Introduction to Intellomx
Q2 2024

Our Mission

"A selective high-quality molecule will never become a medicine if it is modulating the wrong target. This is why target selection is the most important decision we make in research."

Mene Pangalos, AstraZeneca

Deploying AI and ML to extract biological knowledge from OMICS data, identifying causal drivers of disease and expediting the biomarker and drug discovery processes.

Our USP

"We're on an unsustainable path, where the cost of drug development is growing enormously, as well as costs of new medicines. We need to …make the entire process less costly and more efficient. Otherwise we won't continue to realize the practical benefits of advances in science, in the form of new and better medicines."

Scott Gottlieb, FDA 2017-19

- Extensively validated proprietary processes and algorithms
- Algorithm findings have been validated *In vitro*
- Discovery approach takes weeks rather than years.
- Rapid assessment of millions of molecular combinations
- Human diseased tissue used from hundreds to thousands of cases rather than cell line or animal model data for small numbers of cases

How our AI is different…

- Concordance
  - Driver gene products have to rank high across multiple data sets
  - Results very low probability of false discovery
- Network Inference
  - Strength of driver assigned based on the degree of network integration NOT expression levels
  - Approach allows us to assign biological responsibility for disease based on connections not absolute levels

Revealing Causality…

"A selective high-quality molecule will never become a medicine if it is modulating the wrong target. This is why target selection is the most important decision we make in research."

Mene Pangalos, AstraZeneca

Intellomx discovers the biological targets that drive disease.

Revealing Causality…

"A selective high-quality molecule will never become a medicine if it is modulating the wrong target. This is why target selection is the most important decision we make in research."

Mene Pangalos, AstraZeneca

Intellomx discovers the biological targets that drive disease.

We use proprietary Artificial Neural Network (ANN) technologies to identify the most important drivers of disease v healthy

Rank	Gene ID	Influence
1	IO:01	-17.245
2	IO:02	-11.001
3	IO:03	-10.286
n	IO:nn	+22.585

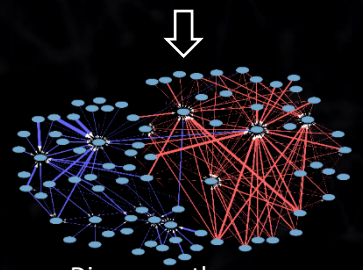
Using ANN and systems biology to identify most influential drivers of disease, prioritised according to level of influence between disease and healthy. Targets are examined at molecular pathway level.

Multiple databases
Thousands of patients
21,000 RNAseq transcripts
50 million models/hr

Revealing Causality…

Rank	Gene ID	Influence
1	IO:01	-17.245
2	IO:02	-11.001
3	IO:03	-10.286
..		
n	IO:nn	+22.585

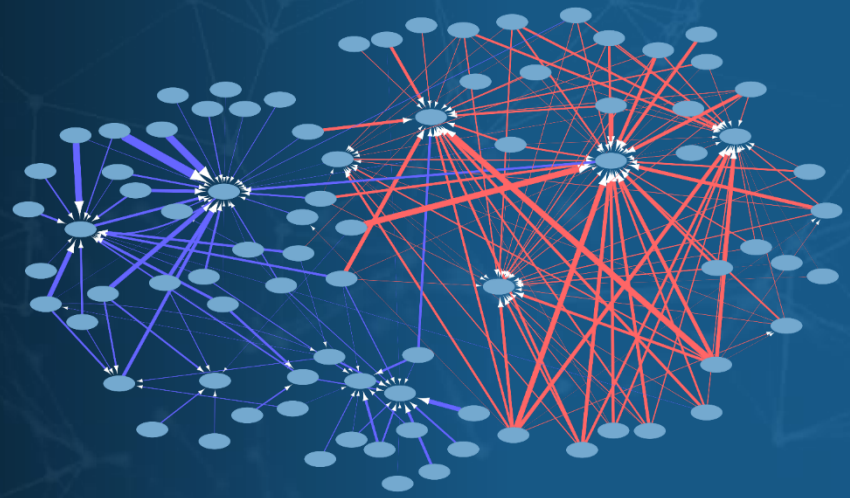
Drivers of disease v healthy



Disease pathway map

Intellomx discovers the biological targets that drive disease.

