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October/November 2020 Report

Update on Deep Genomics

- Since receiving a $40 million series B round, the company has been identifying new drug targets across multiple diseases areas
- The company has since turned up many more prospects than it can pursue on its own
    - Therefore, partnering with other companies has become an essential component to their business strategy
- Brendan Frey, the CEO of Deep Genomics, explains how they had always planned to open up an office into the biotech hotbed of Boston, and that the pandemic actually lent a helping hand with this
    - New norms around remote work and virtual meetings made it easier for Deep Genomics to start recruiting there
- The company's work is based on its AI Workbench – a platform made up of about 30 different machine learning systems, combining deep learning, automation, advanced biomedical knowledge and huge amounts of in vitro and in vivo data

Synex Medical

https://betakit.com/synex-medical-raises-6-99-million-cad-seed-round-for-health-monitoring-technology/ - Oct. 29, 2020

- Synex Medical is a Toronto-based healthcare startup, which offers a wearable solution that measures blood metabolites
    - The wearable device tells the user how their body is performing by measuring the metabolites that affect everything from weight gain to athletic performance to the likelihood of developing diabetes in real-time
- They have raised a $6.99 million CAD seed round of financing
    - The seed round was led by Accomplice – a Boston-based seed venture capital firm
    - Previous investors: Radical Ventures and angel investor Naval Ravikant also participated
    - This will be used to grow Synex Medical's team and support the startup's expansion to the U.S.
- CEO and co-founder Ben Nashman has stated that they are expanding their operations to Boston
- The company was founded in 2017 and their technology is based on magnetic resonance – the same principle used in magnetic resonance imagining
    - The technology is aimed to non-invasively and accurately measure critical blood metabolites like glucose, lactate, and ketones

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XtalPi

- XtalPi is a pharmaceutical technology company that is reinventing the industry's approach to drug research and development with its Intelligent Digital Drug Discovery and Development (ID4) platform

Their Software

XtalForce

- XtalForce is a visual force field calculation software that allows you to either use a general force field to complete simulations, or obtain force field training set from quantum mechanics calculations on one's unique compound library, and train a tailor force field suitable for one's specifical chemical space
- Through the visual interface, users can intuitively operate the molecules, and can click to view the specific parameters corresponding to each term in the molecule
- The user can submit a quantum mechanical calculation task to the cloud, call a more massive computing cluster to shorten the calculation time, and use variable analysis charts to judge the behavior of the calculation result
- The system can connect to the open source database containing millions of molecules and thousands of quantum mechanical data

XtalVision

- XtalVision is a smart tool for delivering crystal structure prediction reports
- All the calculated structures are shown with basic information and 3D visualization
- One can click at the data point in the figure to get more information such as crystal structure, the relative lattice energy, density space group number, cell parameters, and XRD pattern
- One can click on the label of the corresponding torsion angle to see the distribution with a polar coordinate system

Renova

- Renova provides platform support for XtalPi AI Research Center (ZARC) and its AI drug R&D efforts
- The platform helps researchers effectively manage projects through graphical interface by supporting tools integration, computational process management, team collaboration, and other aspects
- Systematization facilitates the use of various AI prediction models and visualization of calculation results, which helps accelerate the discovery of new drugs and avoid the molecular defects that can only be found in the clinical stage as early as possible
- Renova provides various AI models related to new drug discovery, including activity and ADME/T predictions, new drug scaffold design, new binding pocket discovery, and the management of associated computational results

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- Renova also provides complete and customizable computing process support, where users can build customized R&D workflows based on specific needs, assemble models, and analyze the predicted results
- It also provides users with customizable reports to help analyze the results efficiently and quickly
- Renova support teamwork by allowing data sharing with designated authentication/authorization and computational results sharing

