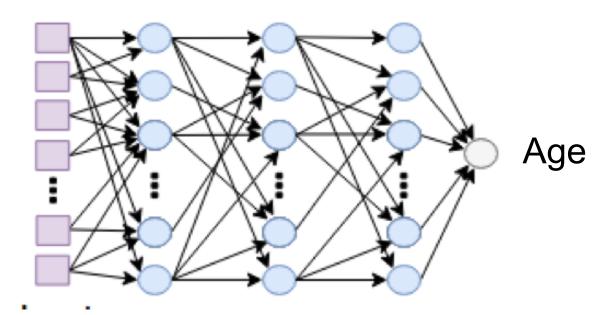
IF I CAN NOT PREDICT YOUR AGE, HOW CAN I CLAIM THAT I CAN PREDICT YOUR HEALTH STATUS?

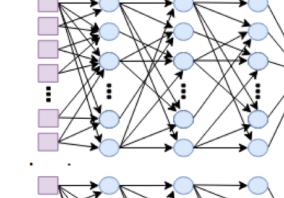
BIG IDEA: USE AGE FOR MULTI-OMICS DATA INTEGRATION

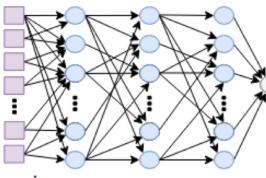


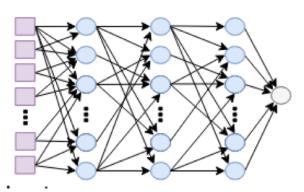












Individual DNNs & Feature Importance Analysis

Features from simple blood tests (biochem.)

Features from simple urine tests (biochem.)

Blood Transcriptome/proteome

Tissue-specific Transcriptome/proteome

Urine Transcriptome/proteome

Genome

Metabolome

Imaging Data (MRI/CT)