We map the key drivers of the pathway, creating the first complete pathway maps for each disease under study



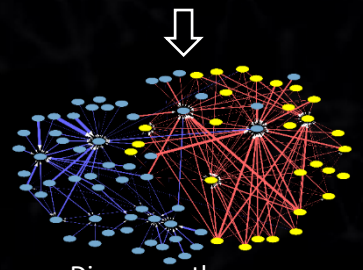
Data are represented in Cytoscape maps, showing disease pathways.

Indications include nodes, direction of influence, degree of influence and network effects for each node.

Revealing Causality…

Rank	Gene ID	Influence
1	IO:01	-17.245
2	IO:02	-11.001
3	IO:03	-10.286
..		
n	IO:nn	+22.585

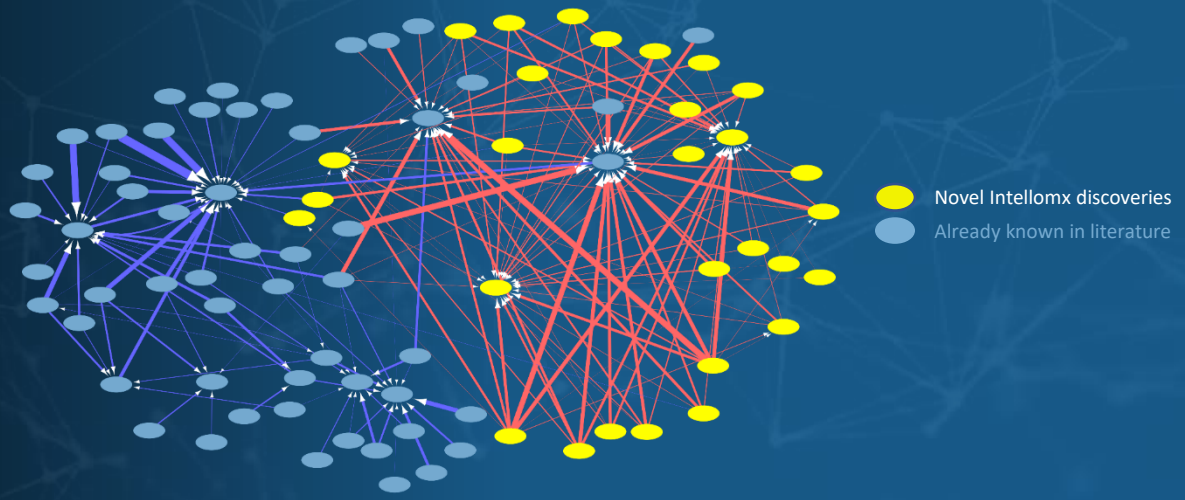
Drivers of disease v healthy



Disease pathway map

Intellomx discovers the biological targets that drive disease.

We compare results to knowledge in the literature to differentiate the novel biological targets from the known



Our AIML approach

"People always ask me where our data comes from, often referencing their own early bioinformatics training and a prejudice about the issue of data quality. Modern RNAseq technologies and our unique ability to eliminate data bias using in-house statistical methods has changed all that."