Key Services

- **Crustal Structure Prediction** – an integrated approach that effectively accelerates the solid-state research and decision-making process to reduce the overall risk in late-stage development
    - By combing CSP with experimental screening, researchers can judge with greater confidence whether the current experimental screening is sufficient, verify the purity of the selected crystal powder, and understand the stability risk of crystal forms obtained in the laboratory
- **Solid-State Screening and Evaluation** – A comprehensive screening that optimizes patent protection and lifecycle management which increases the long-term value of a drug
- **Crystal Structure Determination** – XtalPi has developed a crystal structure analysis technology based on the experimental data and theoretical methods, which can obtain the 3D structure information of drug solids that are traditionally hard to determine solely by experiments
    - With a small amount of solid powder of XRPD spectrum, the 3D structure information can be easily obtained
    - In cases where one has a limited amount of time and material available, this computational analysis could effectively assist in determining the ideal solid form of the drug candidate for early-stage drug development and discovery projects
- **Crystallization Process Development** – Improves the crystallization operation yield
    - Significantly optimize the solvent residue, particle size distribution, bulk density, and other powder properties of API products to improve the overall quality and added value of products
- **Solid-State Testing and Analysis** – XtalPi's Rational Drug Design and Development Experimental Center offers a variety of chemical solid state characterization services
    - Including: X-ray diffractometer (XRD), Thermogravimetric analysis (TGA_, Differential scanning calorimetry (DSC), Dynamic vapor sorption analysis (DS), and Hot stage microscopy (HSM)
- **Small-Molecule Drug Design** –

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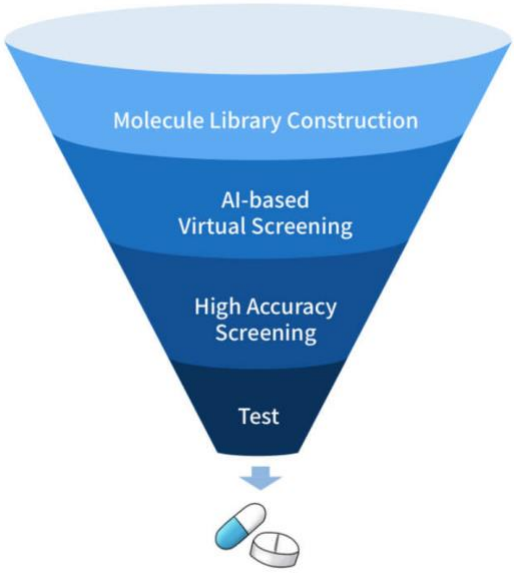
- XtalPi's ID4 platform provides accurate predictions on the physiochemical and pharmaceutical properties of small-molecule candidates for drug design, solid-form selection, and other critical aspects of drug development
- They offer innovative R&D technologies such as, general force field development for drug-like molecules, high-accuracy binding affinity prediction, and AI-based molecule generation, that can accelerate drug discovery and increase pipeline success rate
- XtalPi provides a variety of drug design solutions such as hit identification, hit-to-lead/lead generation, and lead optimization
- Their methods are capable of generating million of new candidate compounds for desired targets, accurately predict their properties like the biological activity, target selectivity, and draggability
- They help their clients accelerate the small-molecule drug discovery and development, reduce R&D costs, and improve the overall success rate of projects
- They have also developed the cloud-based platform to support their ID4 platform
  - Based on this, they provide a variety of automated, efficient, and intelligent drug discovery services
- The company was founded in 2014 by a group of quantum physicists at MIT

Hit Identification Service

- For a specific target, the first step in the drug discovery process is the identification of hit compounds
- Small molecules with novel core structures and reasonable biological activity can be obtained through methods such as high-throughput screening, virtual screening, and de novo design
- XtalPi's service helps:
  - Generate synthesizable molecules with novel core structures and chemical diversity
  - Rapidly filter the compounds using a wide array of descriptors
  - Rank the compounds, cluster the structures, and perform basic SAR analysis



Lead Generation Service

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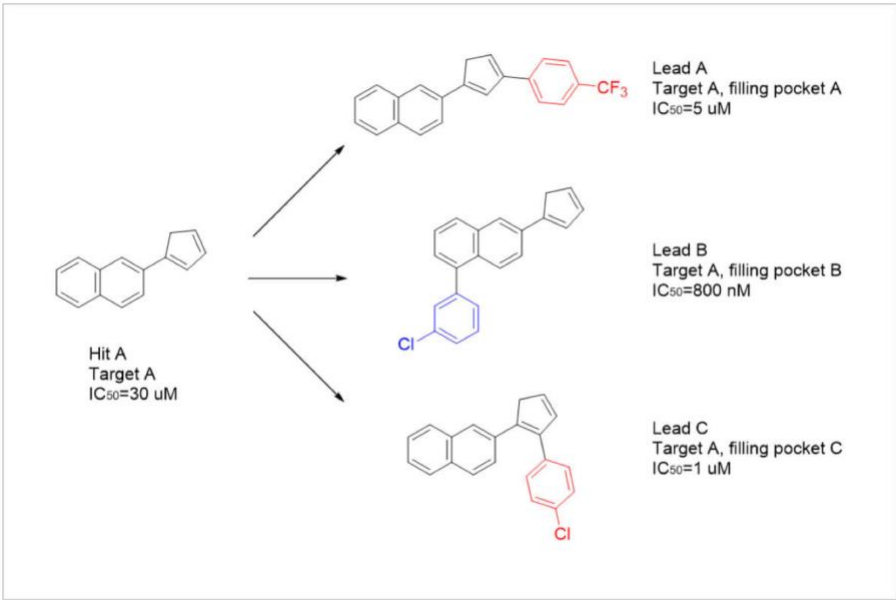
- The next step in the drug discovery process is lead generation – also known as hit-to-lead optimization
  - Starting from the hit compounds emerged from the earlier stage, a combination of scaffold hopping, R-group substitution, structural simplification, and molecular hybridization can be used to modify the structures of hits to achieve better potency, selectivity, and drug-like properties
- XtalPi's service helps:
  - Intelligently design derivatives of hits
  - Rapidly filter compounds using a wide array of descriptors
  - Accurately predict the physiochemical and drug-like properties
  - Accurately predict the binding affinity of newly designed molecules