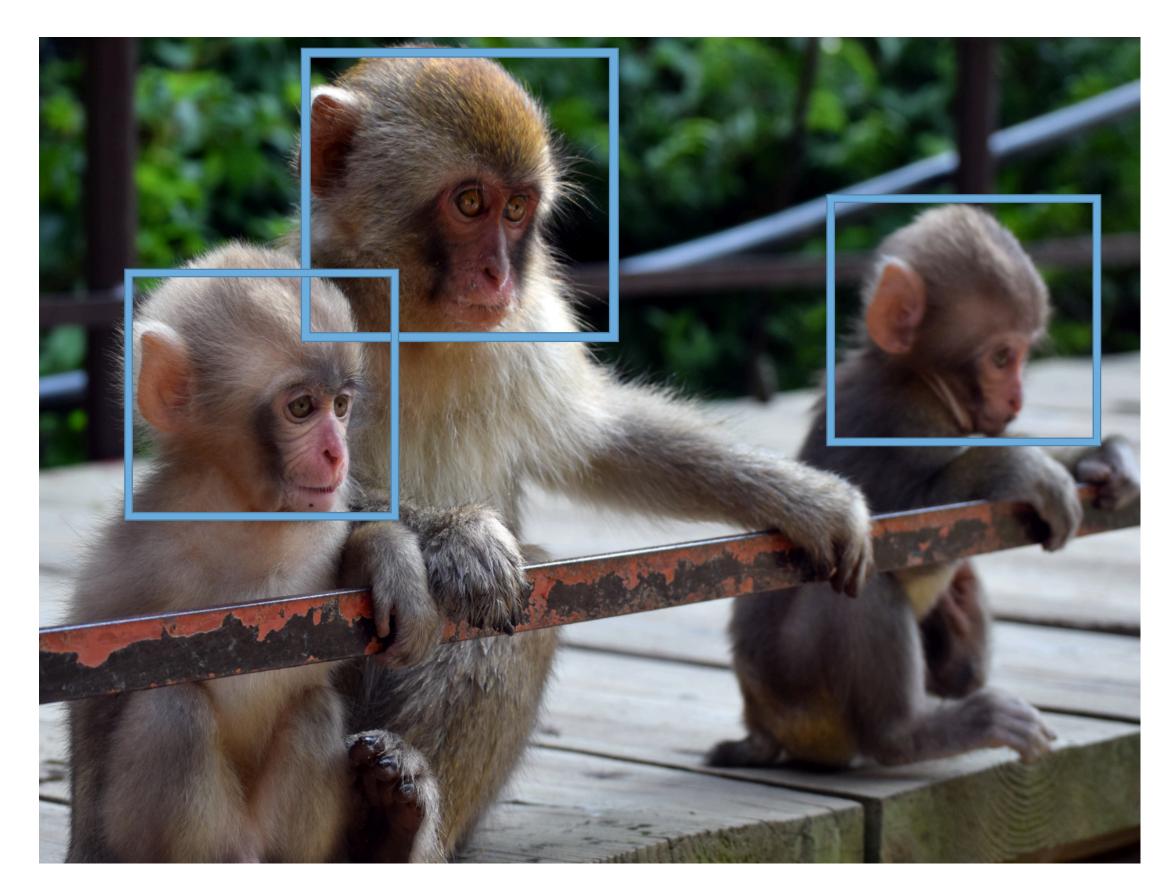
Pictures

Hair/Nail/Skin composition

Multi-modal one-shot learning DNNs & Feature Importance Analysis

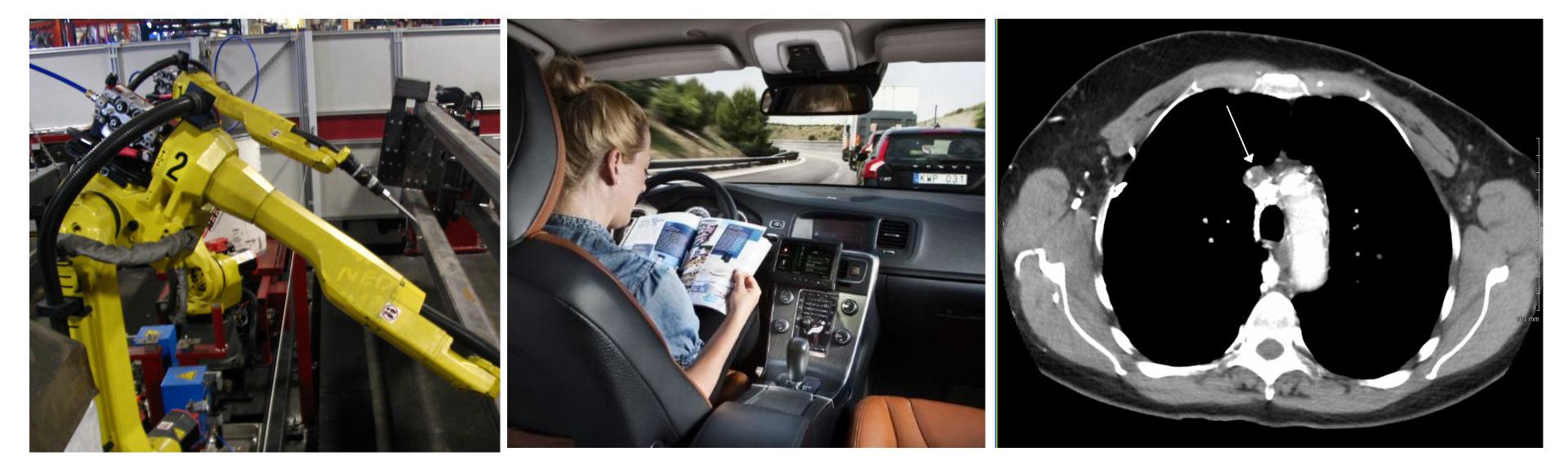
I CAN ACCURATELY PREDICT YOUR AGE **USING THE VARIOUS DIFFERENT DATA TYPES BUT HOW DOES IT CHANGE ANYTHING?**

WHAT IS THE AGE OF EACH MONKEY? LIFESPAN: 25





EVERY INDUSTRY WILL BE TOUCHED OR TRANSFORMED BY AI BEFORE 2020



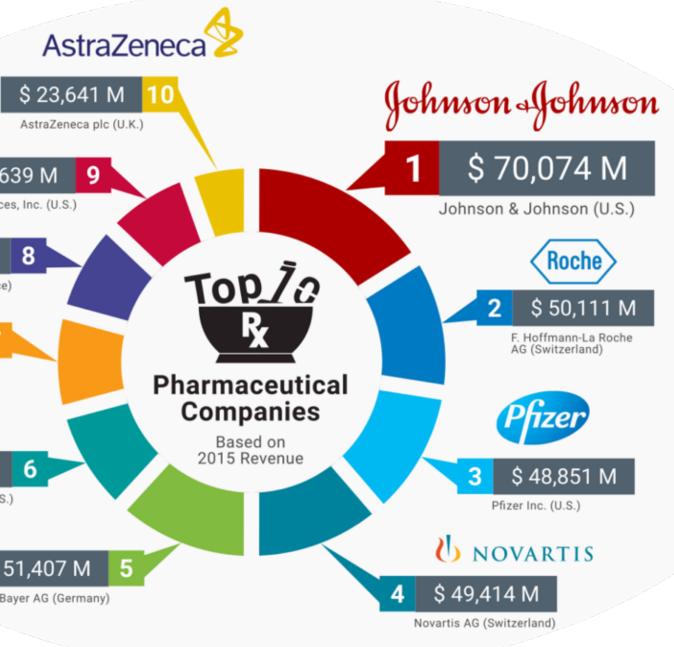
WHAT IS THE MOST INEFFICIENT INDUSTRY TO BE TRANSFORMED BY AI?

