Supplementary Materials

Supplemental Methods

Nucleic Acid Extraction.

DNA was extracted from skin using the Qiagen Extraction Kit (Qiagen, Valencia, CA) according to the manufacturer`s protocol. DNA was detected using PCR as previously described (Iwakiri et al., 2009). EBV viral load was quantified using StepOnePlus Sequence Detector (Applied-biosystems, Life Technologies, Grand Island, NY). The standard curve was created automatically with AB program using EBV-B95-8 quantitated DNA PCR control (Advanced Biotechonologies INC) (Jebbink et al., 2003). Different sets of EBER1 primers were used for PCR (Iwakiri et al., 2009) and qPCR (Strowig et al., 2008).

Fibroblast culture

Primary human dermal fibroblast explant cultures from diffuse SSc lesional (LdSSc) and non lesional (NLdSSc) and healthy donors (HDs) were established as described previously (Jelaska et al., 1996). LdSSc and HD fibroblasts were cultured in DMEM supplemented with 10% FBS and penicillin-streptomycin, utilized at passage 3–6. Fibroblasts were incubated in serum-free DMEM for 24h prior to the addition of TLR agonists: R837 imiquimod, sspolyU/ (1mg/ml) (Invitrogen, Grand Island, NY), CpG-ODN-2006 (5μM) (Invitrogen, Grand Island, NY), TGFβ (5ng/ml) (R&D, Minneapolis, MN).

RNA preparation and real-time polymerase chain reaction (q-PCR).

Human tissue and fibroblasts were processed as describe before (Farina et al., 2010b). The synthesized cDNAs were used as templates for quantitative real-time PCR and primed used as described before (Farina et al., 2010a; Farina et al., 2010b). All real
time-PCR was carried out using StepOnePlus Sequence Detector (Applied Biosystems, Life Technologies, Grand Island, NY) and TaqMan primers and probes were purchased from AppliedBiosystem (Life Technologies, Grand Island, NY) and used as recommended by the supplier. The change in the relative expression of each gene was calculated using \( \Delta\Delta C_t \) formula choosing a healthy human subject (Livak and Schmittgen, 2001). Target and control reactions were run on separate wells of the same q-PCR plate (Farina et al., 2010a).

**Nested RT-PCR.**

Human Skin and PBMCs were processed as described before (Farina et al., 2010a; Pendergrass et al., 2010). The synthesized cDNAs were used as templates for nested RT-PCR. BZLF1 and EBNA-1 were used at condition as described before (Gonnella et al., 1997).

**Primers.**

Primers used to detect viral lytic and latent genes were designed using Primer Express software (Applied Biosystems, Life Technologies, Grand Island, NY) and synthesized by Integrated DNA Technologies. Expression of mRNA for BZLF1, LMP1, and BFLLF1 was detected using SYBRGreen chemistry and TaqMan endogenous control amplification (Applied Biosystems, Life technologies, Grand Island, NY). To assure the specificity of primer set, amplicons generated from PCR reaction were analyzed for specific melting temperatures by using the melting curve software. Primers sets sequences are summarized in Table S8.

**Protein extraction**
Proteins were extracted from SSc and HD skin biopsies using Trizol methods described by the manufacturer (Invitrogen, Grand Island, NY), and suspended in 1% SDS. Samples (30µg) were heat denatured with reducing agent and loaded onto 12% SDS-PAGE gels.

**Western Blot analysis.**

Cellular extracts were prepared by sonication of cells in 10 % NU-PAGE (Invitrogen, Grand Island, NY), in reducing condition. Blotted protein were probed with each primary monoclonal antibody respectively for EBNA2 (DAKO, Carpinteria, CA), BFLF2 (Gonnella et al., 2005) BFRF1 (Farina et al., 2005; Farina et al., 2000), Rta (Argene, bioMérieux, Inc. Durham, NC), Zta (Argene, bioMérieux, Inc. Durham, NC), a-collagen1a1-antibody (SouthernBiotech, Birmingham, Alabama), anti-b-actin-antibody (Sigma, St. Louis, MO), or polyclonal antibodies for BFRF1 (Farina et al., 2005), Rta (kindly provided by Prof. G.Miller), and then probed with secondary antibody and visualized using super signal chemiluminescence kit (Thermo Scientific, Pittsburg, PA).