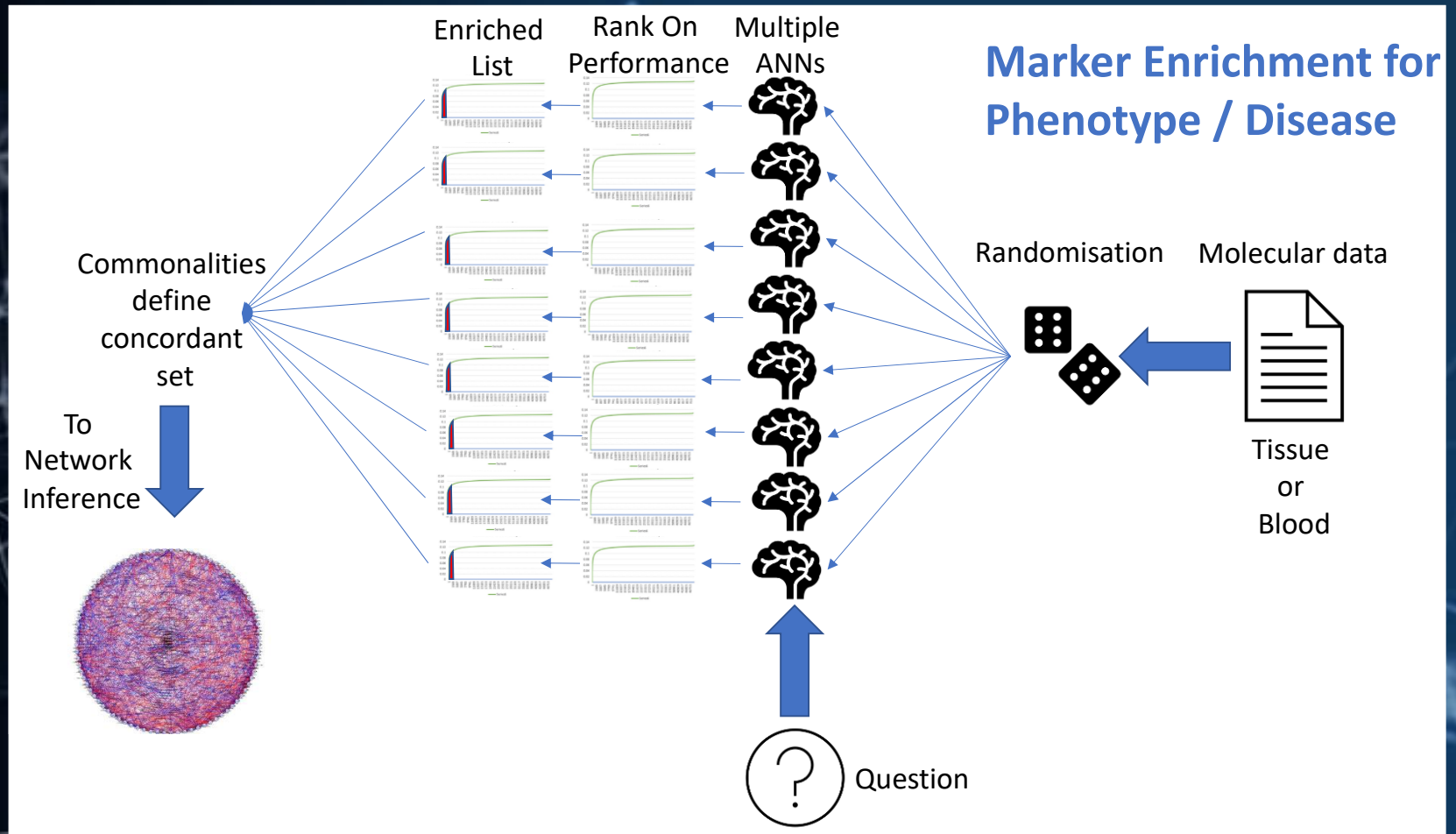
Graham Ball
CSO & co-founder

- Unique concordance-based approach deploys 5 layers of validation across multiple datasets.
- Unique pathway miner approach fills gaps in pathway knowledge based on evidence from the whole transcriptome
- Unique network inference approach to understand the amount of influence of each molecule in a pathway
- Unique stability-based approach identifies level of dysregulation of each molecule in the pathway
- Unique digital twin approach builds comparator pathway models for healthy state in tissue of interest and in off target tissues.

Intellomx Distiller

Our proprietary Distiller platform looks for concordant molecules over hundreds of different views of multiple data sets.

This eliminates the risk of false discovery facilitating robust evidence-based discovery from large scale omics data.