ARTIFICIAL INTELLIGENCE TO TRANSFORM THE PHARMACEUTICAL INDUSTRY

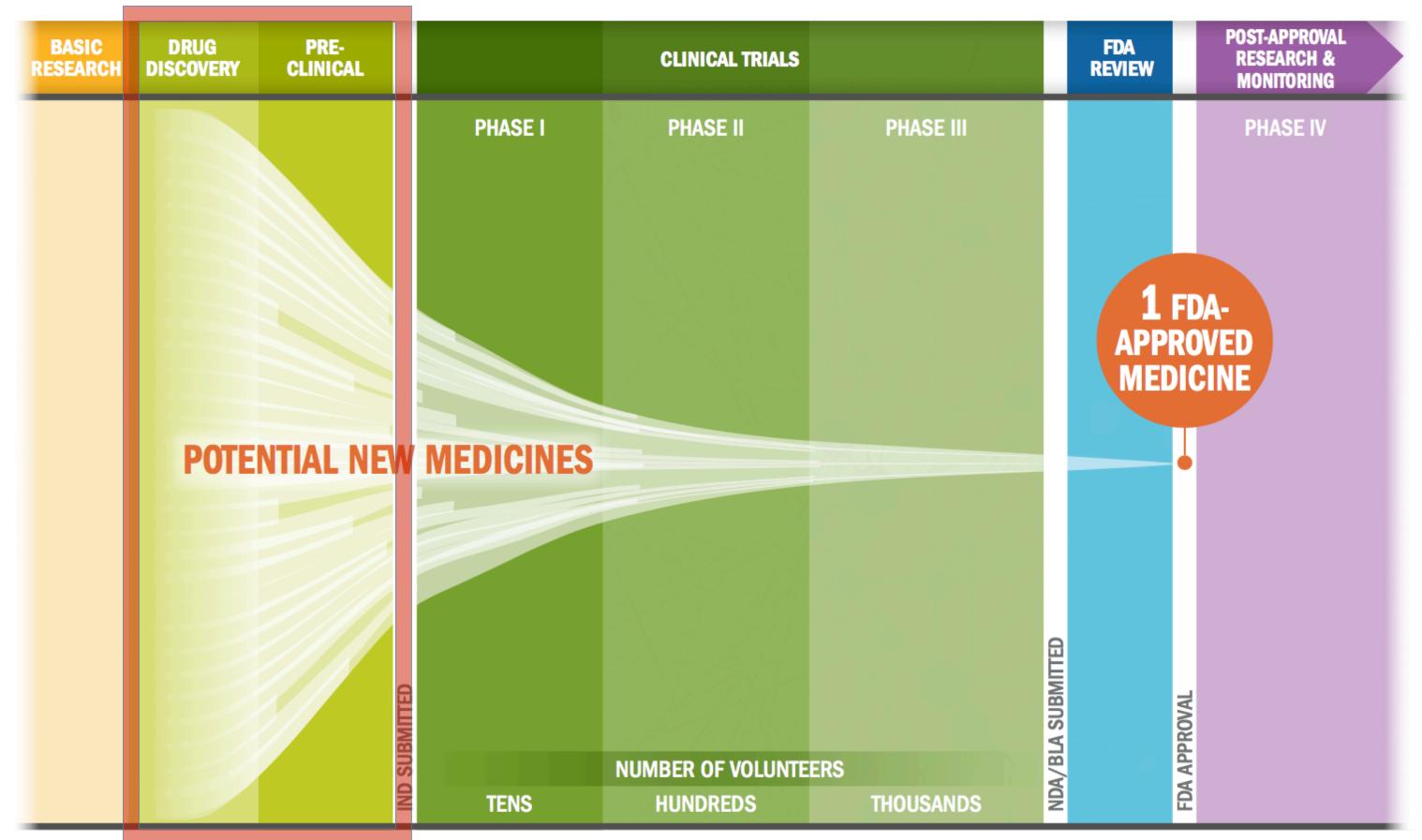


AstraZeneca AstraZeneca \$ 32,639 M \$ 32,639 M Gilead Sciences, Inc. (U.S.) \$ 34,542 M 8 Sanofi (France) \$ 36,566 M 7 GlaxoSmithKline plc (U.K.) \$ 39,498 M 6 Merck & Co., Inc. (U.S.) \$ 51,407 M

Global sales: >\$1 Trillion Global R&D: >\$150 Billion 46 new drugs launched in 2014 >\$2.5B to develop a drug 92% failure rate in clinical trials

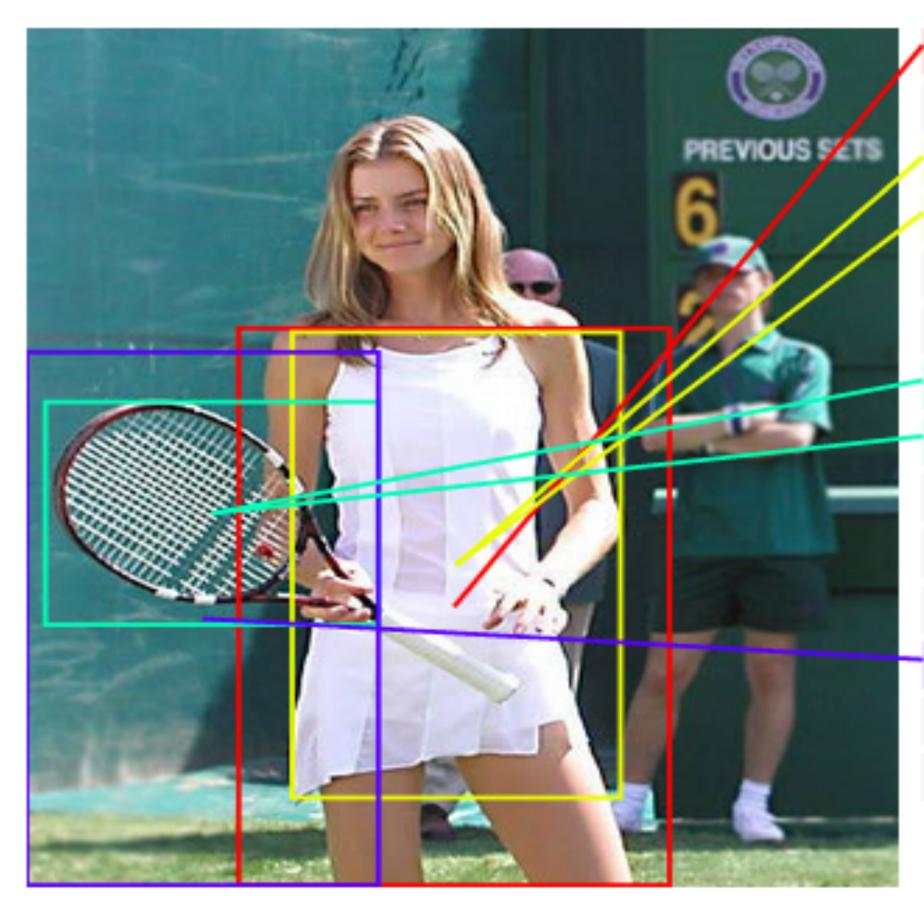


THE BIOPHARMACEUTICAL RESEARCH AND DEVELOPMENT PROCESS



Key: IND: Investigational New Drug Application, NDA: New Drug Application, BLA: Biologics License Application Source: Biopharmaceutical Research & Development, PRMA http://phrma-docs.phrma.org/sites/default/files/pdf/rd_brochure_022307.pdf

