Eugene Consulting Inc.
111 St. Clair Ave W
Toronto, ON
M4V 1N5

February/March 2020 Report

Bill Gates talk at American Association for the Advancement of Science
https://geneticliteracyproject.org/2020/03/03/bill-gates-ai-gene-editing-could-help-us-reach-global-health-goals-exponentially-faster/ - February 15, 2020

- During his keynote address at the annual meeting of the American Association for the Advancement of Science, Bill Gates spoke about how advances in AI and gene editing could accelerate improvement of the state of global health
    - AI and gene editing will be key in to build a new generation of health solutions that are available to everyone
- To fight malaria and other mosquito-borne diseases, CRISPR-Cas9 and other gene-editing tools are being used to change the insects' genome to ensure that they don't pass along the parasites that cause those diseases
    - The Gates Foundation is investing tens of millions of dollars in technologies to spread such genomic changes rapidly through mosquito populations
- For sickle-cell disease Gates' vision is to have in-vivo gene editing techniques where you do a single injection using vectors that target and edit blood-forming cells with high efficiency
    - A similar in-vivo therapy could provide a "functional cure" for HIV patients
- Gates stated that the computational power available for AI applications has been doubling every 3 and a half months on average
- Organ on a chip models – technology that allows in-vitro modeling of human organs in a way that mimics how they work in the human body
    - A proposed model that would accelerate the pace of biomedical research, without putting human experimental subjects at risk
- The Gates Foundation has backed a number of organ-on-a-chip projects over the years
    - Including an experiment that uses lymph-node organoids to evaluate the safety and efficacy of vaccines
- Nortis – a Seattle based organ-on-a-chip venture has gone commercial thanks in part to Gates' support
- However, if the acceleration of medical technologies does manage to happen around the world, Gates also insists that could have repercussions – growing inequality between the rich and poor
    - "Disease is not only a symptom of inequality but it's a huge cause"

Eugene Consulting Inc.
111 St. Clair Ave W
Toronto, ON
M4V 1N5

Nortis
http://www.nortis.us
Company focus*:* opening the door to tissue-engineered microenvironmentsof human organs as an alternative to traditional in vitro tools and animal models in scientific research and drug development

- Nortis provides an efficient, affordable alternative to animal testing that can accelerate research and advance scientific exploration
- Their technology supports fluid flow, 3D tissue culture, and robust analysis in 1 scalable, user-friendly platform
- Nortis innovation makes it easy to:
    - Engineer a variety of 3D tissue microenvironments
    - Expose engineered tissues to flow and shear force via fluidic perfusion
    - Perform real-time visualization under variable conditions
    - Research human disease without relying on interspecies extrapolation
-

Technology
ParVivo Chips: Nortis' unique microfluidic chips

- About the size of a credit card and comes in different configurations for different organ applications
    - 1-3 experiments can be performed simultaneously
- These chips are used for growing microscopic human organs by seeding cells into tubular voids within extracellular matrix gels
    - 3D tubules are fully surrounded by matric allowing cells to self-organize into *in-vivo*- like structures
- Chip design offers the flexibility to generate a variety of tissue architectures based on cell types and matrix materials selected
- Each chip supports a wide range of readout methods including fluorescent microscopy, effluent analysis, permeability studies, histology, and gene expression analysis

ParVivo Perfusion System

- Consists of 12 small perfusion platforms – each the size of a well plate
- Each platform houses 1 ParVivo chip and supporting media reservoirs
- A standard cell culture incubator can house up to 24 perfusion platforms
- The ParVivo incubator gas pump powers the system and provides precise control of flow rates – the pump recirculates incubator air to maintain specific gas conditions without any additional consumables

Eugene Consulting Inc.
111 St. Clair Ave W
Toronto, ON
M4V 1N5

Other Leading Players

- Emulate
- TissUse
- Hesperos
- CN Bio Innovations
- Tara Biosystems
- Draper Laboratory
- Mimetas
- Micronit Microtechnologies B.V.
- Kirkstall
- Cherry Biotech SAS
- Else Kooi Laboratory

Using "organs-on-a-chip" to model complicated diseases

http://news.mit.edu/2020/organ-on-microfluidic-chip-0318 - March 18, 2020

- MIT biological engineers have created a multi-tissue model that lets them study the relationships between different organs and the immune system, on a specialized microfluidic platform seeded with human cells
    - Using this, the research team was able to explore the role of circulating immune cells in ulcerative colitis and other inflammatory diseases
    - They also discovered that a metabolic byproduct generated by bacteria living in the human gut plays an important role under these inflammatory conditions
- This leads to options to decrease or increase the level of disease complexity, under controlled and systematic conditions
- Their approach was published in the journal *Cell Systems*
    - Martin Trapecar, an MIT postdoc and lead author of the paper
    - Linda Griffith – the School of Engineering Professor of Teaching Innovation and professor of biological engineering and mechanical engineering is a senior author of the study
- In their paper in *Cell Systems*, Martin and Linda set out to model interactions between two organs – the colon and the liver
    - They also wanted to study how the immune system, especially T-cells, influences those organs
- They found that when these tissues were connected, their physiological behavior completely changed as compared to when they are isolated
    - Inflammation in ulcerative colitis gut tissue decreased when the tissue was exposed to healthy liver cells
    - At the same time, genes and cellular pathways involved in metabolism and immune function became more active in both organs

