

OPEN SEARCH FOR BLOOD-BASED BIOMARKERS OF PSYCHOSIS THROUGH A NOVEL DATA-DRIVEN APTAMER-BASED APPROACH: A PROOF-OF-CONCEPT STUDY

Chen-Fang Chung^(a,b), Julien Ouellet^(b,c), Murielle M. Akpa^(b), Laurent Elkrief^(a,d), Madline Sauvage^(a,b), Roshita Anandani^(e), Robert-Paul Juster^(a), Stéphane Potvin^(a)
^(a) Université de Montréal _ ^(b) OneCare Biotechnologies Inc. _ ^(c) University of Toronto _ ^(d) Centre hospitalier de l'Université de Montréal (CHUM) _ ^(e) McGill University

Bringing Precision Medicine to Psychiatry ~ OneCare Biotechnologies

Summary

Introduction: Objective blood-based biomarkers for psychosis remain lacking. Aptamer-based biosensing offers a hypothesis-free approach for biomarker discovery.

Objective: Evaluate the potential of aptamer-based biosensing combined with machine learning for psychosis classification.

Methods: Plasma samples from psychosis patients and controls were screened using a hypothesis-free aptamer selection process and analyzed by NGS, qPCR, and machine learning.

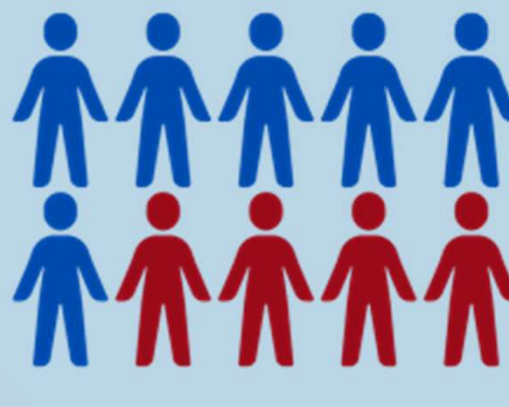
Results: An initial model using 5 aptamers achieved **65% accuracy**. Validation in an independent cohort (n = 200) using all 12 aptamers improved classification accuracy to **71%**. This proof-of-concept study supports the use of **hypothesis-free aptamer-based biosensing** for objective blood-based psychosis classification and represents a promising step toward **precision psychiatry**.

Introduction



800M

individuals suffer from a psychiatrist condition.



40%

are misdiagnosed and on the wrong treatment



0

objective blood-based diagnostic test



Delayed treatment & poor patient outcomes

Need

An objective blood-based diagnostic tool for psychosis.

- **Psychosis** affects **0.3–2.0%** of the global population and remains a leading cause of disability¹.
- **40% of patients** are misdiagnosed and receive inappropriate treatment².
- In **Canada**, psychotic disorders represent an annual economic burden of **> \$50 billion**, while in **Ontario** they account for **\$2.1 billion** in healthcare costs, a **15-year reduction in life expectancy**, and a **2.5-fold increase in all-cause mortality**³.
- Despite a **70 - 80% heritability**, objective blood-based biomarkers remain unavailable due to the biological heterogeneity of psychosis and the limitations of reductionist approaches⁴.
- Current diagnosis relies primarily on **subjective DSM-5/ICD clinical assessment**, with schizophrenia inter-rater reliability as low as $\kappa = 0.39$ ⁵.

Objective

We aim to evaluate the potential of available aptamer technologies in identifying psychosis-specific biomarkers.

Materials & Methods

Study Cohort

- **300 plasma samples** from the Signature Biobank⁶.
- Adults (≥ 18 years) admitted to the Institute's psychiatric emergency service⁷.
- **Psychosis group:** acute psychotic symptoms (PSYRATS).
- **Control group:** no DSM-5 psychiatric disorder.
- Exclusion: arthritis, cancer, stroke, inflammatory bowel disease, epilepsy.
- All samples were **anonymized** and collected with informed consent and psychiatrist approval.

Aptamer Discovery Workflow

- 1- **Hypothesis-free aptamer selection** using plasma samples from psychosis and control participants.
- 2- **NGS quantification** to identify enriched aptamers associated with psychosis.
- 3- **qPCR validation** of selected aptamarkers across the remaining plasma samples.
- 4- **Machine learning analysis** to identify biosignatures and develop a diagnostic model.
- 5- **Data-driven diagnostic prediction** using computational analysis and machine/deep learning to classify pathological conditions.



Results

- **Pilot cohort:** 100 plasma samples
50 psychosis + 50 controls
 - **5 candidate aptamers** selected.
 - **qPCR validation** across the entire cohort.
- 65% overall classification accuracy.**

Table 1. Psychosis Pilot Study Using 5 aptamarkers with N=99 (Ctrl:50 vs PE:49)					
ML Model - Rtp	Accuracy	Precision	Recall	F1-Score	Specificity
sPLDA	0.52	0.48	0.51	0.47	0.57
SVM-linear	0.59	0.59	0.58	0.58	0.61
Random Forest	0.58	0.65	0.60	0.59	0.61
LDA	0.62	0.63	0.58	0.60	0.66
LogisticRegression	0.58	0.63	0.48	0.54	0.68
extra Tree	0.61	0.61	0.56	0.58	0.66
Ensemble_5_Classifiers	0.65	0.70	0.70	0.69	0.62

- **Independent validation cohort:**
200 plasma samples.
119 psychosis + 81 controls
 - **12 selected aptamer biosensors.**
 - Successfully replicated the pilot study.
- 71% overall classification accuracy.**

Table 2. Confirmatory Study Using 12 aptamarkers with N=200 (Ctrl:81 vs PE:119)					
ML Model - Rtp	Accuracy	Precision	Recall	F1-Score	Specificity
sPLDA	0.64	0.66	0.83	0.73	0.37
SVM	0.63	0.65	0.91	0.75	0.21
RF	0.71	0.74	0.81	0.77	0.56
LDA	0.64	0.65	0.84	0.73	0.34
Logistic Regress	0.63	0.66	0.80	0.71	0.37
ExtraTree	0.70	0.71	0.86	0.77	0.44
Ensemble_5_classifiers	0.66	0.71	0.78	0.74	0.44
PMLE m=6	0.65	0.69	0.81	0.75	0.39
Symbolic Classification	0.70	0.70	0.85	0.77	0.45

Conclusion

Our findings demonstrate the potential of **hypothesis-free aptamer-based biosensing** combined with machine learning to enable **objective blood-based classification of psychosis**, paving the way toward precision psychiatry.

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