DEEP LEARNING: HUMAN LEVEL



Andrej Karpathy, Stanford, http://cs.stanford.edu/people/karpathy/deepimagesent/

1.12 woman

-0.28 in

1.23 white

1.45 dress

0.06 standing

-0.13 with

3.58 tennis

1.81 racket

0.06 two

0.05 people

-0.14 in

0.30 green

-0.09 behind

-0.14 her



LEE SEDOL 00:01:00

GENERATIVE ADVERSARIAL NETWORKS

GENERATIVE ADVERSARIAL NETWORKS (GANs)

this small bird has a pink breast and crown, and black almost all black with a red primaries and secondaries.

the flower has petals that are bright pinkish purple with white stigma

this magnificent fellow is crest, and white cheek patch.



this white and yellow flower have thin white petals and a round yellow stamen





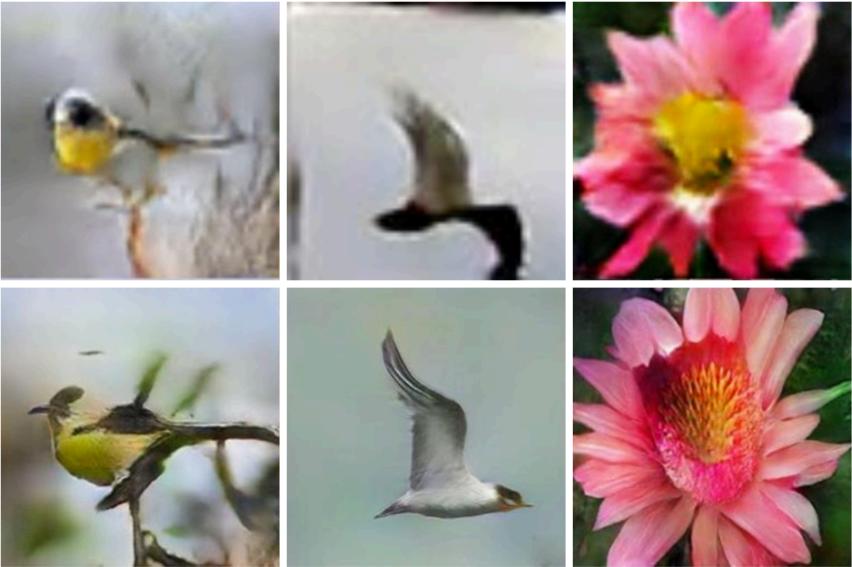
Figure 1. Examples of generated images from text descriptions. Left: captions are from zero-shot (held out) categories, unseen text. Right: captions are from the training set.

Reed et al, ICML 2016

ACHIEVING PHOTOREALISM WITH GANs

This bird has a yellow This bird is white belly and tarsus, grey back, wings, and brown throat, nape with a black face