Lead Optimization Services

- The last step before arriving at a clinical drug candidate is the optimization of lead compounds
- The structures of the drug candidates are modified to fully enhance their selectivity, physiochemical and ADMET properties, while maintaining their biological activity
- Eventually, a safe and effective preclinical candidate compounds is obtained
- The traditional lead optimization process usually costs a significant amount of time and resources, no matter whether it is related to the development of me-too, me-better, or first-in-class drugs
- XtalPi's service helps:
  - Generate structures of novel drug candidate with similar scaffolds

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- Accurately predict the physiochemical and drug-like properties
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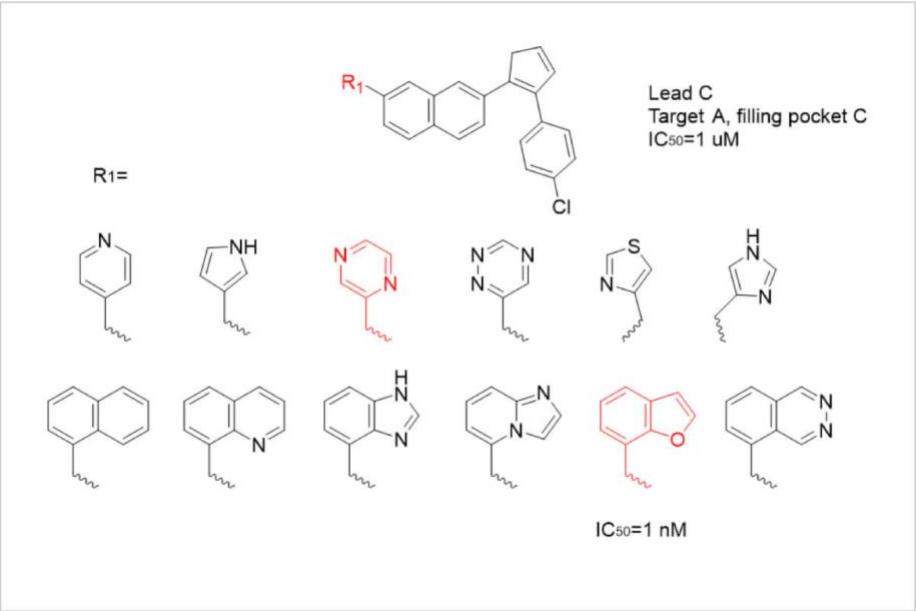

- **Peptide R&D Collaboration** – XtalPi AI Research Center (XARC) provides active peptide generation, prediction, and recommendation solutions that are based on AI< theoretical calculation, and cloud computing, which can effectively improve R&D efficiency and shorten the peptide drug R&D cycle
    - The peptide sequence generational module (XARCP Io algorithm) is based on the deep learning algorithm
    - Combined with a large-scale databse of peptide sequences and properties, XARC IO can rapidly generate million of new peptide sequences and cover the physiochemical properties space of desired peptides
    - The machine-learning-based peptide function prediction mode, XARCP, is combined with expert judgement model, to quickly screen and recommend candidate peptide sequences
    - XARC's peptide drug design and function prediction services can be used for the rational design, prediction, and refined multi-dimensional analysis of various types of peptide compounds, including antihypertensive peptides, HIV inhibitory peptides, neuropeptides, hemolysis peptides, anti-parasite peptides, anti-cancer peptides, antimicrobial peptides, cell-penetrating peptides, anti-viral peptides, peptide hormones, the blood-brain barrier peptides, anti-angiogenic peptides, and toxic peptides.
    - With feedback from further experimental results, the model can be optimized in future iterations for increased screening efficiency