**Immunohistochemistry.**

Tissue sections were deparaffinised as described before using primary antibodies described above in western-blotting and immunocytostaining (Farina et al., 2009). Hematoxylin (Thermo Scientific, Pittsburg, PA) was used to counterstain the cells.

**Immunocytochemistry.**

Infected cell were washed with PBS, trypsinized and spotted on to coverslip as previously described (Farina et al., 2004; Farina et al., 2000; Gonnella et al., 2005). Slides were stained with mouse monoclonal antibodies against EBNA2 (PE2), BZLF1 (Argene), BFLF2(Gonnella et al., 2005), CD20 (DAKO, Carpinteria, CA ), CD21 (DAKO, Carpinteria, CA), BDCA-1 (MiltenyiBiotec, Auburn,
CA), BFRF1 (Farina et al., 2005), polyclonal antibodies against Collagen1 (SouthernBiotech, Birmingham, Alabama), and BFRF1-R319 (Farina et al., 2000) and secondary-antibodies-Cy3-conjugated (Jackson IR, West Grove, PA), Alexafluor-350 goat-anti mouse antibody (Invitrogen, Grand Island, NY), or 488-labeling (Zenon kit; Invitrogen, Grand Island, NY). Cell nuclei were counterstained with DAPI (Sigma, St. Louis, MO).

**EBV-VCA-IgG/EBNA1-IgG bio-assay quantification.** EBV- EBNA1-IgG ELISA was conducted in sera from 34 HDs and 78 SSc patients according to the supplied protocol (NovaGnost, Siemens Victoria, Australia); EBV-VCA-IgG ELISA ELISA was conducted in sera from 34 HDs and 78 SSc patients according to the supplied protocol (Novagnost SIEMENS, Victoria, Australia).
Fig. S1. **EBER probe in the skin of healthy donors.**

(a and b) Representative images of EBER in situ hybridization (ISH) in the skin from 2 healthy donors (HDs) (left panels); α-smooth muscle actin (αSMA) staining by IHC in serial sections from skin of 2 HDs (right-panels) (scale/bars upper-panels, 100µm, lower-panel 50µm).
Fig. S2. Expression of EBV transcripts in skin and PBMCs of SSc patients.

(a) Representative gel electrophoresis of EBV-lytic/latency genes (BZLF1/EBNA1) RT-PCR products from 6 lesional diffuse SSc (LdSSc) and one representative normal skin (HD); 293 and Raji cells were use as negative and positive control respectively. (b) RT-PCR products of EBV-lytic-gene BZLF1 in (LdSSc) and non/lesional (NLdSSc) from 2 representative patients. (c) RT-PCR products of EBV-lytic-gene BZLF1 in PBMCs from dSSc and 2 representative HDs subjects. (d) PCR products of EBV DNA (EBER1) in LdSSc and in 2 HDs representative skin; DNA from B95-8-EBV-positive cells were used as positive control, GAPDH used as internal control; incidence of EBV DNA and BZLF1/EBNA1 transcripts in screened skin section are summarized in Supplemental Table 2. (e-f) Detection of EBV-load by q-PCR; each sample was tested in duplicates and normalized by endogenous internal control. Shown here are copies of viral nucleic acid in the skin calculated by standard curve. 293 cells and Foreskin dermal skin were used as negative control. The average of copies number is represented by horizontal line ± SE. p-values calculated using Wilcoxon two samples test.
Fig. S3. Expression of EBV proteins in the skin of SSc patients.
(a-c) Immuno-histochemistry (IHC) in serial tissue sections from lesional (LdSSc) and non-lesional (NLdSSc) skin samples. Nuclear localization of EBV-lytic-protein/Zebra in scattered fibroblasts (square insert) and in the matrix, and expression of the early lytic BFLF2 protein in LdSSc deep dermis obtained from the same patient (a-b). Expression of Zebra and early-lytic-BFLF2 proteins in LdSSc and NLdSSc skin from the same patient (c). Crude lysate from skin and PBMCs of representative SSc patients and HDs (d and e), skin and PBMCs samples obtained from the same patients (f), were separated on SDS-PAGE, blotted on PVDF and probed with the indicated antibodies; lysate from B95-8 EBV infected cells were used as positive control; β-actin was used as loading control. Numbers represent distinct patients enrolled in the study. (red-staining bar scale 100µm (upper-panels) and 10µm (lower and squares panels).
Fig. S4. EBV RNAs and antigens in the skin of SSc patients.
(a-c) Representative images of EBERs in situ hybridization (ISH), and (d-f) immuno-histochemistry (IHC) of EBV- lytic-protein Zebra in serial tissue sections from lesional skin (LdSSc) of two SSc cohort patients naïve vs immunosuppressed treatment (arrows indicate vessels positive or negative for EBERs staining). Numbers on the side represent distinct patient enrolled in the study, whose clinical characteristics are summarized in Table S5. Bar scale 100µm (upper panels) and 10µm (lower and squares panels).
Fig. S5. **EBV antigens expression in the skin.**