with some black on its head and wings, and has a long orange beak



(a) Stage-I images

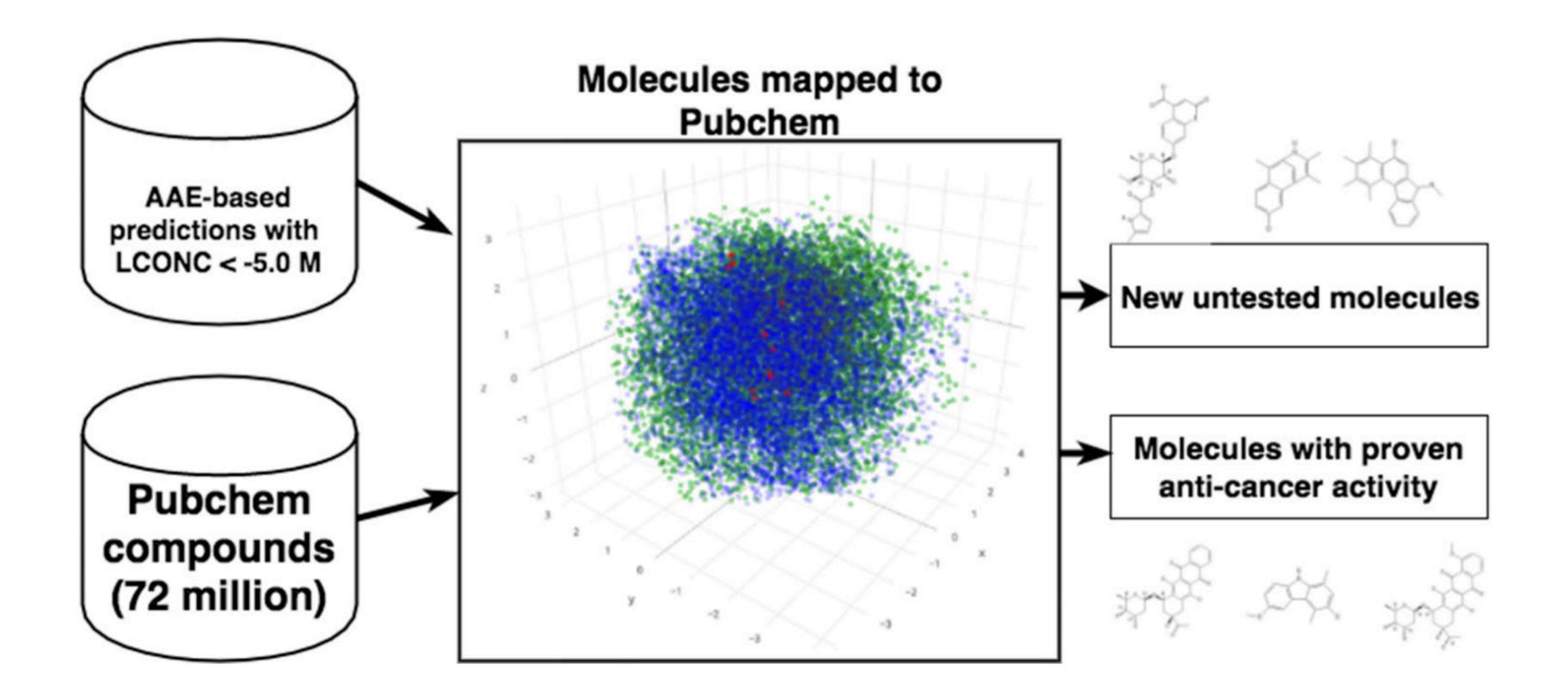
(b) Stage-II images

Zhang et al, StackGAN: Text to Photo-realistic Image Synthesis with Stacked **Generative Adversarial Networks**

arXiv:1612.03242v1 [cs.CV] 10 Dec 2016

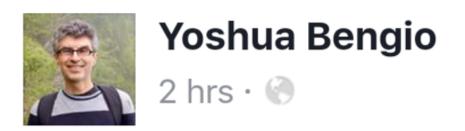
This flower has overlapping pink pointed petals surrounding a ring of short yellow filaments

AT INSILICO WE ARE MAKING DRUGS USING GANs

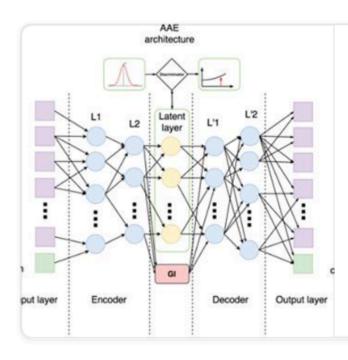


NOTICED BY THE MASTERS

Yann LeCun liked this.



Auto-encoders with a GAN objective in the latent layer for cancer drug discovery:



Oncotarget | The cornucopia of meaningful leads: Applying...

