

Data driven insights for improved drug development

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Drug development: Lengthy, expensive and risky



Current likelihood of success limited - based on trial and error:

5.1%

Oncology*

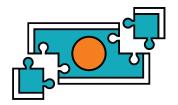
11.1%

Autoimmune / inflammation*

Development costs

\$1.78B

Doubled in the last 10Y



Development time

13.5Y

6-7Y in the clinic

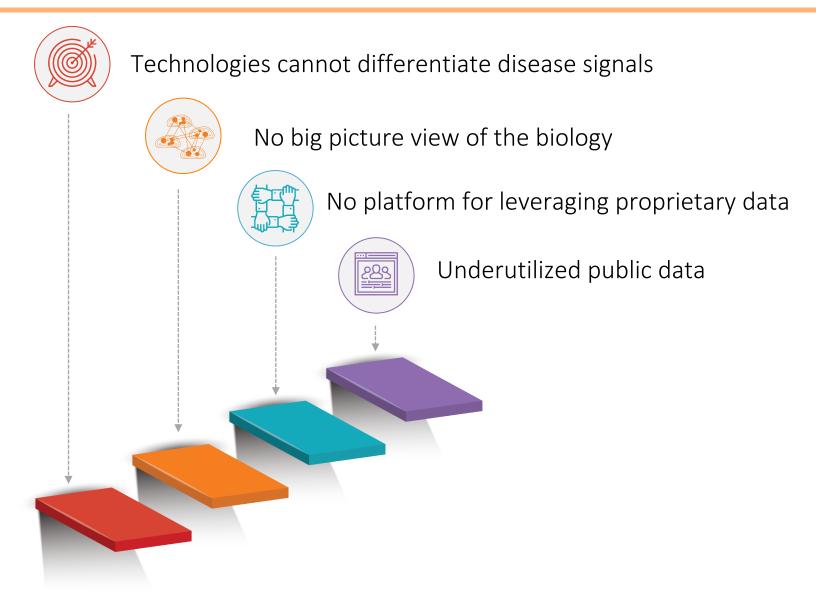


Identifying the existing gaps can push these rates much higher

The gaps preventing higher success rates







CytoReason is using its machine learning cell-centered-model, trained on proprietary and public data...



...to support discovery, pipeline and portfolio decision-making

CytoReason in a nutshell





Founded Oct '16

located in Tel Aviv



Based on 10 years' research from

Stanford and Technion



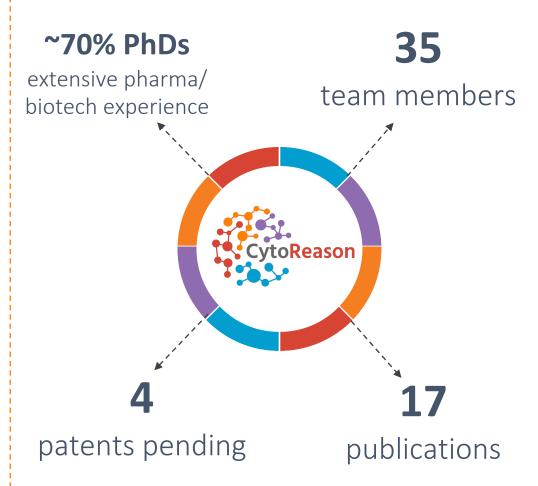
Revenue funded

from inception



8 collaborations

with the likes of **Pfizer**, **Janssen**, **GSK** and **Parker Institute for Cancer Immunotherapy**