Immuno-histochemistry (IHC) in serial skin tissue sections from lesional (LdSSc), non-lesional (NLdSSc) and healthy-donor (HD) skin sample of indicated EBV-proteins (red-staining bar scale 50µm). Numbers on the side represent distinct patient enrolled in the study.
**Fig. S6.** EBV-p2089-recombinant-virus infects human SSc-fibroblasts “*in vitro*”.  
(a) Inverted microscope image of 2 EBV-p2089-infected-SSc-fibroblast 4 week/post infection (PI). GFP expression indicates recombinant ebv- infected cells. (left panel: phase-contrast-light-microcopy; bar scale 20 mm).  
(b) Western-blot analysis of Poly (ADP-ribose) polymerase (PARP) protein in cell lysates from EBV-p2089 and mock-infected-SSc-fibroblast-cultures at 4-week-PI. B95-8 EBV-activated was used as positive control.
Fig. S7. Expression of TGFβ-responsive genes in fibroblasts infected with EBV.
mRNA expression of indicated genes in EBVp2089-infected, mock-infected and control fibroblasts from SSc patients after 4/week post infection, evaluated by qPCR. Fold-changes shown on the graph are normalized to mRNA expression by each corresponding untreated cell lines. Bars represent mean ± S.E.M. from 3 separate experiments from different SSc-fibroblast-cell-lines. p-values calculated using two-tailed T-test. *= p<0.05; **= p<0.01; ***= p<0.001
Fig. S8. Expression of Interferon-stimulated-genes (ISGs) in human dermal fibroblasts by TLRs stimulation.

Fibroblasts explanted from healthy donors (HDs) (a) and from lesional skin of patients with dSSc (b), were starved o/n and incubated with TLR-agonist-ligands as indicated for 24hrs. mRNA was harvested and analyzed by qPCR. Fold-changes shown on the graph are normalized to mRNA expression by each corresponding untreated cell lines. Bars represent mean ± S.E.M. from 3 separate experiments using 3 different cell lines. p-values calculated using two-tailed T-test. *= p<0.05; **= p<0.01; ***= p<0.001. (c-d) Western blot analysis was performed to determine type I collagen secretion in the media of indicated fibroblasts cultures after indicated treatment. Total protein loading was determined by Ponceau-S staining of the filter after western transfer (bottom panel).
Fig. S9. Expression of Interferon-stimulated-genes (ISGs) in human dermal fibroblasts by TLRs chronic stimulation. Fibroblasts explanted from healthy donors (HDs) (a) and from lesional skin of patients with dSSc (b), were incubated with TLR-agonist-ligands as indicated and treated for 3 times/week for 4 weeks in presence of FBS 10%. mRNA was harvested and analyzed by qPCR. Fold-changes shown on the graph are normalized to mRNA expression by each corresponding untreated cell lines. Bars represent mean ± S.E.M. from 3 separate experiments using 3 different cell lines. p-values calculated using two-tailed T-test. *= p<0.05; **= p<0.01; ***= p<0.001.
Table S1. Demographics and Clinical characteristics of SSc patients and Healthy Donor (HD) subjects