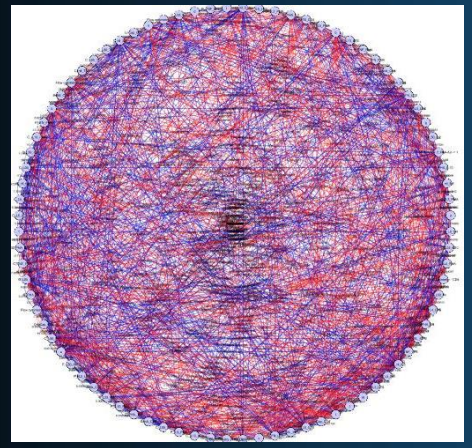


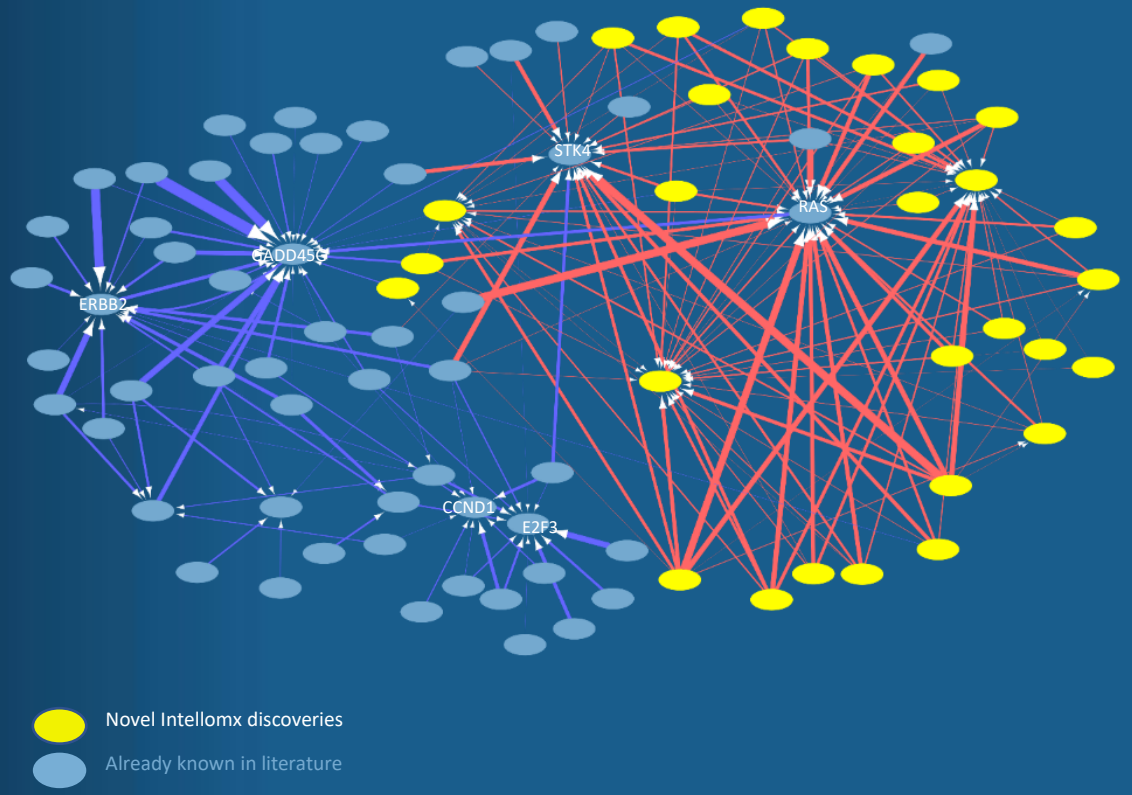
Intellomx Driver

Our driver discovery process models the interactions between molecules identifying the most connected and influential molecules in a system.

Our discovery doesn't just rely on fold change and p values but gets to the core of the molecular processes that drive a biological system.

This approach builds a model of the interaction space which can be interrogated to discover the most influential molecular features for drug target discovery and the level of dysregulation of a molecular feature.