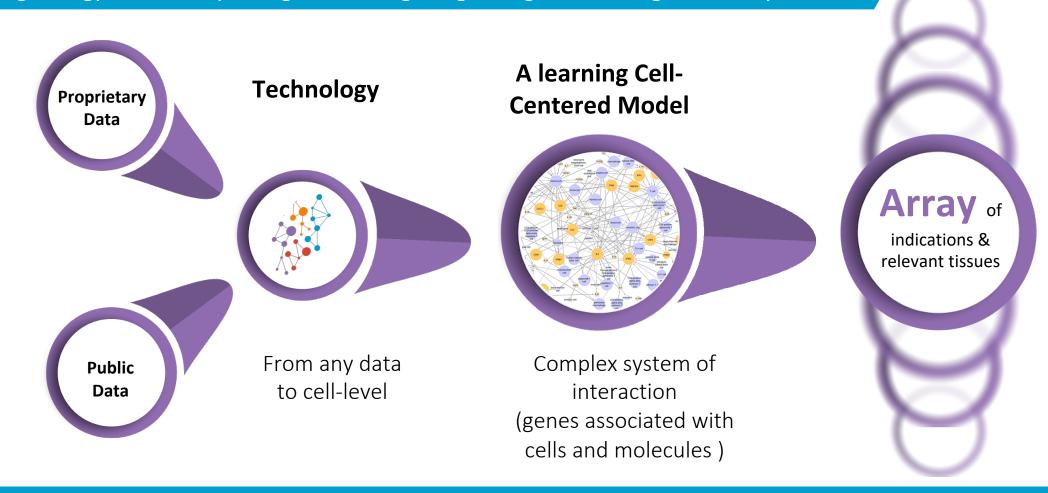


At the heart of it all: The CytoReason Cell-Centered Model



Built on a cellular level:

Replicating biology to crack key biological challenges – growing and learning from every data set



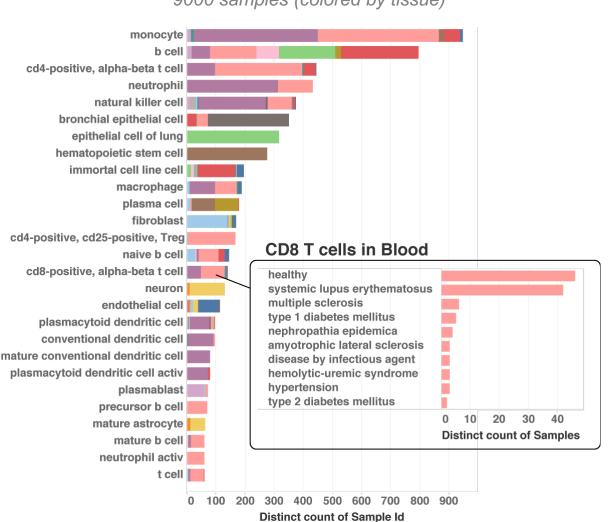
CytoReason's data assets

Cell signatures and disease / treatment references



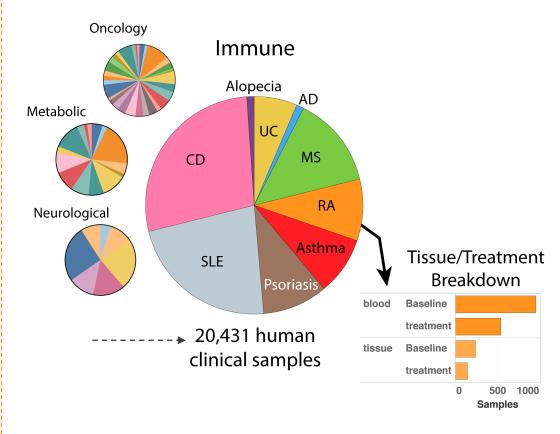
Cell Signature Database

9000 samples (colored by tissue)



Disease Reference Database

Human clinical samples (colored by disease)



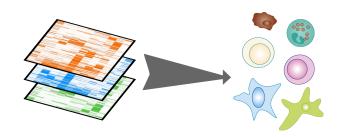
CytoReason's technology assets

The six building blocks



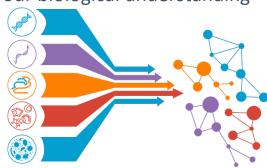
Deconvolution

Rebuilding cellular proportion and information from bulk measurement data



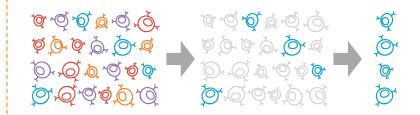
Multi omics

Integrating data types to improve our biological understanding



Cell Specificity

Removal of non-specific cell signals to reveal pure disease-related cell / gene maps



Disruption networks

Generating insights from small data sets



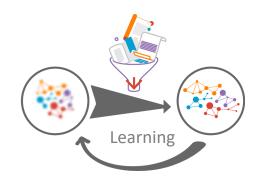
Natural Language Processing

Generating biological correlations from the literature



Statistical learning

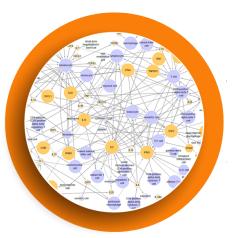
Incorporating prior knowledge to improve prediction power and accuracy