|                      | SSc     | HD      |
|----------------------|---------|---------|
| Subjects (n)         | 89      | 36      |
| Age mean ± SE (years)| 47.9 ± 2.1 | 42 ± 2.8 |
| Sex (F/M)            | 72/17   | 27/9    |
| Race %               |         |         |
| Caucasian            | 86.6    | 93.4    |
| African-American     | 6.7     |         |
| others               | 6.6     | 6.6     |
| diffuse SSc (dSSc) (n)| 80      | -       |
| limited SSc (ISSc) (n)| 9       | -       |
| EBV seropositive (anti-EBNA1) | 100% (78/78) | 100% (34/34) |
Table S2. Detection of Epstein-Barr virus genomes and their products in PBMCs and skin tissues of patients with SSc and HD subjects

|                  | PBMC RT-PCR | Skin RT-PCR | RNA in situ | DNA¹ |
|------------------|-------------|-------------|-------------|------|
|                  | BZLF1 | BZLF1 | EBNA1 | EBER | EBER1 |
| dSSc (n=80)      | 10/21 (47%) | 22/59 (37%) |             |      |       |
| LdSSc (n=50)     | -     | 17/50 (34%) | 23/64 (36%) | 11/23 (47%) | 20/22 (90%) |
| NLdSSc (n=9)     | -     | 5/9 (55%)  | 3/9 (33%)  | 2/4 (50%)  | 3/3 (100%) |
| ISSc (n=9)       | -     | 1/7 (14%)  | 3/9 (33%)  | 2/5 (40%)  | 6/6 (100%) |
| HD (n=36)        | 2/20 (10%) | 0/16 | 0/16 | 0/15 | 2/7 (26%) |
| p value LdSSc vs HD | p<0.01 | p<0.05 | p<0.05 | p<0.0001 | p<0.05 |

¹: DNA detected by PCR
Table S3: serological profile to EBV in patients with diffuse (dSSc) and limited (lSSc) SSc disease.

|     | Age (years) | d.d.  | ANA (auto-ab) | IgG-VCA* ELISA | Immunosuppressant Therapy |
|-----|-------------|-------|---------------|----------------|--------------------------|
| dSSc#67 | 35 |       |               | 300            | none                     |
| dSSc#68 | 26 | 3     | n/a**         | 243            | mycophenolate             |
| dSSc#69 | 36 | n/a   | n/a           | 282            | none                     |
| dSSc#70 | 67 | n/a   | n/a           | 261            | none                     |
| dSSc#71 | 52 | 4     | Scl-70        | 181            | gleevec                  |
| dSSc#72 | 71 | 4     | n/a           | 175            | none                     |
| dSSc#73 | 61 | 6     | n/a           | 175            | methotrexate             |
| dSSc#74 | 29 | n/a   | n/a           | 170            | none                     |
| dSSc#75 | 55 | n/a   | Scl-70        | 158            | none                     |
| dSSc#76 | 53 | 5     | +             | 163            | prednisone               |
| dSSc#77 | 38 | 10    | +             | 113            | cyclophosphamide         |
| dSSc#78 | 67 | 6     | +             | 44             | cyclophosphamide         |
| dSSc#79 | 53 | 4     | n/a           | 12             | gleevec                  |
| dSSc#80 | 42 | 8     | Scl-70        | 12             | prednisone               |
| dSSc#81 | 54 | 7     | Scl-70        | 11             | none                     |
| dSSc#82 | 55 | 7     | Scl-70        | 9              | none                     |
| lSSc#19 | 66 | 12    | +             | 241            | none                     |
| lSSc#20 | 71 | 8     | +             | 191            | none                     |
| lSSc#21 | 84 | 15    | +             | 66             | none                     |
| lSSc#22 | 63 | 6     | n/a           | 57             | methotrexate             |
| lSSc#23 | 63 | 5     | n/a           | 48             | mycophenolate             |
| lSSc#24 | 45 | 10    | n/a           | 41             | prednisone               |
| lSSc#25 | 48 | n/a   | +             | 28             | prednisone               |
| lSSc#26 | 41 | 7     | n/a           | 8              | none                     |
| lSSc#27 | 67 | 4     | +             | 6              | none                     |

