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Abstract Electrochemical Immunosensor for Simultaneous Determination of Emerging Autoimmune Disease Biomarkers in Human Serum ⁺

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Abstract: Rheumatoid arthritis is an autoimmune disorder characterized by persistent erosive syn-12 ovitis, systemic inflammation and the presence of autoantibodies, which play an important role in 13 inducing inflammation and joint damage, releasing pro-inflammatory cytokines from monocytes 14 and macrophages [1,2]. Likewise, neutrophil activating protein-2 (CXCL7) is a platelet-derived 15 growth factor belonging to the CXC chemokine subfamily, which is expressed in serum, synovial 16 fluid and synovial tissue of patients developing rheumatoid arthritis during the first twelve weeks, 17 being useful to reflect local pathological changes [3]. Besides, matrix metalloproteinase-3 (MMP-3), 18 which is induced by inflammatory cytokines such as interleukin-1 (IL-1) and tumor necrosis factor 19 alpha (TNF- α) in rheumatoid synovium, degrades several extracellular matrix components of car-20 tilage and plays central roles in rheumatoid joint destruction [4]. Thereby, monitoring serum CXCL7 21 and MMP-3 levels is useful for predicting the disease activity in rheumatoid arthritis. In this work, 22 the construction and analytical performance of a dual electrochemical platform for the simultaneous 23 determination of CXCL7 and MMP-3 is described. After the optimization of experimental variables 24 involved in the preparation and implementation of the biosensor, the analytical usefulness of the 25 developed configuration was demonstrated by its application to the determination of these bi-26 omarkers in serum samples from healthy individuals and patients with rheumatoid arthritis. In 27 addition, the results obtained using the dual immunosensor were compared with those provided 28 by the respective ELISA immunoassays, yielding no significant differences between the two meth-29 ods. 30

Keywords: rheumatoid arthritis; CXCL7; MMP-3; immunosensor; simultaneous determination; human serum samples. 32

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References

1.	Bos, W.H.; Wolbink, G.J.; Boers, M.; Tijhuis, G.J.; de Vries, N.; van der Horst-Bruinsma, I.E.; Tak, P.P.; van de Stadt, R.J.; van der	6
	Laken, C.J.; Dijkmans, B.A.C.; van Schaardenburg, D. Arthritis development in patients with arthralgia is strongly associated	7
	with anti-citrullinated protein antibody status: a prospective cohort study. Ann Rheum Dis 2010, 69, 490–494.	8
2.	Scott, D.L.; Wolfe, F.; Huizinga, T.W.J. Rheumatoid arthritis. Lancet, 2010, 376, 1094–1108	9
0		

- Guerrero, S.; Cadano, D.; Agüí, L.; Barderas, R.; Campuzano, S.; Yáñez-Sedeño, P.; Pingarrón, J.M. Click chemistry-assisted 10 3. antibodies immobilization for immunosensing of CXCL7 chemokine in serum. J Electroanal Chem 2019, 837, 246–253. 11 12
- 4. Sugiyama, E. Role of matrix metalloproteinase-3 in joint destruction in rheumatoid arthritis. Clin Calcium 2007, 17, 528-534