Eugene Consulting Inc.
111 St. Clair Ave W
Toronto, ON
M4V 1N5

    - Additing 2 types of T cells to the system (CD4+ T regulatory cells and TH17 cells) to the gut-liver interaction quickly increased inflammation and recreated certain features of both IBD and autoimmune liver diseases
- The new MIT study also found that adding SCFAs to the ulcerative colitis model greatly exacerbated inflammation throughout the liver and gut, but only if T cells were already present

Organ-chip platform enables new insights into human diseases and toxicity mechanisms

https://www.eurekalert.org/pub_releases/2020-03/tyn-ope031820.php - March 19, 2020

- Organs-on-Chips technology has entered the mainstream and reached 150 installations for use by researchers across many industries
- The 150 installations include customers in 10 of the top 25 biopharmaceutical companies and U.S. government laboratories
- Organ-chips currently available for use in the lab-ready platform developed by Emulate, Inc, = Liver-chip, kidney-chip, and new intestine-chip (launched commercially earlier this year)
- Ongoing R&D is supporting the development of additional organ-chips such as the brain-chip + new applications in key areas of biology and diseases (ex. applications in neurodegenerative disease, gastrointestinal diseases, and infectious diseases such as COVID-19)
- Researchers can culture the organ-chips using Emulate's portfolio of protocols, enabling research to understand how the human body responds to disease, medicines, chemicals, and foods
    - The lab-ready platform recreates key factors of the body's dynamic cellular microenvironment, including tissue-to-tissue interfaces, fluid flow, and mechanical forces
- Emulate's lab-ready platform allows researchers with no experience with organ-on-chips to conduct studies, using the platform's supporting protocols and software to collect, analyze, and share data
    - This platform integrates into the workflows of researchers developing new drugs and products
    - This can help them assess safety risks and make informed, efficient decisions throughout the drug discovery and development process

Emulate's platform includes:

- Organ-chips that have a proprietary design to support dynamic cellular interactions that mimic the appropriate microenvironment cells need for accurate biological translation

Eugene Consulting Inc.
111 St. Clair Ave W
Toronto, ON
M4V 1N5

- Zoe Culture Module – a lab-ready instrument that automates the dynamic flow of cell culture media and the mechanical forces required for any user to work with organ-chips in a robust and reproducible manner
    - Can run up to 12 organ-chips at the same time
    - Is powered by the Orb Hub Module which provides the precise required mixture of gas, power, and vacuum stretch
- Experimental applications content that provides users with protocols, study plans, and representative data sets for specific applications of the platform
- Software applications that enable study design and management, data analysis, integration with standard analytical tools, and collaboration among teams using the platform

- Emulate's lab-ready platform was inspired by a $37 million grant from the Defense Advanced Research Projects Agency (DARPA) in 2012 to the Wyss Institute for Biologically Inspired Engineering at Harvard University to create organ-chips
    - This research enabled the development of chips with a level of human-relevant biological complexity not feasible with conventional cell-based systems
    - Based on the success of this early research, Harvard established a worldwide license agreement to form the start-up company, Emulate (the company became operational in January 2015)
- Emulate's platform could be used in other industries such as cosmetics, food, chemical-based consumer products, and personalized health, to allow new understanding of human response to products

Emulate Inc.
https://www.emulatebio.com
- Emulate Inc, is a privately held company that creates living products for understanding how diseases, medicines, chemicals, and food affect human health
- Their lab-ready platform provides a window into the inner workings of human biology and disease
- Emulate's proprietary organ-chips contains tiny hollow channels lined with tens of thousands of living human cells and tissues and are about the size of an AA battery
    - An organ-chip is a living, micro-engineered environment that recreates the natural physiology and mechanical forces that cells experience within the human body

Organ-on-chips Market to growth speculation
https://www.whatech.com/market-research/industrial/641595-organ-on-chip-market-to-grow-170-million-by-2023-cagr-of-63-2-according-to-a-new-research-report

Eugene Consulting Inc.
111 St. Clair Ave W
Toronto, ON
M4V 1N5

- The global organ-on-chip market was valued at $5 million in 2016 and is projected to reach at $170 million by 2023
- Heart-on-chip segment is anticipated to witness the highest growth rate during the forecast period
- North America was the highest revenue contributor in the global market in 2016
- Rise in demand for lung- and kidney-based organ culture devices is expected to boost the market growth
- Asia-Pacific is anticipated to witness a significant growth rate during the forecast period

https://siliconcanals.com/news/british-cell-culture-company-funding/

- Cambridge-based CN Bio Innovations = one of the leading bioengineering companies specializing in innovative lab technologies
    - Led by Dr. David Hughes
    - They aim to provide systems that generate clinically translatable data that can enhance the development of tomorrow' medicines
- Recently, CN Bio Innovations raised $9 million funding in a round led by CITIC Securities Investment Co. Ltd.
    - With this, they will focus on the commercial development of its products
    - They also intend to strengthen its position in the U.S (its key market) and expand operations across Europe