**Anti-VCA** = antibody to the viral capsid antigen, positive >1.1 U/mL; negative < 0.37;

**n/a** = not available
### Table S4. Demographics and clinic characteristics of two cohorts of SSc patients Treatment Naïve vs Treatment

| LdSSc  | Age | EBER “in situ” RNA | d.d. (mo)* | MRSS | Medications |
|--------|-----|--------------------|------------|------|-------------|
| LdSSc #42 | 64  | +++                | 5          | 31   | naive       |
| LdSSc #43 | 62  | ++                 | 36         | 12   | naive       |
| LdSSc #44 | 37  | +++                | 9          | 21   | naive       |
| LdSSc #45 | 39  | ++++               | 192        | 29   | naive       |
| LdSSc #46 | 61  | ++                 | 12         | 26   | naive       |
| LdSSc #47 | 53  | +++                | 8          | 42   | naive       |
| LdSSc #48 | 61  | ++                 | 12         | 26   | naive       |
| LdSSc #49 | 42  | neg                | 24         | 27   | naive       |
| LdSSc #50 | 65  | neg                | 9          | 50   | naive       |
| LdSSc #51 | 62  | neg                | 252        | 20   | naive       |
| LdSSc #52 | 53  | neg                | 18         | 42   | naive       |
| LdSSc #53 | 61  | ++                 | 14         | 26   | naive       |
| LdSSc #54 | 58  | ++                 | 18         | 31   | naive       |
| LdSSc #55 | 41  | +                  | 6          | 30   | naive       |
| LdSSc #56 | 57  | +++                | 3          | 42   | naive       |
| LdSSc #57 | 53  | neg                | 38         | 28   | naive       |
| LdSSc #58 | 55  | neg                | 30         | 5    | mycophenolate |
| LdSSc #59 | 47  | neg                | 50         | 2    | mycophenolate |
| LdSSc #60 | 38  | neg                | 21         | 24   | methotrexate |
| LdSSc #61 | 54  | +                  | 44         | 27   | mycophenolate |
| LdSSc #62 | 49  | ++                 | 6          | 10   | cellcept    |
| LdSSc #63 | 53  | ++                 | 53         | 31   | cytoxan     |
| LdSSc #64 | 53  | +++                | 18         | 23   | cytoxan     |
| LdSSc #65 | 51  | +++                | 35         | 16   | prednisone  |
| LdSSc #66 | 54  | neg                | 55         | 31   | Ab-interferon type I |

LdSSc = Lesional diffuse SSc  
*d.d. mo= duration of disease in months; MRSS: Modified Rodnan skin score
**Table S5.** Comparison of EBER “in situ” RNA expression in SSc patients Treatment-Naïve vs Treatment-Immunosuppressed

|                      | Treatment-naïve (TN) | Treatment-immunosuppressed (T) |
|----------------------|----------------------|--------------------------------|
| LdSSc (n total)      | 16                   | 9                              |
| EBERs positive (n) (%)| 11 (68%)             | 5 (55%)                        |
| EBERs negative (n) (%)| 5 (32%)              | 4 (44%)                        |
| TN vs T (Fisher exact test) |                      | P=0.6                          |
**Table S6.** (part I): EBV expression pattern in lesional skin (LdSSc) and auto-antibodies profile in patients with SSc diffuse disease.