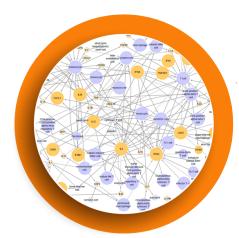
A cell-centered-model for each disease-related tissue

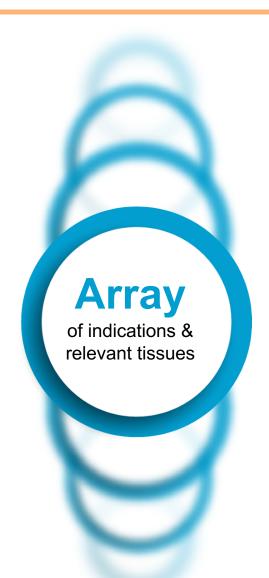


Psoriasis (lesion)

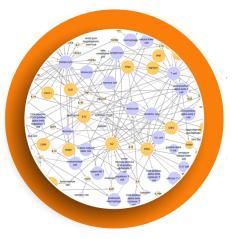


Melanoma (blood)

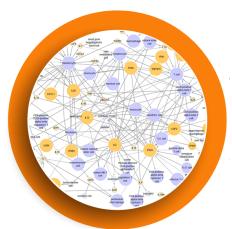




CRC (tumor tissue)

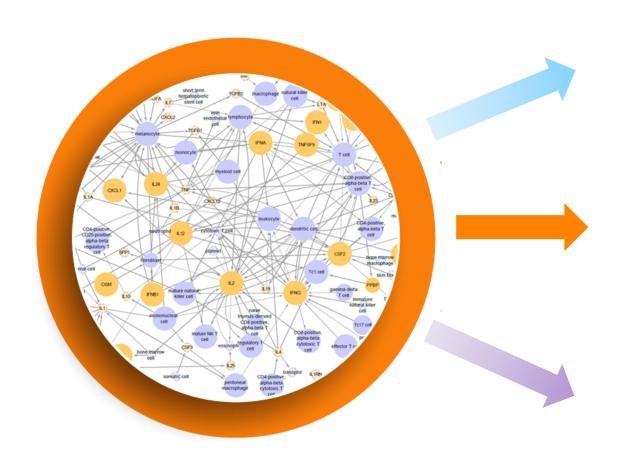


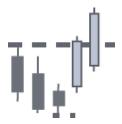
UC (inflamed tissue)



The critical questions our Cell-Centered Model can solve





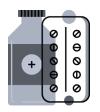


MODES OF ACTION

- Target identification
- Target validation
- Adverse events
- Combination therapy
- Multi-functional biologics

BIOMARKERS

- Disease sub-populations
- Disease severity
- Predictive biomarkers
- Companion diagnostics



