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RESEARCH PAPER

SERS-based liquid biopsy of saliva and serum from patients with Sjögren's syndrome

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Abstract

In this preliminary study, we employed surface-enhanced Raman scattering (SERS) of saliva and serum samples for diagnosing Sjogren's syndrome (SjS), a systemic autoimmune disease characterized by dryness of the mouth and eyes. The saliva and serum samples from $n = 29$ patients with SjS and $n = 21$ controls were deproteinized with methanol and then the SERS spectra were acquired using silver nanoparticles synthesized by reduction with hydroxylamine hydrochloride. In the case of both saliva and serum, the SERS spectra were dominated by similar bands attributed to purine metabolites such as uric acid, xanthine, and hypoxanthine. Principal component analysis-linear discriminant analysis (PCA-LDA) models built from SERS spectra of saliva and serum yielded an overall classification accuracy of 94% and 98%, respectively. These results suggest that the SERS analysis of saliva and serum is able to capture the complex biochemical perturbations that accompany the onset of SjS, a strategy which could be translated in the future into a novel point-of-care diagnosis method.

Keywords Surface-enhanced Raman scattering (SERS) · Sjogren's syndrome · Saliva · Serum · PCA-LDA

Introduction

Primary Sjogren's syndrome (SjS) is the second most common systemic autoimmune disease, with an incidence of around 15 cases per 100,000 individuals [1]. The typical presentation of SjS involves the classic triad: dryness of the mouth and eyes (sicca syndrome), fatigue, and arthralgia, although in around 60% of cases, the patients also present with fever and weight loss as well as end organ damage of the kidneys, lungs, GI tract, and the bone marrow [2]. When systemic symptoms are the lead complaints, the disease is termed occult SjS or non-sicca onset SjS [3].

SjS can sometimes be superimposed on another systemic autoimmune disease such as systemic lupus erythematosus, rheumatoid arthritis, or dermatomyositis, in which case the SjS is considered a secondary disease [4].

Although the exact etiology of SjS is unclear, several lines of evidence suggest that the disease is caused by epithelial cells acting as atypical antigen-presenting cells, resulting in an aberrant immune response involving both innate and acquired immunity [2]. For instance, circulating antibodies against Ro (also called Sjögren's syndrome–associated antigen A (anti-SSA)) and/or La (Sjögren's syndrome–associated antigen B (anti-SSB)), two antigens which are preferentially expressed in the epithelium tissue lining the salivary glands, can be found in around 30% of the cases [5]. There is also data suggesting that besides factors related to the immune system, endocrine perturbations also contribute to the onset of SjS [6].

The mainstay treatment of SjS is represented by topical medications and patient education aiming to mitigate the sicca syndrome, which is the main factor impacting quality of life

Andrei Stefancu and Maria Badarinza contributed equally to this work.

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