| LdSSc | Lytic/genes | Latency/genes | Lytic/proteins | auto-antibodies |
|-------|-------------|---------------|----------------|-----------------|
|       | Zta         | EBERs         | EBNA1 (Zebra/Rta/BFLF2) | Scl-70          |
| #1    | +           | +             | +               | negative        |
| #3    | +           | +             | +               | negative        |
| #4    |              | +             |                 | positive        |
| #5    | negative    | negative      | +               | negative        |
| #6    | +           | negative      | +               | Scl-70          |
| #7    | +           | negative      |                 | positive        |
| #8    | +           | negative      | +               | Scl-70          |
| #9    | +           | negative      | negative        | positive        |
| #10   | negative    | negative      | negative        | Scl-70          |
| #11   | negative    | negative      | negative        | Scl-70          |
| #12   | +           | negative      | +               | Scl-70          |
| #13   |              | +             |                 | positive        |
| #14   | +           | +             | +               | Scl-70          |
| #15   | negative    | negative      | negative        | Scl-70          |
| #17   | negative    | negative      |                 | positive        |
| #18   | negative    | negative      |                 | Scl-70          |
| #19   | negative    | negative      |                 | negative        |
| #20   | negative    | negative      | negative        | Scl-70          |
| #21   | negative    | negative      | Scl-70          |                 |
| #22   | +           | +             | +               | negative        |
| #23   | +           | negative      |                 | Scl-70          |
| #24   |              |               |                 | Scl-70          |
| #25   | negative    | +             |                 | positive        |
| #26   | negative    | +             | +               | positive        |
| #28   |              |               |                 | positive        |
| #29   | +           | negative      |                 | positive        |
| #30   | negative    | negative      |                 | negative        |
| #32   | +           | +             | +               | Scl-70          |
| #33   | +           | +             | +               | negative        |
Table S6. (part II): EBV expression pattern in lesional skin (ISSc) and auto-antibodies profile in patients with limited SSc disease.

| ISSc | Lytic/gene | Latency/genes | Lytic-proteins | auto-antibodies |
|------|------------|---------------|----------------|----------------|
|      |            | Zta | EBER | EBNA1 | (Zebra/Rta/BFLF2) |         |
| #27  | negative   | negative |       |       |                   |         |
| #31  | negative   | +   |       |       |                   | +       |
| #34  | +          | neg  |       |       |                   | + ACA   |
| #36  | negative   | neg  |       |       |                   | negative |
| #37  | negative   | +   | neg  |       |                   | +       |
| #38  | negative   | negative | neg  | negative |               | +       |
| #39  | negative   | negative | neg  |       |                   | +       |
| #40  | +          | +   |       |       |                   | +       |
| #41  | negative   | +   |       |       |                   | +       |
Table S7. Detection of Epstein-Barr virus products in PBMCs and skin tissues of patients with SSc and HDs

|                | Zebra* | RTA*       | BFRF1* | BFLF2* | EBNA2* |
|----------------|--------|------------|--------|--------|--------|
| **LdSSc skin** |        |            |        |        |        |
| (n=50)         | 11/50  | 10/50      | 13/50  | 4/6    | 24/50  |
|                | (22%)  | (20%)      | (26%)  | (66%)  | (48%)  |
| **HD skin**    | 0/10   | 1/20       | 1/20   | 0/4    | 1/20   |
| (n=10)         | (3.3%) | (3.3%)     | (3.3%) | (3.3%) | (3.3%) |
| **SSc PBMC**   | 11/21  | 11/21      | 11/21  | 6/21   | 10/21  |
| (n=21)         | (52%)  | (52%)      | (52%)  | (28%)  | (47.6%)|
| **HD PBMC**    | 3/20   | 1/20       | 1/20   | 1/20   |
| (n=20)         | (15%)  | (5%)       | (5%)   | (5%)   |

*= evaluated by Western-blot
Table S8. Real-time PCR primers used for detection of viral cDNAs.

| GENE | Forward (5’-3’) | Reverse (5’-3’) |
|------|----------------|----------------|
| qPCR |                |                |
| BZLF1| -TCGCATTCCTCCAGCGAT- | -AACCTGGAGACAATTCTACTGTCTCAA- |
| LMP1 | -CAGTCAGGCAAGCTATGA-  | -CTGGTTCCGGGTGGAGATGA-  |
| BLLF1| -CATTGGTAGCCGTTCTGATGATAAT- | -GCGAGCAATCGGACATTTTGACAT- |
Supplemental References

Farina A, Cardinali G, Santarelli R, Gonnella R, Webster-Cyriaque J, Bei R, et al. (2004) Intracellular localization of the Epstein-Barr virus BFRF1 gene product in lymphoid cell lines and oral hairy leukoplakia lesions. Journal of medical virology 72:102-11.