doi:10.18632/oncotarget.14073. Artu... impactjournals.com

Yann LeCun and 340 others



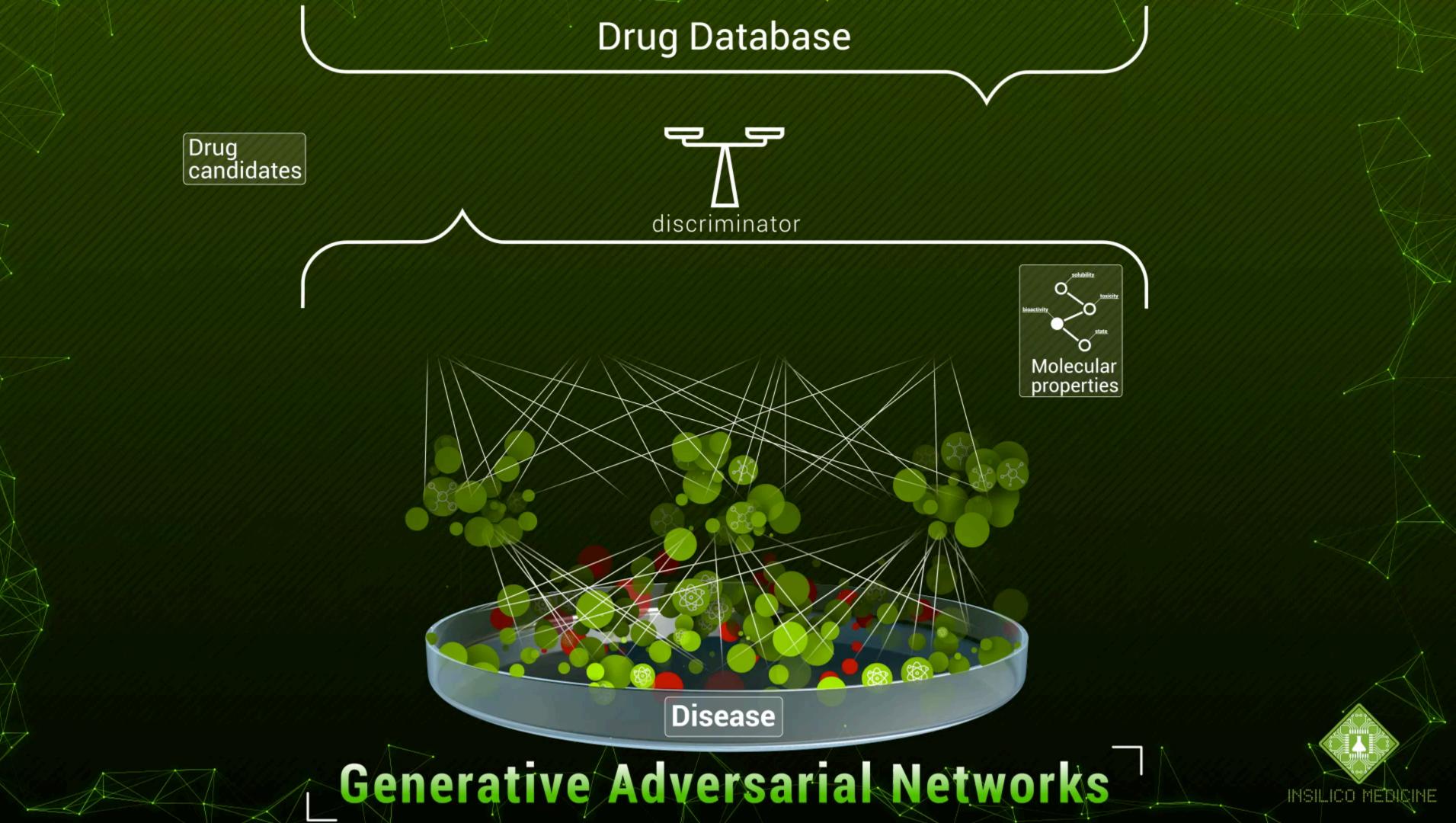






64 Shares

Share



WE NEED NEW STRATEGIES FOR RAPID VALIDATION

WE ARE BRIDGING THE PHARMACEUTICAL AND **CONSUMER INDUSTRIES**

Α

0-0

0-0

DRUG DISCOVERY

BIOMARKER DEVELOPMENT

AGING RESEARCH

PERSONALIZED **MEDICINE**

HEALTH & MEDICINE

BEAUTY

COSMETICS

NUTRITION

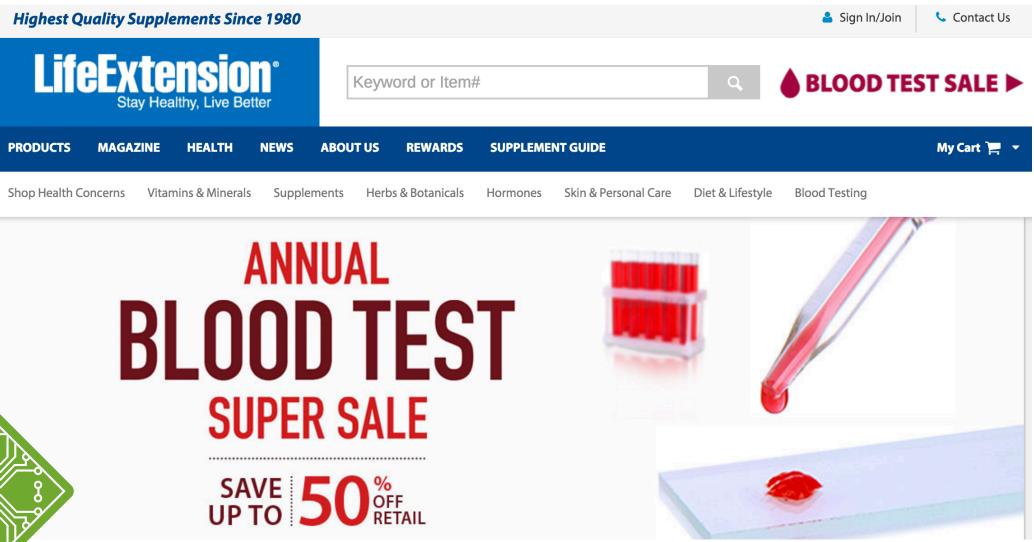
RECOMMENDATION **ENGINES**

CONSUMER INDUSTRY

EXAMPLE: NATURAL COMPOUNDS WITH SUBSEQUENT BLOOD TESTING



www.geroprotector.com







www.lifeextension.org

EXAMPLE: NATURAL COMPOUNDS WITH SUBSEQUENT BLOOD TESTING



25 weeks



ONE ORGAN, WHERE WE CAN VALIDATE QUICKLY IS SKIN

HAPPY TO ANNOUNCE THAT INSILICO KOREA WILL BE FOCUSED ON SKINCARE

CAN WE FORCAST BEYOND 5 YEAR HORIZON?



HOW WILL THE FUTURE LOOK LIKE IN 5 YEARS?



along the R&D pipeline to optimize the discovery and development of novel

therapies with better outcomes, faster and more cost effectively.

Other Companies include:



Apply AI to De-Risk Drug Discovery and Development

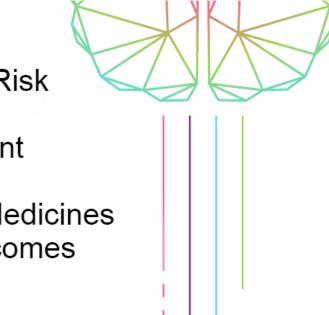
Deliver Better Medicines with Better Outcomes Faster & More Cost Effectively



Alex Zhavoronkov CEO **Insilico Medicine**



Guido Lanza CFO Numerate



Confirmed Speakers Include:





Numerate



Jason Raines Head, Biometrics Data Sciences & Operations Biogen



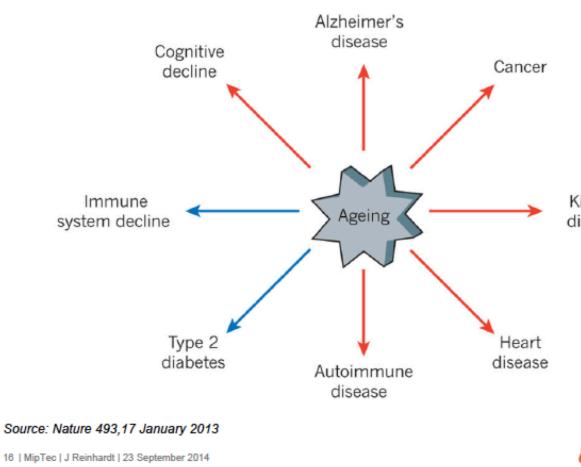
Ranga Sarangarajan Senior Vice President & CSO BERG



Shahar Keinan CSO Cloud **Pharmaceuticals**

4th ANNUAL AGING FORUM 1st AI & BLOCKCHAIN FOR DRUG DISCOVERY FORUM AT BASEL LIFE

Better understanding of mechanisms involved in ageing will help to address many different diseases