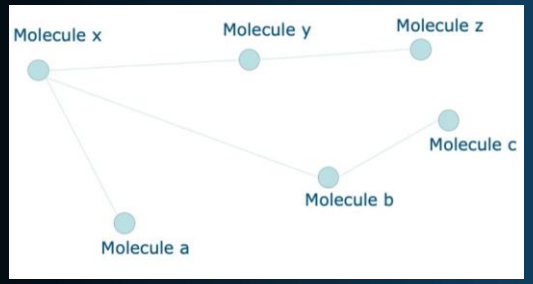


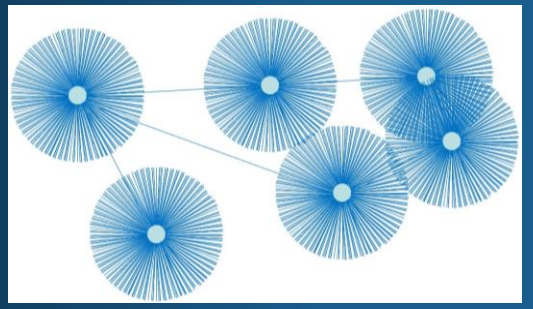


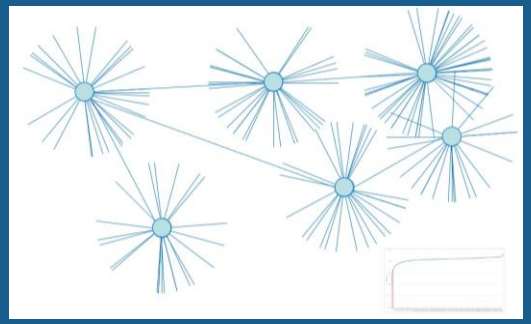
Intellomx Pathway Miner

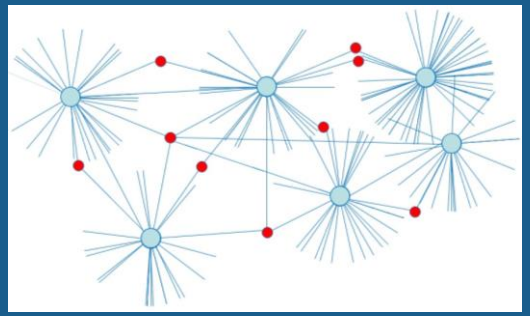
Intellomx pathway miner uses a molecular pathway or gene list as a framework. Deploying the principles of Intellomx Distiller we can discovery new evidence-based features.

The approach mines the whole transcriptome to identify new members or associations with the pathway based on evidence from the whole transcriptome.





