

Accepted Manuscript

Title: Piezoelectric immunosensor based on antibody recognition of immobilized Open-tissue transglutaminase: An innovative perspective on diagnostic devices for celiac disease

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PII: S0925-4005(14)00537-1
DOI: <http://dx.doi.org/doi:10.1016/j.snb.2014.05.018>
Reference: SNB 16892

To appear in: *Sensors and Actuators B*

Received date: 25-2-2014
Revised date: 21-3-2014
Accepted date: 4-5-2014

Please cite this article as: A. Manfredi MattarozziM. GiannettoM. Careri Piezoelectric immunosensor based on antibody recognition of immobilized Open-tissue transglutaminase: an innovative perspective on diagnostic devices for celiac disease, *Sensors and Actuators B: Chemical* (2014), <http://dx.doi.org/10.1016/j.snb.2014.05.018>

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1 **Piezoelectric immunosensor based on antibody recognition of immobilized Open-tissue**
2 **transglutaminase: an innovative perspective on diagnostic devices for celiac disease**

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15 **Abstract**

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17 A piezoelectric immunosensor was developed for the first time for direct detection of anti-tissue
18 transglutaminase antibodies (anti-tTG), very specific biomarkers for reliable and early diagnosis of
19 celiac disease. Since the inflammation processes associated to the pathology's occurrence involve
20 tTG structural changes from closed to open conformation as well the extended structure has been
21 demonstrated to have higher diagnostic accuracy if compared with closed conformation, the new
22 strategy undertaken in this study was based on the immobilization of tTG enzyme in its open
23 conformation as receptor on immunosensor surface. Ten nm-sized gold nanoparticles conjugated
24 with secondary antibodies were exploited for signal amplification. Liquid phase detection
25 conditions using a laminar flow cell were properly selected in order to have a good signal stability
26 both in dynamic and in static modes. Optimization of the operating conditions, by experimental
27 design on mouse anti-tTG antibodies in serum, allowed us to obtain a model for the realization of a
28 reliable piezoelectric immunosensor with high potential as diagnostic device for the determination
29 of human autoantibodies of celiac patients.

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31 **Keywords:** Quartz crystal microbalance (QCM) immunosensor, Open-tissue transglutaminase,
32 Anti-tissue transglutaminase antibodies, Flow-through cell, Nanogold amplification, Celiac disease

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