Farina A, Feederle R, Raffa S, Gonnella R, Santarelli R, Frati L, et al. (2005) BFRF1 of Epstein-Barr virus is essential for efficient primary viral envelopment and egress. Journal of virology 79:3703-12.

Farina A, Santarelli R, Gonnella R, Bei R, Muraro R, Cardinali G, et al. (2000) The BFRF1 gene of Epstein-Barr virus encodes a novel protein. Journal of virology 74:3235-44.

Farina G, Lafyatis D, Lemaire R, Lafyatis R (2010a) A four-gene biomarker predicts skin disease in patients with diffuse cutaneous systemic sclerosis. Arthritis and rheumatism 62:580-8.

Farina G, Lemaire R, Pancari P, Bayle J, Widom RL, Lafyatis R (2009) Cartilage oligomeric matrix protein expression in systemic sclerosis reveals heterogeneity of dermal fibroblast responses to transforming growth factor beta. Annals of the rheumatic diseases 68:435-41.

Farina GA, York MR, Di Marzio M, Collins CA, Meller S, Homey B, et al. (2010b) Poly(I:C) drives type I IFN- and TGFbeta-mediated inflammation and dermal fibrosis simulating altered gene expression in systemic sclerosis. The Journal of investigative dermatology 130:2583-93.

Gonnella R, Angeloni A, Calogero A, Farina A, Santarelli R, Gentile G, et al. (1997) Transcription of latent and replicative Epstein-Barr-virus genes in bone-marrow and peripheral-blood mononuclear cells of healthy donors. International journal of cancer Journal international du cancer 70:524-9.

Gonnella R, Farina A, Santarelli R, Raffa S, Feederle R, Bei R, et al. (2005) Characterization and intracellular localization of the Epstein-Barr virus protein BFLF2: interactions with BFRF1 and with the nuclear lamina. Journal of virology 79:3713-27.

Iwakiri D, Zhou L, Samanta M, Matsumoto M, Ebihara T, Seya T, et al. (2009) Epstein-Barr virus (EBV)-encoded small RNA is released from EBV-infected cells and activates signaling from Toll-like receptor 3. The Journal of experimental medicine 206:2091-9.
Jebbink J, Bai X, Rogers BB, Dawson DB, Scheuermann RH, Domiatì-Saad R (2003) Development of real-time PCR assays for the quantitative detection of Epstein-Barr virus and cytomegalovirus, comparison of TaqMan probes, and molecular beacons. The Journal of molecular diagnostics : JMD 5:15-20.

Jelaska A, Arakawa M, Broketa G, Korn JH (1996) Heterogeneity of collagen synthesis in normal and systemic sclerosis skin fibroblasts. Increased proportion of high collagen-producing cells in systemic sclerosis fibroblasts. Arthritis and rheumatism 39:1338-46.

Livak KJ, Schmittgen TD (2001) Analysis of relative gene expression data using real-time quantitative PCR and the 2(-Delta Delta C(T)) Method. Methods 25:402-8.

Pendergrass SA, Hayes E, Farina G, Lemaire R, Farber HW, Whitfield ML, et al. (2010) Limited systemic sclerosis patients with pulmonary arterial hypertension show biomarkers of inflammation and vascular injury. PloS one 5:e12106.

Strowig T, Briot F, Arrey F, Bougras G, Thomas D, Muller WA, et al. (2008) Tonsilar NK cells restrict B cell transformation by the Epstein-Barr virus via IFN-gamma. PLoS pathogens 4:e27.