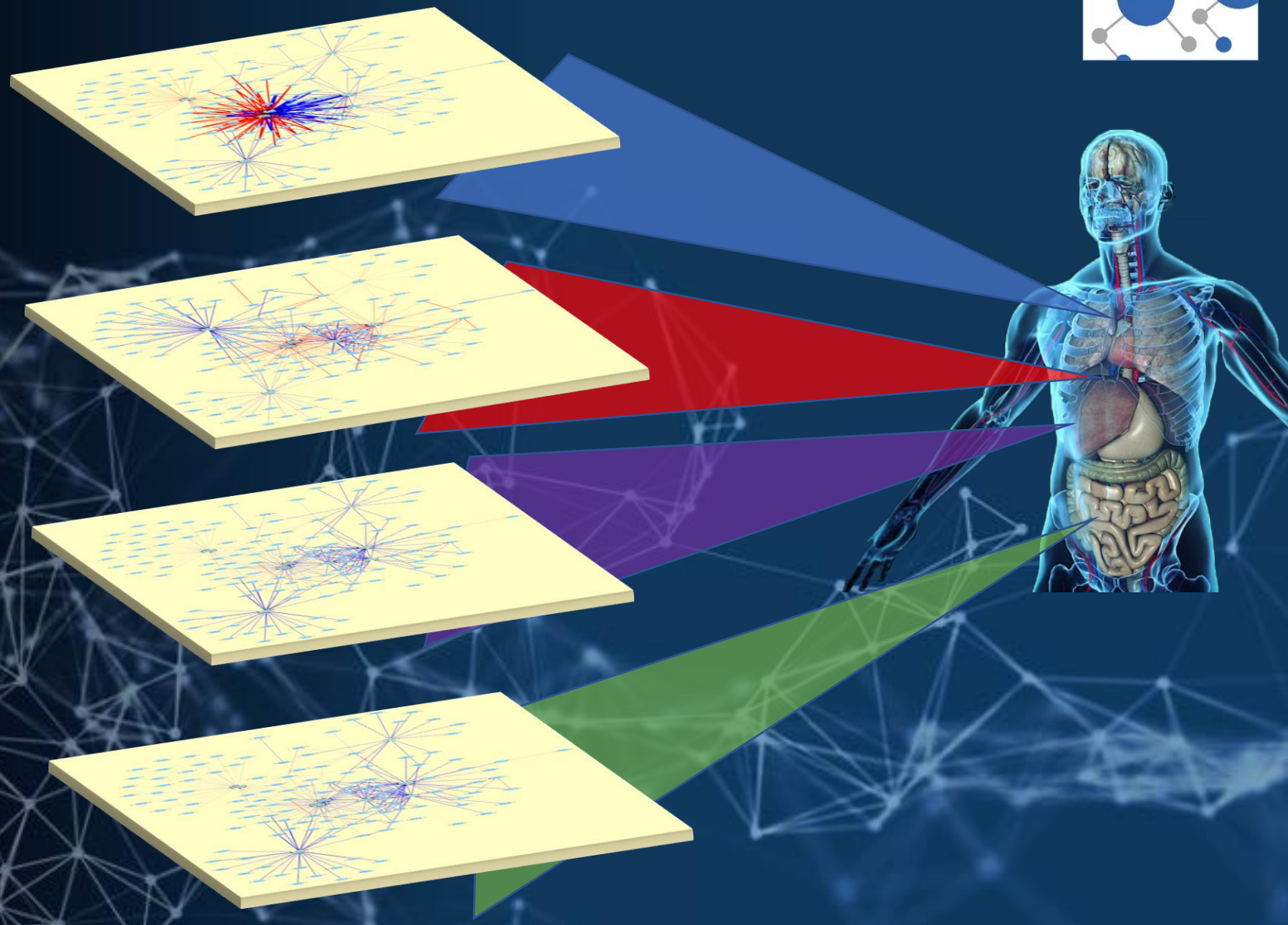




Digital Twin

"The Intellomx Digital Twin gives us the opportunity to test drugs in development in a human model without risk, giving a clear indication of off-target toxicity effects:

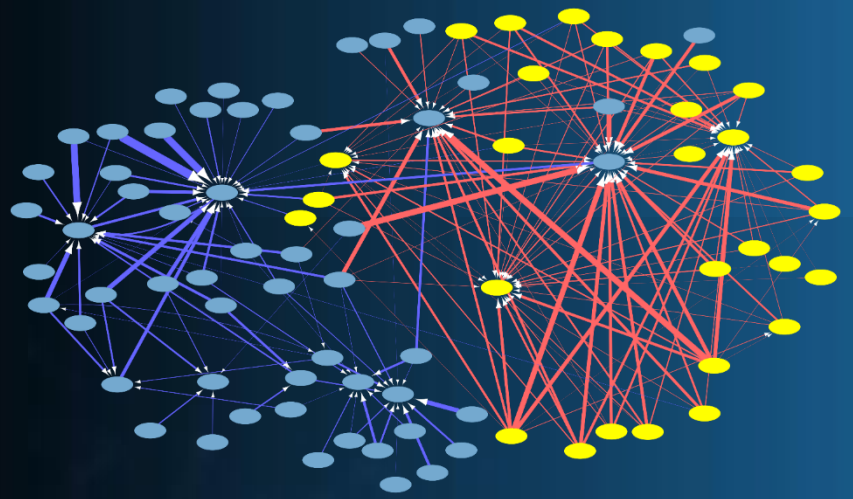
- We can now **predict the specific off-target effects for any molecule under study** by applying our pathway analysis regarding the brain, kidney, skin, blood, liver and other organs.
- In turn this enables us to prioritise molecules for development, eliminating up to 90% of projects that would fail due to toxicity in later, high-cost stages.



Case Study: Lung Cancer (KRAS)

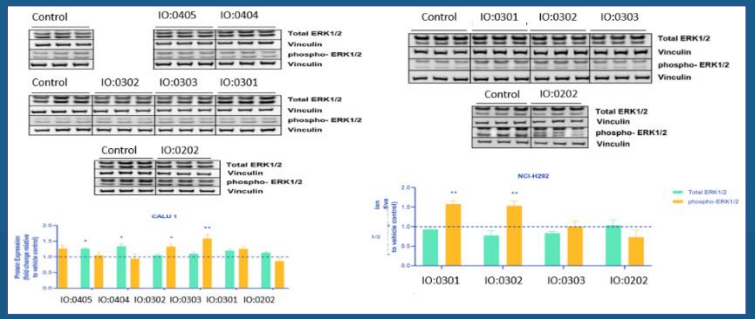
Project supported by Innovate Grant 2021. Intelligent OMICS led the program, supported by subcontractors Medicines Discovery Catapult and cell-line robotics company Arctoris Ltd.

