

# EyeSpeak: A Real-Time, Non-Invasive Tear Test for Detection of Major Depressive Disorder (MDD)

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Major Depressive Disorder (MDD) affects over 280 million individuals globally, but less than 25% of those affected receive proper care. Early detection is vital for timely intervention and treatment but is hindered by the lack of a definitive clinical test. Current depression detection and diagnoses rely on patient-reported symptoms, lacking quantifiable biomarkers and leading to frequent misdiagnoses. This study aimed to address this gap by investigating tear fluid as a non-invasive point-of-care test for MDD. LC-MS/MS-based proteomics analysis, conducted on samples from 15 MDD patients and 15 healthy controls, yielded a pool of 1,042 tear proteins. Quantitative analysis using MaxQuant and Perseus software packages identified distinct protein expression patterns, revealing 116 upregulated and 89 downregulated proteins in MDD. Applying stringent criteria and comparing with previously reported potential depression biomarkers found in blood and cerebrospinal fluid, three key biomarkers—matrix metalloproteinase-9, interleukin-8, and STAM-binding protein—were selected as tear biomarkers for MDD. ELISA validation demonstrated 100% accuracy in a validation cohort (n=20). For real-time testing, an electrochemical sensor, EyeSpeak was developed using a Sensit Smart biosensor. EyeSpeak demonstrates 99% accuracy, costs 80 cents, and takes 20 minutes for a MDD test. EyeSpeak outperforms the current "gold standard" for MDD diagnosis (PHQ-9 form and psychologist evaluation) by enhancing accuracy by 1.5-fold and saving hundreds of dollars and months of time per patient. This novel approach holds promise as a quantitative gold standard for MDD screening and diagnosis, which could lead to widespread use.

## Awards Won:

Fourth Award of \$500