# Machine learning combined with diagnostic chip technology for personalized dynamic management of idiopathic pulmonary fibrosis

## Blavatnik Application

2019

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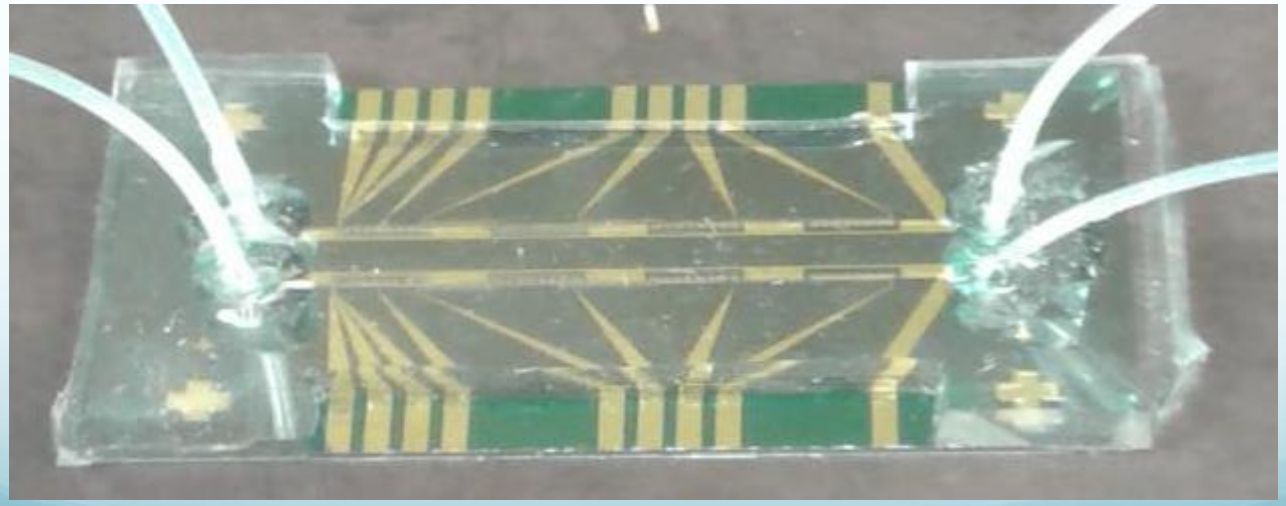
# Problem: No FDA approved biomarkers for management of idiopathic pulmonary fibrosis

- Idiopathic pulmonary fibrosis (IPF) is a deadly chronic lung disease with median survival of 3 years and with a worse prognosis than lung cancer
- 6 million worldwide affected, 200,000 in North America affected with 45,000 dying each year
- The progressive decline of lung function is interspersed with unpredictable disease flares called acute exacerbations of IPF (AE-IPF) that accelerate lung function loss and increase morbidity and mortality
- The annual incidence of AE is up to 20% with a mortality ranging from 35-90%, demonstrating the severity of IPF disease progression and the importance for active disease monitoring (ER visits and hospital stays can amount to >$11,500 per case)
- **We remain unable to predict how an individual patient will progress and whether they will respond to available interventions**
- **Market size for biomarker chip detection is ~3B**

# First key finding – Chip technology to measure disease progression from home

- Diagnostic chip technology that can measures genes and proteins in parallel from 5ul of human whole blood or serum
- Chip with fast readouts is planned to enable home monitoring of disease progression
- Patent: Soleymani, L. Nanostructured microelectrodes and biosensing devices incorporating the same. US Patent Office Patent Number: US 10 , 274 , 453 B2 (2019). (McMaster University)
- The technology has been patented and undergone limited licensing for diagnosis of infectious diseases and endometriosis (Canada)
- There is a potential contract manufacturer to scale up
- Competitors (Abbot (Free style precision NEO), Cepheid, Spartan Bioscience)
- The cost of device on the market would be ~ $50-100





- *Soleymani, L. et al. Programming the detection limits of biosensors through controlled nanostructuring, Nature Nanotechnology, 2009*

# Second key finding – Gene biomarker signature predictive of IPF patient survival to be used on the chip

- 52-gene blood-based signature from a cross-sectional study was able to divide IPF patients in high and low risk groups, thus successfully predicting survival. The signature is validated in 425 participants.