- Assessment of KRAS/MEKK inhibition in Lung Cancer
- Top 200 drivers evaluated via analysis of 9 lung cancer datasets, generating 30 novel targets in KRAS (22 in MEKK)
  Results presented in Cytoscape …



Novel Intellomx discoveries
Already known in literature

+



Validation:

WP 1.1 siRNA Screen: phenotypic outcome 24, 48, 72 and 96h
WP 1.2 Pathway Analysis screen: siRNA transfection. Target depletion confirmed
WP 2 Compound Screen: siRNA transfection. Target depletion confirmed

Results validated in Wild Type and Mutated cell lines by Arctoris

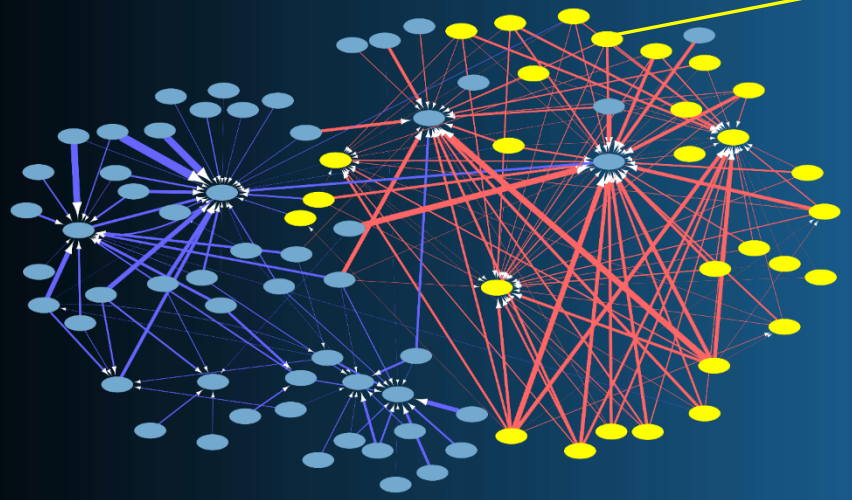
Lung Cancer (KRAS)

ARCTORIS

"Our system validated the targets and then tested drugs against those targets. Results were clear – the targets identified by Intelligent OMICS are indeed important, previously unknown targets in lung cancer and the novel drugs identified by the team modulate those targets, all as predicted by the AI."

Martin Bittner
CEO

3 biological targets and 7 molecules prioritized for development and partnering



IO:03 KRAS inhibitor

IO:0301 Small molecule	wild type
IO:0302 Small molecule	wild type
IO:0303 Small molecule	wild type+G12C
IO:0304 Monoclonal	wild type+G12C

IO:04 KRAS/MEKK inhibitor

IO:0404 Small molecule	G12C
IO:0405 Small molecule	G12C

IO:02 MEKK inhibitor

IO:0202 Small molecule	wild type+G12C

Differentiation

	Intellomx	Other AI	Traditional R&D
New source of biological targets	✓	✓	✗
Fast	✓	✓	✗
de novo research	✓	✗	✓
Human data only	✓	✗	✗
Intellomx Digital Twin	✓	✗	✗
Reduced animal trials	✓	✗	✗
Improved resource use + sustainability	✓	✗	✗

Key papers + illustrations:

Lancet oncology

Supplementary data available on request

SPAG5 as a prognostic biomarker and chemotherapy sensitivity predictor in breast cancer: a retrospective, integrated genomic, transcriptomic, and protein analysis

Frontiers in oncology

Comprehending Meningioma Signaling Cascades Using

Frontiers in biology

Development of a Bioinformatics Framework for Identification and Validation of Genomic Biomarkers

Blood advances

A parsimonious 3-gene signature predicts clinical outcomes in an acute myeloid leukemia multicohort study

Plant physiology

Network Inference Analysis Identifies an *APRR2-Like* Gene Linked to Pigment Accumulation in Tomato and Pepper Fruits[1][W][OA]

Jama network

Association of Sperm-Associated Antigen 5 and Treatment Response in Patients With Estrogen Receptor–Positive Breast Cancer

CONNECT

OBN supporting and bringing together the UK's life sciences companies, corporate partners and investors

DDI & drug

Press service

Conquering KRAS!

