## Author's Accepted Manuscript

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PII: S0956-5663(18)30419-6

DOI: https://doi.org/10.1016/j.bios.2018.05.059

Reference: BIOS10517

To appear in: Biosensors and Bioelectronic

Received date: 11 March 2018 Revised date: 29 May 2018 Accepted date: 31 May 2018

Cite this article as: Keisuke Watanabe, Munetaka Nomoto, Fumio Nakamura, Shoji Hachuda, Akihiro Sakata, Takumi Watanabe, Yoshio Goshima and Toshihiko Baba, Label-free and spectral-analysis-free detection of neuropsychiatric disease biomarkers using an ion-sensitive GaInAsP nanolaser b i o s e n s o r , *Biosensors and Bioelectronic*, https://doi.org/10.1016/j.bios.2018.05.059

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### **ACCEPTED MANUSCRIPT**

# Label-free and spectral-analysis-free detection of neuropsychiatric disease biomarkers using an ion-sensitive GaInAsP nanolaser biosensor

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#### **Abstract**

The emission intensity of GaInAsP semiconductors that show an ion sensitivity is altered by the surface charge. In this study, we propose a biosensing technique using GaInAsP photonic crystal nanolasers based on this principle. Here, simple and rapid detection of collapsin response mediator protein 2 (CRMP2) is demonstrated, which is a promising biomarker candidate for neuropsychiatric diseases existing in peripheral white blood cells. We prepared CRMP2 as a standard protein and introduced sodium dodecyl sulfate (SDS) as an anionic surfactant to enhance the net negative charge of the protein. The nanolaser was modified in advance with an anti-CRMP2 antibody and then photopumped at a constant power. The laser emission intensity was monitored during the antibody–antigen reaction. Consequently, CRMP2 was detected as a decrease in the emission intensity. We achieved a lower limit for detection of 3.8 µg/mL that satisfies the requirement for clinical biomarker testing. Without the requirements of any kind of labels and spectral analyses, this technique allows for simple, rapid, and low-cost biomarker detection.

Keywords: GaInAsP; label-free; photonic crystal; nanolaser; biomarker; collapsin response mediator protein

#### 1. Introduction

Biomarker tests as quantitative clinical indicators are useful for the early detection and evaluation of progress and treatment effects of severe diseases. Neuropsychiatric diseases, including schizophrenia, are mainly diagnosed through clinical interviews based on the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5), which is *de facto* the world's standard diagnostic criteria (Tandon et al.,

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