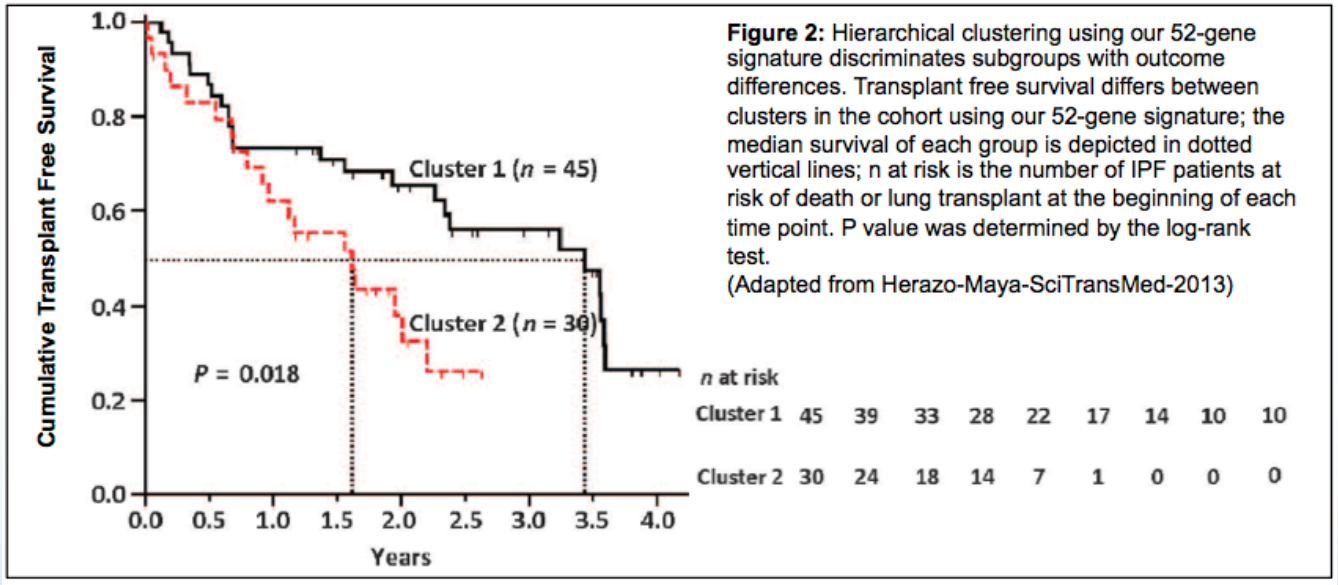
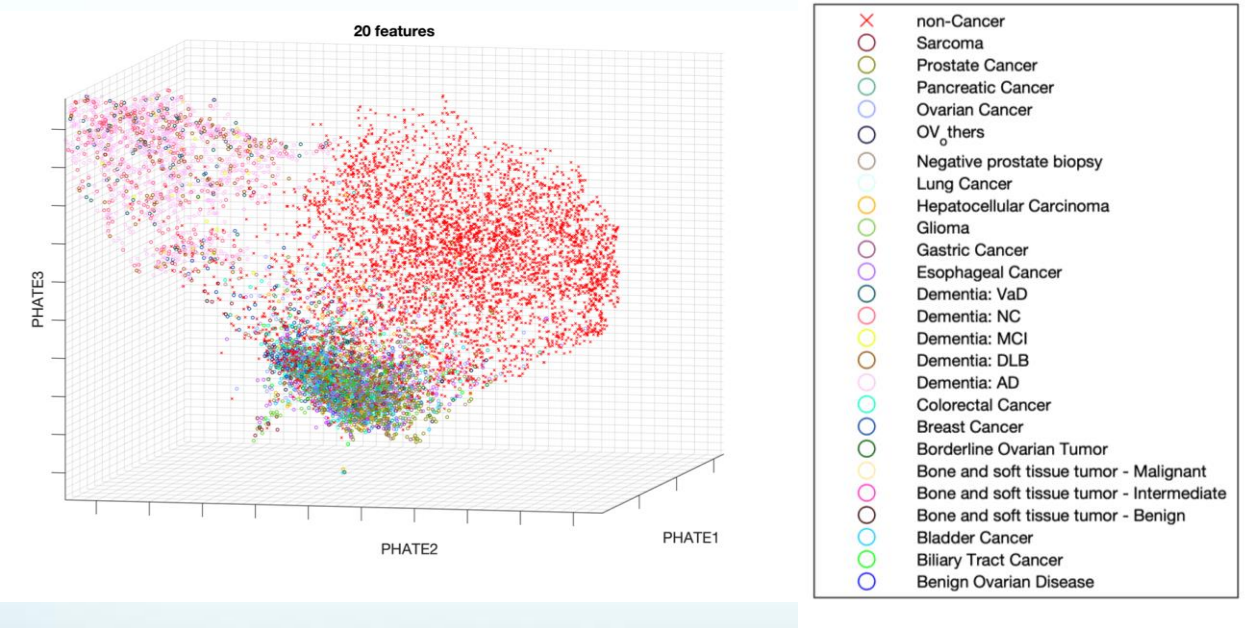



**Figure 2:** Hierarchical clustering using our 52-gene signature discriminates subgroups with outcome differences. Transplant free survival differs between clusters in the cohort using our 52-gene signature; the median survival of each group is depicted in dotted vertical lines; n at risk is the number of IPF patients at risk of death or lung transplant at the beginning of each time point. P value was determined by the log-rank test.
(Adapted from Herazo-Maya-SciTransMed-2013)