The AI drug discovery revolution that is here to stay

Intelligent OMICS is delighted to announce successful completion of its recent Innovate UK grant program, in collaboration with the Medicines Discovery Catapult (MDC) and Arctoris Limited.

5 key conclusions:

- Application in oncology identifies novel KRAS-inhibiting drugs for lung cancer, one of which is even effective regardless of KRAS mutation;
- AI-driven drug discovery is at last proven, and ready for application across multiple diseases;
- The AI approach discovers new drugs because it focusses on the drivers or causes of the disease state, rather than focussing on the symptoms or effects of a disease state;
- The evidence-based analysis produces original results, without reliance on prior hypotheses or literature, allowing creation and control of new Intellectual Property.
- AI discovery methods can achieve greater than 90% reduction in carbon footprint compared to traditional high-throughput screening

The project, led by Intelligent OMICS and funded by Innovate UK, sought to demonstrate the carbon efficiency of an AI-based drug discovery program compared to traditional pharma methods. The case study used in the project was assessment of Non-Small Cell Lung Cancer – thought to account for over 80% of all lung cancer cases.

Method

The team analysed nine lung cancer datasets from the Intellomx Curated Data Library, using the Intelligent OMICS I³ platform. The datasets include human transcriptomic data plus confirmation of a disease v healthy diagnosis for lung cancer for approximately 2,000 patients. Proprietary AI was used to model the underlying systems biology - first creating a list of the most important genes defining the disease v healthy diagnosis, then modelling the interaction of those genes in a disease pathway map based on the evidence in the data.

"The real benefit of our technology is evident when we compare our results with what is known in the literature," says Intellomx CEO Dr Simon Haworth. **"We can immediately spot errors and omissions in pathway maps documented in KEGG, for example, and because our analysis only focusses on the most influential drivers in each pathway we know that any such differences are genuinely important. For our lung cancer work, focussing on EGFR and KRAS, the comparison led us to 8 really exciting new lung cancer targets."**

The next step of the process was to validate *in silico* targets in the wet lab, to link validated targets to possible drugs and then to test the impact of those novel drugs on cancer cells.

Subcontractor Arctoris, with its world leading fully automated drug discovery platform and robotic cell line system, provided rapid validation of the targets using knock down analysis on KRAS G12C mutant and KRAS wild type cell lines. Data from Arctoris proved the validity of the targets by

Our Clients

SERVIER

"I love this collaboration already – in under 4 weeks you have provided a clearer picture of [disease] than we have achieved from 4 years of hard work. Let's move to the next level!"

Philippe Moingeon
Director,
Laboratoir Servier

Corporate contracts

Takeda	Dengue vaccine	RANDOX	Sepsis	SERVIER	Sjogren's, SLE
Public Health England	TB, Sepsis	biose	Pro-biotic response		
LGC	Cell therapy, Toxicity	Exonate	AML	ALMAC	
MOLOGIC	Sepsis, COPD	apitope	Rh Arthritis	Johnson&Johnson	Oncology
dstl	Sepsis, Viral infection	AstraZeneca	Prostate cancer		
onyvax	Prostate cancer	Oxford Biomedica	Renal cancer		
syngenta	Tomato ripening	武汉市肺科医院/武汉市结核病防治所 Wuhan Pulmonary Hospital/Wuhan Institute for Tuberculosis Control	TB		
PharmaEngine	Oncology asset	SERVIER	Autoimmune		

Academic collaborations

University of Leicester	Preeclampsia,resp,renal	University of Dundee	Breast cancer	London School of Hygiene & Tropical Medicine	Tuberculosis
The University of Nottingham	Breast, ovarian	UCL	Cell-based therapy		
The Open University	Prostate, campylobacter	University of Southampton	Melanoma		
Cardiff University / Prifysgol Caerdydd	Breast, Sepsis	University of Leeds	Melanoma		
Nottingham Trent University	Oncology, diabetes				

Contact :

Rob Grundy, CEO	rob.grundy@intellomx.com	+44 7976 600016
Dr. Bill Mason, NED	bill.mason@intellomx.com	+44 7785 950134