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- **Antibody R&D Collaboration** – CADD+AI prediction method can assist the development of antibody drugs, significantly speed up the R&D process, improve the success rate, and reduce the cost and risk
- **Customized AI Model Development** – XtalPi offers correlation analysis between sequencing data and phenotypes as well as drug-target-disease association analysis
    - XtalPi has developed an AI-empowered process optimization method which is applicable to a variety of scenarios, including synthesis, cell culture, and screening of crystallization conditions
    - They also offer deep-learning-based analysis service of experimental results to get fast results on experimental statistics such as cell count, cell size and shape measurements, and more
    - They provide technical consultation and customized system and model development services so that users can effectively utilized digital and intelligent tools to address their needs
    - XtalPi provides both cloud and local deployment options for different users to reach an optimum balance between efficiency, cost, and security based on their needs

Xtalpi raises $318M from Softbank, Tencent, and others
https://www.fiercebiotech.com/medtech/ai-drug-molecule-designer-xtalpi-raises-318m-for-digital-twin-simulation-efforts - September 28, 2020

- Artificial intelligence=based drug molecule designer, XtalPi, has secured a series C funding round totaling $318.8 million
    - The round was co-led by SoftBank's Vision Fund 2, PICC Capital and Morningside Venture Capital
    - Follow-on investments were also made from the company's previous backers, Tencent, Sequoia China, China Life and SIG
    - This will help XtalPi expand the reach of its AI and cloud computing-powered platform
- By integrating its virtual R&D work with real-world laboratory testing data, the company aims to develop a new digital twin simulation system for modeling the activity of potential new drugs, making it easier for biopharmaceutical companies to pick the best candidates for clinical studies
- The company states that it plans to take a "three-pronged approach" to expanding its platform by simultaneously developing its algorithms, drug-like molecule database, and computing power
- Currently, XtalPi's system incorporates over 100 algorithms to predict the interactions between molecules and proteins at the atomic level and map out its pharmacologic properties
- By tapping international cloud-computing providers, the company assembles supercomputing clusters consisting of over a million processing cores

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- The company technology platform combines quantum physics, AI and cloud computing, to improve the efficiency and accuracy of drug research and development

Microsoft, Illumina, and Twist forms an alliance to make big data small
https://www.fiercebiotech.com/medtech/microsoft-illumina-twist-work-to-make-big-data-small-weaving-it-into-dna-archives - November 13, 2020

- Microsoft, Illumina, Twist Bioscience, Western Digital among others to establish a roadmap for the industry toward the wider use of DNA data storage
    - This alliance was announced at the virtual Flash Memory Summit
    - The goal of this alliance is to set technology and formatting standards with the goal of building interoperable commercial systems capable of housing the exponential amounts of data expected to be generated in the future
- Their plan is to use the idea that DNA is an incredible molecule that, by its very nature, provides ultra-high-density storage for thousands of years
- To store data in DNA, a file is converted from its binary sequence of ones and zeros into the four labelled compounds that make up out genomes: A's, C's, T's, and G's.
    - The information is then broken up into short segments of 200 to 300 genetic bases which are tagged to an index, synthesized and stored
- The companies estimate that 10 full-length movies could be written into DNA molecules and packed to a volume the size of a grain of salt and that this can last for a very long time under the proper conditions in capsules or glass beads
- By mirroring biologic processes, DNA data can also be cheaply and quickly duplicated and read
- In a collaboration with University of Washington, Microsoft demonstrated a fully automated end-to-end system capable of storing and retrieving data from DNA
    - They have also separately stored 1GB of data in DNA synthesized by Twist and recovered data from it
- Twist Bioscience, Illumina, Western Digital and Microsoft will serve as founding members of the DNA Data Storage Alliance, and are joined by Ansa Biotechnologies; Catalog; DNA Script; Imec; Iridia; Molecular Assemblies; and the Molecular Information Systems Lab at the University of Washington—as well as The Claude Nobs Foundation, which works to preserve audiovisual recordings through the Montreux Jazz Digital Project, alongside the Swiss Federal Institute of Technology's locations in Lausanne and Zurich.