

Extended Abstract

IFI16 and Anti-IFI16 as Novel Biomarkers for Sjogren's Syndrome: Preliminary Data †

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Sjogren's syndrome (SS) is a chronic autoimmune disease characterized by sicca syndrome and systemic manifestations [1]. IFN γ -inducible protein-16 (IFI16) is a viral DNA sensor involved in infections and autoimmune diseases. In SS patients, IFI16 and anti-IFI16 antibodies can be detected in serum and salivary glands [2]. However, to date none of these findings were correlated with SS severity and disease activity.

IFI16 and anti-IFI16 in serum, minor salivary glands and saliva were evaluated together with clinical characteristics and EULAR SS disease activity index (ESSDAI) of SS patients.

Serum and tissue samples were analyzed as previously described [2], salivary anti-IFI16 IgG/IgA detection via ELISA based on horseradish peroxidase–conjugated rabbit anti-human IgG/IgA.

Table 1 describes patient characteristics. Patient (a), with moderate systemic SS (Figure 1a), showed increased IFI16 expression in inflammatory and epithelial cells not only in nuclei, but also in the cytosol, very high serum IFI16 (472 ng/mL), and serum anti-IFI16 IgG (116 U/mL). Patient (b), with localized SS (Figure 1b), showed moderately increased nuclear expression of IFI16 both in inflammatory and epithelial cells and no serum IFI16/anti-IFI16 IgG. In patient (c), with mild systemic SS (Figure 1c), we observed poor inflammatory infiltrate, although salivary anti-IFI16 IgA (10 U/mL) and serum anti-IFI16 IgG (147 U/mL) were found.

In saliva, IFI16 was not detected by Western blot. Recombinant IFI16 incubated at 37 °C was markedly degraded after 1h and completely degraded after 6 h in controls; completely degraded after 1h in patient (a), and more slowly degraded in patients (b) and (c).

Our results suggest that the expression and localization of IFI16 and anti-IFI16 may vary based on disease severity and activity of SS. Further experiments in a larger cohort of patients will allow us to better define the diagnostic and prognostic value of these biomarkers.

Table 1. Characteristics of patients.

Parameter	Patient (a)	Patient (b)	Patient (c)
ESSDAI	12	0	3
RF	+	-	-
Anti-SSA/Ro	+++	++	+
Anti-IFI16 IgG U/mL Serum	116 (+)	102 (-)	147 (+)
IFI16 ng/mL Serum	472 (++)	0.00 (-)	0.00 (-)
Anti-IFI16 IgA U/mL Saliva	4.7 (-)	5.4 (-)	10 (+)
Hypocomplementemia	+	-	+
Hypergammaglobulinemia	+	-	+

EULAR Sjogren Syndrome Disease Activity Index, IFI16 IFN γ -inducible protein 16, RF rheumatoid factor, - negative, + positive, ++ high titre positivity, +++ very high titre positivity.

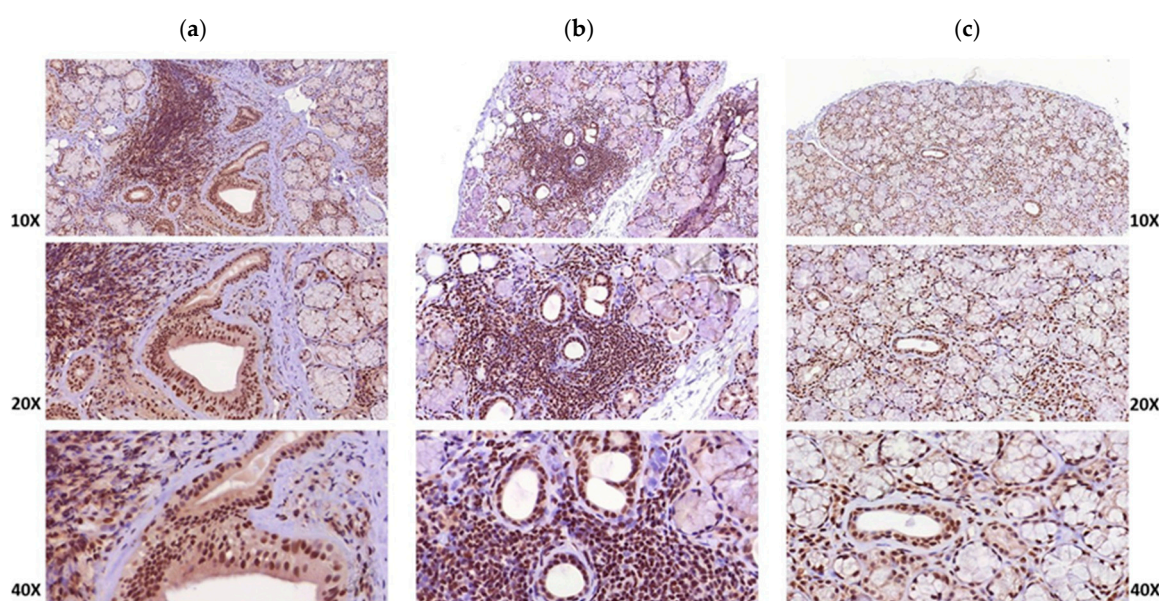


Figure 1. Immunohistochemistry for IFI16 expression in minor salivary glands in three patients. IFI16 staining is shown in brown and hematoxylin staining to highlight nuclei is in blue. (a) moderate systemic disease, (b) localized disease, (c) mild systemic disease.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Brito-Zerón, P.; Baldini, C.; Bootsma, H.; Bowman, S.J.; Jonsson, R.; Mariette, X.; Sivils, K.; Theander, E.; Tzioufas, A.; Ramos-Casals, M. Sjogren’s syndrome. *Nat. Rev. Dis. Primers.* **2016**, *2*, 16047.
2. Alunno, A.; Caneparo, V.; Carubbi, F.; Bistoni, O.; Caterbi, S.; Bartoloni, E.; Giacomelli, R.; Gariglio, M.; Landolfo, S.; Gerli, R. Interferon gamma-inducible protein 16 in primary Sjögren’s syndrome: A novel player in disease pathogenesis? *Arthritis Res. Ther.* **2015**, *17*, 208.



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