- 4th Annual International Aging Research for Drug Discovery Forum, Basel, Basel Congress Center, September 12-13 (with GSK)
- 1st Artificial Intelligence & BlockChain for Drug Discovery Forum, Basel, Basel Congress Center, September 13-14 (with NVIDIA) www.BaselLife.Org

b NOVARTIS

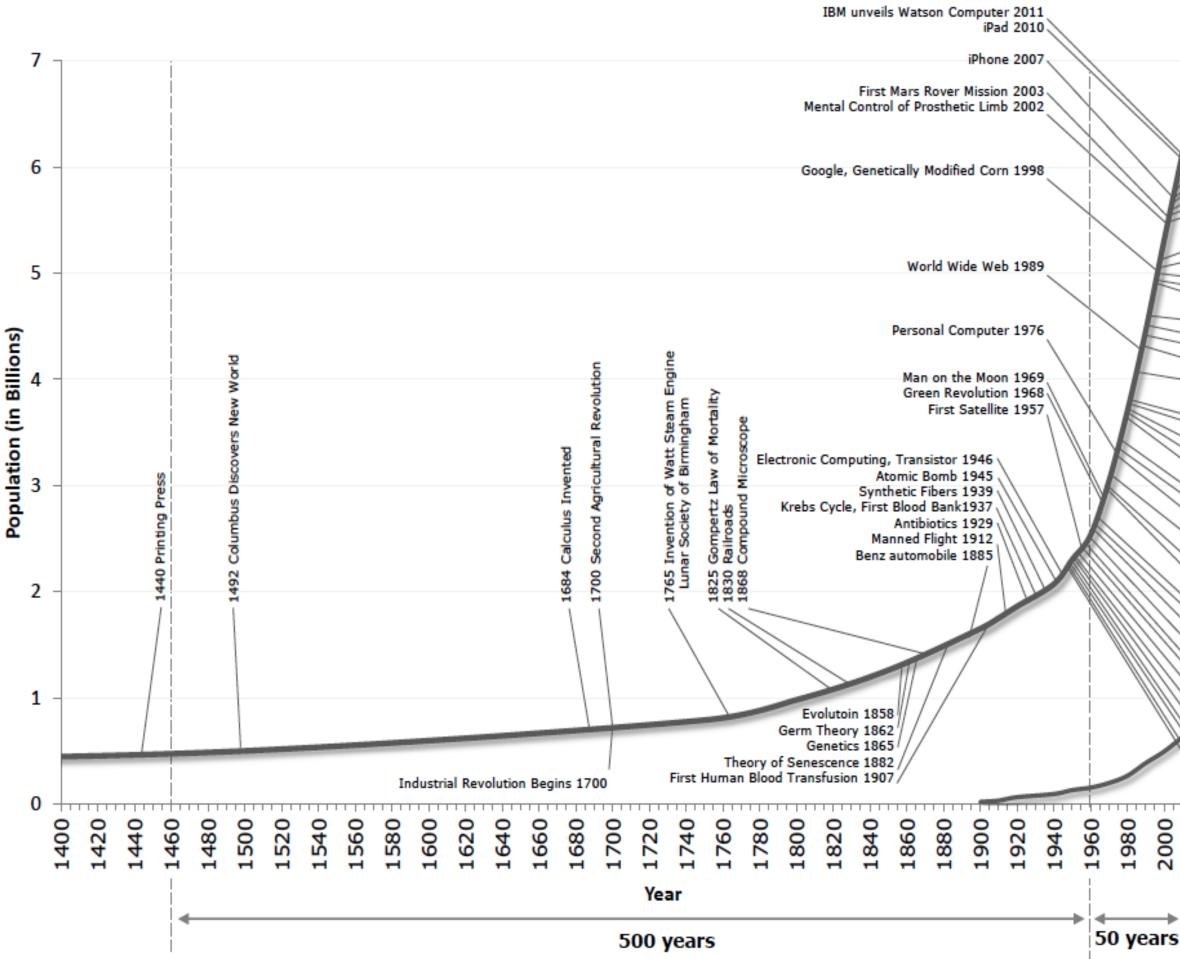
Kidney disease



SUPPORT SLIDES

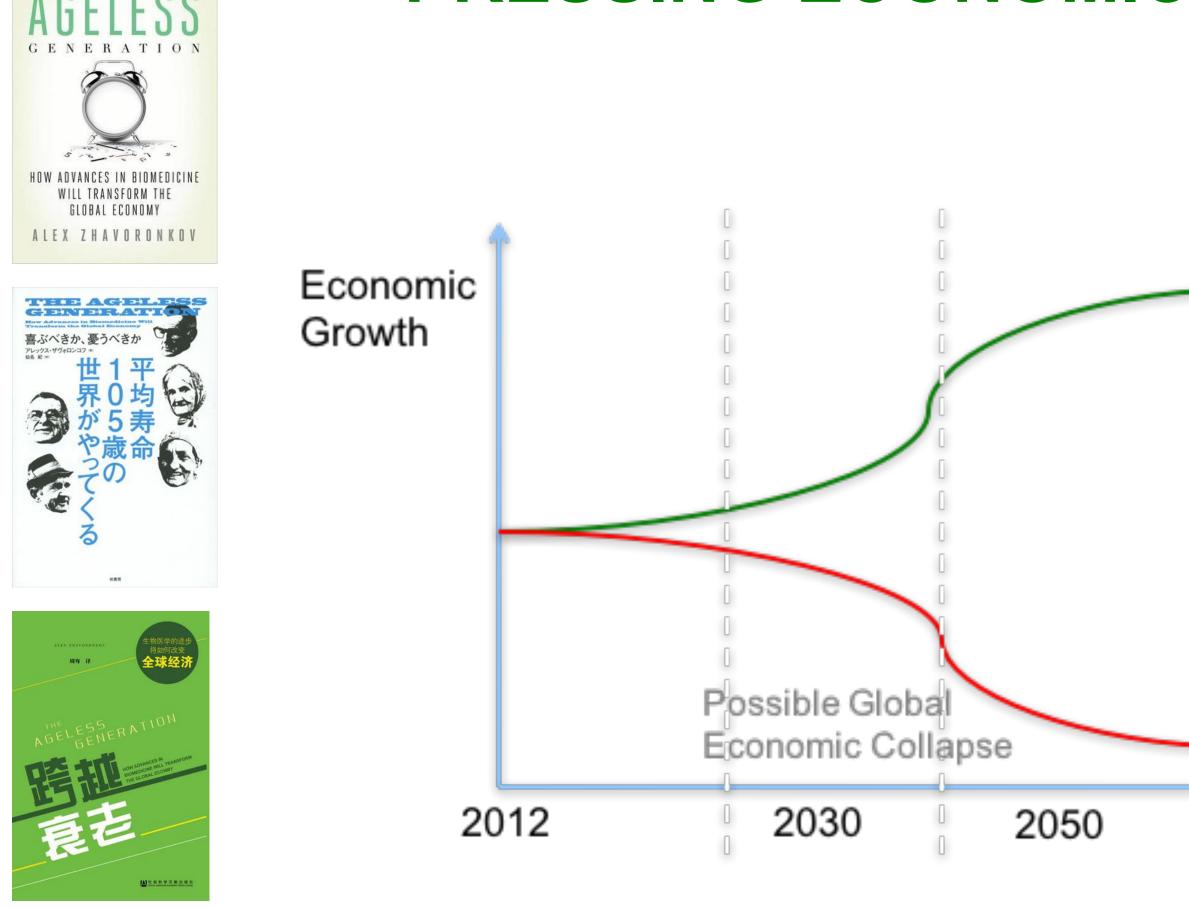


World population and Elderly population (>65)



- 2011 First Transplant of Lab Grown Trachea, Skin turned into Beating Heart Cells 2010 Intestinal Tissue Grown from Stem Cells, Skin Transformed into Blood Cells Stem cells used to Grow Teeth in the Mouth, Embryonic Stem Cells turned into
- Retinas, Synthetic Bacterial Cells, p21 and Relation to Regeneration
- 2009 First Methods Developed to Create iPS without the use of Retroviruses
- 2008 Personal Genomics goes Mainstream,
- Human Embryonic Stem Cell Lines Generated without Destruction of the Embryo
- 2007 Induced Pluripotent Stem Cells (Human)
- 2006 Human Vision Improves from Transplanted Stem Cells,
- First Artificial Liver Grown from Stem Cells
- 2004 Evidence of Stem Cell-Based Disease Therapy Potential
- 2003 Completion of Human Genome Sequencing
- 2002 Adult Stem Cells are shown to have the Capacity to Differentiate into Unrelated Cell Types like Nerve and Blood Cells
- 1999 First Artificial Lab-Grown Bladder Transplanted into Dogs
- 1998 Construction Begins on International Space Station, RNA Interference, First Embryonic Stem Cells from Humans Mice Cloned using Nuclear Transfer, First Human Embryonic Stem Cells (hES) are Isolated
- 1997 Proof of Concept for Epigenetic Reprogramming
- 1996 Dolly the Sheep is Cloned
- 1995 Hepatitis A Vaccine
- 1993 Identification of Longevity Genes
- 1992 First Cultivation of Neural Stem Cells In Vitro
- 1991 Discovery of APOE4