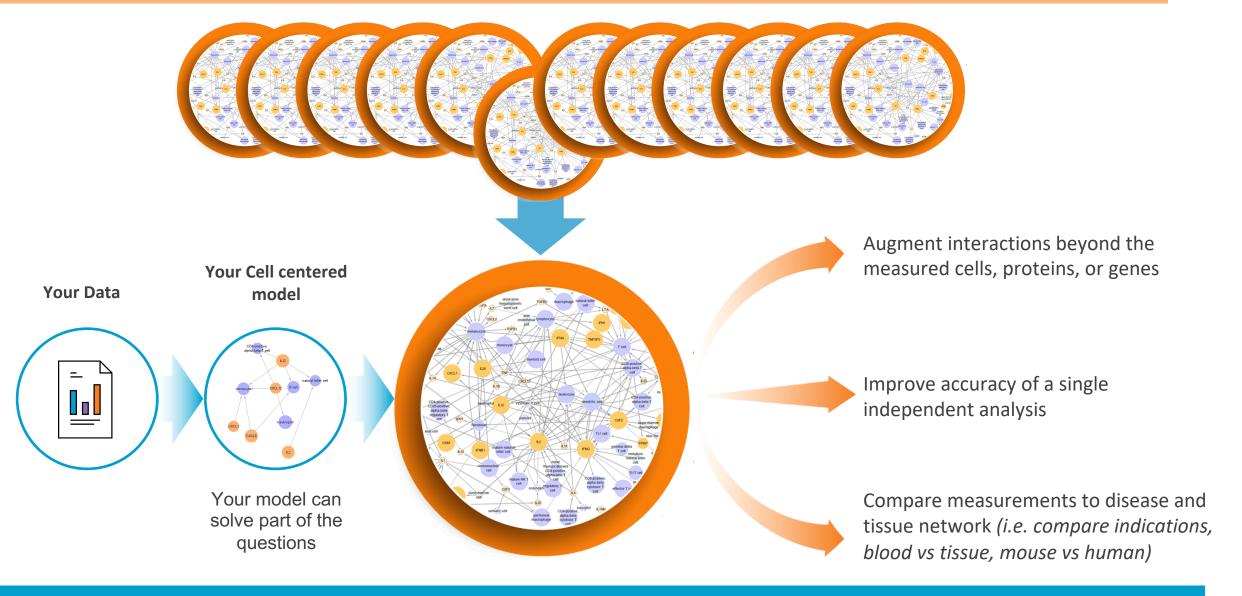
INDICATION

- Prioritization
- Expansion

CytoReason's two steps process



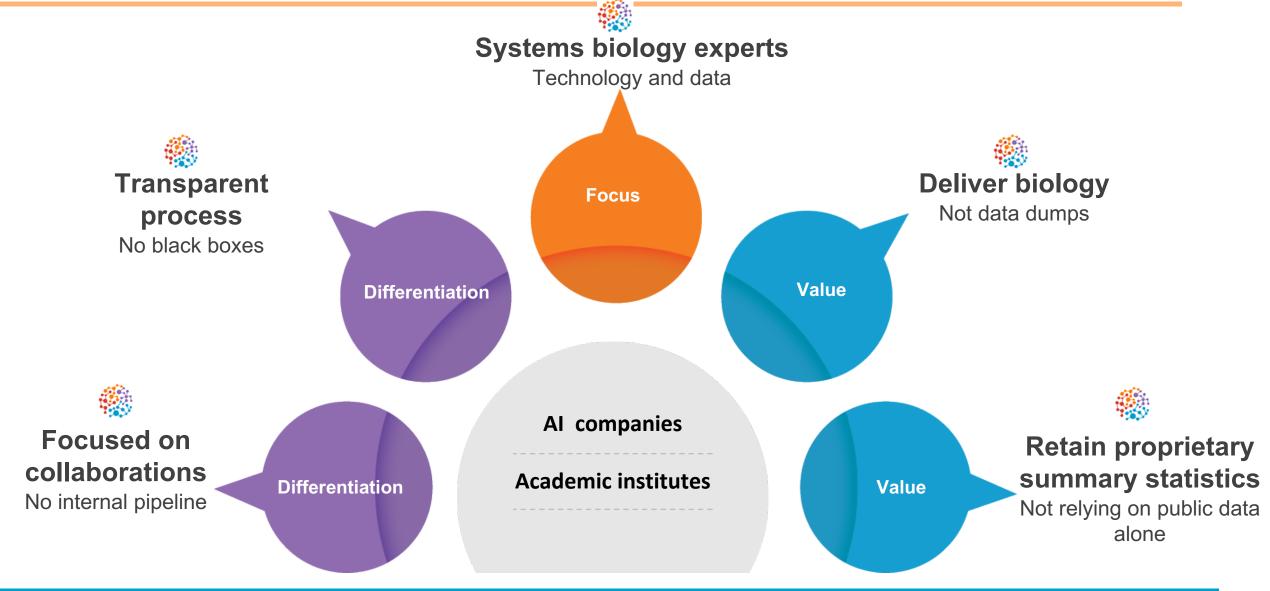




Competitive edge

Clear value, differentiation and focus







CytoReason as a partner

CytoReason collaboration plan



Technology PoC project *MoA. targets, indications*

MoA, targets, indications and biomarkers

Long term collaboration

MoA, targets, indications

and biomarkers

GOAL	Evaluate the model/technologies capabilities	Leverage CytoReason's model and know-how to support drug discovery and development
SCOPE	3-6 months, two projects	2-3 years, one or more parallel workstreams each with consecutive projects
OUTPUT PROVIDED PER PROJECT	Project report, presentation and interactive data visualization reports (which can be updated periodically)	Project report, presentation and interactive data visualization reports (which can be updated periodically)

Collaboration outline



Data retention – machine learning

- By the nature of the machine learning system, a summary statistics of the data will remain in the model
- No raw data or project-based questions and answers retained
- Strict data retention policy



Use of retained data

- Data cannot be backtracked
- No disclosure of the data source (company name)
- No disclosure of the drug tested
- No collaborator has access to CytoReason cell centered model



Intellectual property

- All IP arising from the collaboration will be assigned to the Collaborator upon IP option exercise
- Exclusions: Any improvements to CytoReason's model and/or technologies



Scientific Publications of Methods and Results



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A clinically meaningful metric of immune age derived from high-dimensional longitudinal monitoring *Nature Medicine, March 2019.*



The first ever method to reliably quantify a person's "immune age" providing a much more reliable predictor for the status of your immune system potentially leading to fundamental changes in drug & vaccine development and medical practice.



method

Found In Translation: a machine learning model for mouse-tohuman inference.