- Yale IP - US8846341B2 (issued in 2014, Naftali Kaminski)
- ***Herazo-Maya, J. D. et al. Validation of a 52-gene risk profile for outcome prediction in patients with idiopathic pulmonary fibrosis: an international, multicentre, cohort study. The Lancet. Respiratory medicine 5, 857-868, (2017)***

# Third key finding – BIER
## Biomarker Identification via Embedding Recapitulation

- This approach will be used to refine the existing biomarker signature for expanded applications by predicting behavior of IPF biomarkers in large patient populations and prioritize for clinical development




- Using BIER, 20 features (miRNAs) were shown to be enough to recapitulate embedding of 2500 features and distinguish specifically amongst 27 diseases. This approach will be adopted for lung fibrosis phenotypes.

*Moon, K. et al. Visualizing Structure and Transitions for Biological Data Exploration, Nature Biotechnology vol 37(12), 2019,* pages1482–1492

# Our approach

1. We plan to optimize the existing diagnostic chip prototype technology for the IPF biomarker panel

2. We have access to well-phenotyped, large longitudinal cohorts of IPF patients (discovery and validation) to test the chip performance

3. We plan to refine the patented 52-gene signature for IPF disease outcome and expand to new signatures for AE-IPF, disease progression and response to therapy

4. Our approach will include:
   - Testing and validation of the IPF chip with human samples
   - Development of advanced artificial intelligence (AI) algorithms for data driven next generation IPF biomarker development

5. We have access to USA and Canadian regulatory agencies and newly formed pharma consortium for IPF biomarker development

6. Our chip and AI technologies are easily scalable to other chronic lung diseases (Asthma, COPD)

# Development

$300.000

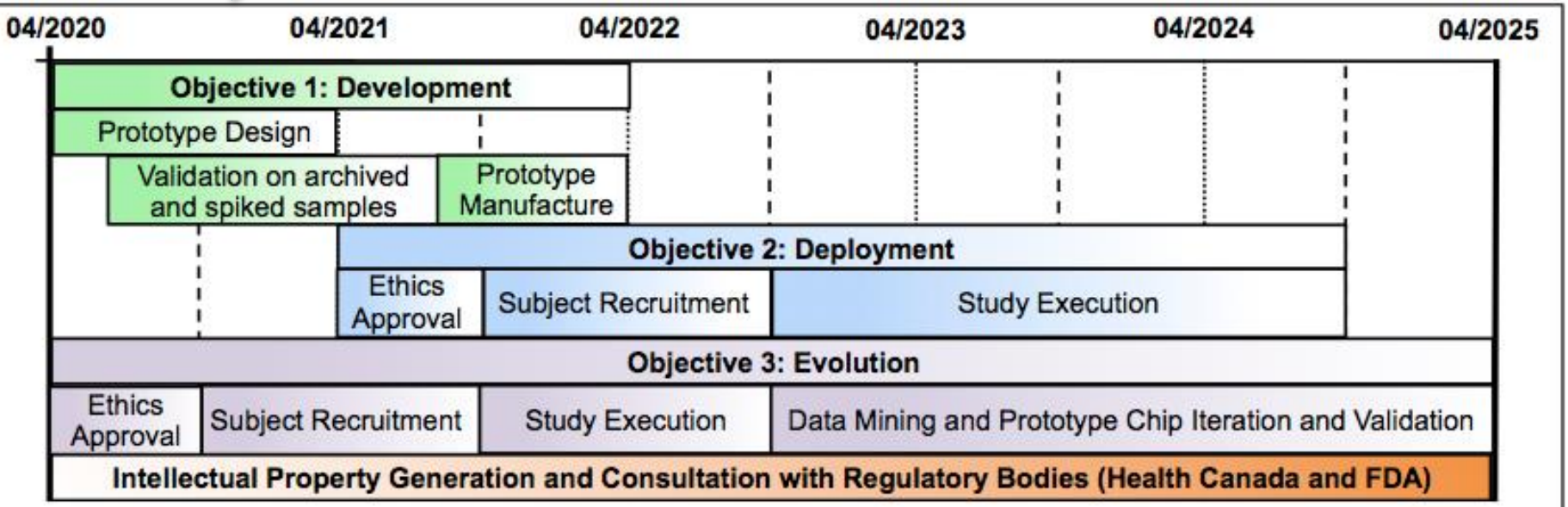



**Figure 3**: Gantt chart timeline of Objective 1 - Development (green shade), Objective 2 - Deployment (blue shade), and Objective 3 - Evolution (grey shade) demonstrating a transition from task execution (bold shade) to completion (light shade). Throughout the proposal, all avenues for intellectual property generation will be explored for downstream commercialization opportunities (orange shade – increasing over time). In parallel, consultation with regulatory bodies will be performed to ensure diagnostic approval requirements are confirmed.