- 1990 Gene Silencing, microRNA, Discovery of Amyloid Precursor Protein (APP)
- 1988 Experiments Showing that Manipulating One Gene is Enough to Convert Skin Cells into Muscule Cells
- 1984 Discovery of Telomereses and Telomerase
- 1983 Polymerase Chain Reaction (PCR), Discovery that Mammalian Cell Differentiation is Reversible
- 1982 First Artificial Heart Transplant (Human)
- 1981 Hepatitis B Vaccine, Derivation of Embryonic Stem Cells from Mice Mouse Embryonic Stem Cells Described, First Recombinant Human Growth Hormone 1980 Ribozymes
- 1978 In Vitro Fertilization, Discovery of Haematopoietic Stem Cells
- 1977 DNA Synthesizing Machines, DNA Sequencing, Introns, RNA Splicing
- 1976 Genentech Biotech Industry, Complete Bacteriophage Nucleotide Sequence Determined
- 1973 Recombinant DNA, First Successful Bone Marrow Transplant, Recombinant DNA Technology, First Statin
- 1971 Intel Silicon Valley
- 1970 Reverse Transcriptase
- 1967 First Human Heart Transplant
- 1965 Hayflick Limit
- 1962 Frogs Cloned using Nuclear Transfer, Discovery that Adult Cells have all the Genes Necessary to Create an Organism
- 1960 First Documentation of Stem Cells
- 1959 Research Triangle Park
- 1958 Human Leukocyte Antigens
- 1957 First Artificial Heart Tranplant (Dog)
- 1956 Free Radical Theory of Aging, Discovery of Angiotensin-Converting Enzyme (ACE), First Successful Bone Marrow Transplant
- 1954 First Kidney Transplant Between Identical Twins
- 1953 DNA Discovered, First Heart-Lung Machine (Human)
- 1952 Polio Vaccine
- 1951 HeLa Cell Line Derived
- 1950 Beta Blockers

AGING IS WORLD'S MOST IMPORTANT AND PRESSING ECONOMIC CHALLENGE



 Accelerate Aging Research & Mass Adoption of Preventative and Regenerative Strategies

- Proactive Increase of Retirement Age
- Lifelong Learning & Career
 Planning

- Longevity gains from prior research
- Retroactive adjustments in retirement age
- Massive austerity measures