Nature Methods, November 2018.



Groundbreaking model translates the results of new mouse experiments into the equivalent human condition, outperforming traditional methods of extrapolation by up to 50%. Leveraging existing mouse and human gene expression data, the new approach demonstrates ability to uncover novel disease-related genes, providing new disease understanding and new targets for drug discovery.



Immune-centric network of cytokines and cells in disease context identified by computational mining of PubMed.

Nature Biotechnology, June 2018.



Immune-Focused AI Model Creates the Largest Library of Inter-Cellular Communications - Uses It to Predict 335 Novel Cell-Cytokine Interactions.

2018

application

Cell-centred meta-analysis reveals baseline predictors of anti-TNF α non-response in biopsy and blood of patients with IBD. *GUT*, 2018



Application of our deconvolution and machine learning methods to predict biomarkers of non-responders prior anti-TNF α treatment.

method

Alignment of Single-cell trajectories to compare cellular expression dynamics.

Nature methods, 2018



A new method for comparing expression dynamics within and between single-cell trajectories.

application

Multi-cohort analysis reveals baseline transcriptional predictors of influenza vaccination responses.

Science Immunology, 2017



Application of our cross-trial data integration used to identify novel gene biomarkers that are predictive of Influenza vaccination responders.

Integrated analysis of multi-modal immune data over three years of aging adults, detecting novel predictor

2017

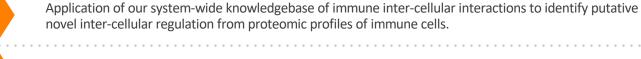
application

Social network architecture of human immune cells unveiled by quantitative proteomics.

Defective signaling in the JAK-STAT pathway tracks with chronic

Nature Immunology, 2017

Cell Systems, 2016



2016

application

A single-cell transcriptomic map of the human and mouse pancreas reveals inter-and intra-cell population structure. *Cell Systems*, 2016

inflammation and cardiovascular risk in aging humans.



of atherosclerosis burden.

A new method of gene expression deconvolution methodology used to infer cell specific expression profiles from heterogeneous biopsy data using single cell profiles.

method

CytoReason Ltd., Proprietary Information | Non-Confidential

Scientific Publications of Methods and Results (continued)



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method

application

method

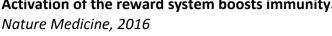
Tofacitinib for polyarteritis nodosa: a tailored therapy. Annals of the Rheumatic Diseases, 2016



Repositioning case study of tofacitinib for vasculitis with potential for companion diagnostic based on JAK-STAT baseline and response levels.



Activation of the reward system boosts immunity.





A new method of high dimensional cellular immune profiling coupled with novel algorithm for increased signal to noise detection.



Systems immunology reveals markers of susceptibility to West-Nile Virus infection. method

Clinical and Vaccine Immunology, 2015



A new method for identifying cell type specific gene expression differences, undetectable otherwise, via flow cytometry and NanoString data integration.



Systems analysis of immunity to Influenza vaccination across multiple years and in diverse populations reveals shared molecular signatures.

Immunity, 2015



Application of our gene expression deconvolution techniques to estimate cell type proportions where flow data was missing, validating the observed cell differences post-vaccination.



2013

Reconstructing the genomic content of microbiome taxa through shotgun metagenomic deconvolution.

Computational Biology, 2013



A new method for increased resolution of meta-genomic data



Sensitivity analysis for inference with partially identifiable covariance matrices. Computational Statistics, 2013



A new method for an ultra-high dimensional single cell cytometry measurement by estimation from overlapping marker panels.

method

Extracting cell-type-specific gene expression differences from complex tissues Nature Methods, 2010



A new method for estimating cell-type specific expression differences from whole blood. Applied to identify a signature of graft rejection in specific cell-type, undetectable otherwise.



2009

Towards a cytokine-cell interaction knowledgebase of the adaptive immune system.



A novel method for generating an immune inter-cellular interactions from the literature using text-mining.

method

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Pacific Symposium on Biocomputing, 2009

Thank you!



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