**Table S1: Detailed characteristics of the cohort of patients with IgG4-RD.**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **IgG4-RD patients** | **Age (yrs)** | **Sex** | **Serum IgG4 (g/L)**  | **Serum IgE (KIU)** | **Eosin (count)** | **Atopy** | **Organs involved** | **IgG4-RI DA index** | **Stage of disease at sampling** | **Disease duration (yrs)** |
| **1** | 80 | M | 39.0 | 698 | 0.15 | No | AIP, Lung, LN | 15 | Diagnosis, No Tx | 0.75 |
| **2** | 80 | F | NR | NR | 0.18 | Yes | Biliary, LN, Liver, Lung | 6 | Relapse, no Tx | 15 |
| **3** | 64 | M | 2.45 | 17.3 | 0.18 | No | AIP, Lung | 8 | Diagnosis, no Tx | 0.5 |
| **4** | 79 | M | 3.61 | 389 | 0.11 | Yes | AIP, SMG, LN | 11 | Relapse, on MMF | 2 |
| **5** | 40 | F | 1.63 | 41.9 | 0.26 | Yes | Biliary, Lung, LN | 13 | Relapse on Aza | 9 |
| **6** | 66 | M | 11.6 | 1461 | 0 | Yes | AIP, TIN | 10 | Relapse, on Pred | 2 |
| **7** | 70 | M | 5.12 | 463 | 0.22 | Yes | AIP, SMG | 8 | Diagnosis, No Tx | 2 |
| **8** | 60 | M | 38.1 | 643 | 1.63 | No | Biliary, LN, Colon | 14 | Diagnosis, No Tx | 2 |
| **9** | 65 | M | 1.86 | 123 | 0 | Yes | Lung, Nasal, Aortitis | 13 | Diagnosis, No Tx | 0.5 |
| **10** | 50 | F | 0.37 | 11.4 | 0.17 | No | AIP, LG, SMG, Orbit | 16 | Diagnosis, No Tx | 1 |
| **11** | 80 | F | 7.15 | 269 | 0.22 | Yes | AIP, Biliary, SMG | 16 | Relapse, No Tx | 14 |
| **12** | 55 | M | 1.94 | 152 | 0.28 | Yes | AIP/Biliary | 12 | Diagnosis, No Tx | 0.08 |
| **13** | 66 | F | 0.11 | 6.29 | 0 | No | LG, Orbit, AIP | 4 | Inactive, on MMF and CsP | 2.5 |
| **14** | 63 | M | 3.62 | 72 | 0.19 | Yes | AIP/Biiary | 2 | Inactive, on Aza | 7.5 |
| **15** | 69 | M | 2.38 | NR | 0.11 | Yes | AIP, LN, SMG | 3 | Inactive, prior surgery | 2.5 |
| **16** | 58 | M | 1.33 | NR | 0.12 | No | Biliary | 2 | Inactive, prior Pred | 3 |
| **17** | 42 | F | 0.65 | NR | 0.1 | Yes | Biliary | 1 | Inactive, on Aza | 3.5 |
| **18** | 80 | M | 0.81 | 73.5 | 0.12 | Yes | AIP, Biliary, TIN | 1 | Inactive, on MMF | 6 |

Abbreviations: yrs; years; g/L: grams per litre; KIU: international units; IgG4 RI DA index: IgG4 responder index disease activity index; M: male; F: female; NR: not recorded; AIP: autoimmune pancreatitis; Biliary: IgG4-sclerosing cholangitis; LN: lymph node; TIN: renal tubulointerstitial nephritis; SMG: sub mandibular gland; LG: lacrimal gland; Tx: treatment; Aza: azathioprine; MMF: mycopheonlate mofetil; CsP: cyclophosphamide; Pred: prednisolone.

**Table S2:** **Circulating PD1+ Tfh cells correlate with IL4 and IL21 cytokine production in patients with active IgG4-SC/AIP.**

Correlation of PD-1+ Tfh cells and cytokine production in cultured supernatants of active IgG4-SC/AIP patients. Spearman’s Rank correlation and p values are expressed as NS≥0.05, \*p<0.05.

|  |  |  |
| --- | --- | --- |
| Cytokine | Spearman Rank Correlation  | p value |
| IL-4 | 0.83 | 0.03 \* |
| IL-5 | 0.71 | 0.06 |
| IL-6 | 0.09 | 0.46 |
| IL-8 | 0.49 | 0.18 |
| IL-10 | 0.60 | 0.12 |
| IL-13 | 0.77 | 0.05 |
| IL-17A | 0.49 | 0.18 |
| IL-21 | 0.89 | 0.02 \* |
| TGF-Beta | 0.03 | 0.5 |
| BAFF | -0.2 | 0.36 |

**Table S3:** Qualitative histological staining for T-fh cells, activation and chemokine homing markers.

|  |  |  |
| --- | --- | --- |
| **Cases and Controls** | **Specimen**  | **Markers** |
| **CD4** | **CXCR5** | **ICOS** | **CXCL13** |
| **IgG4-RD (n=12)** |
| Liver | B | ++ |  + |  + |  ++ |
| Bile duct | R | ++ |  + |  +++ |  + |
| Mesenteric mass & Lymph node | R | ++ |  ++ |  + |  +++ |
| Mesenteric mass | B | ++ | NS | 0 | 0 |
| Salivary gland | R | ++ |  ++ |  + |  +++ |
| Salivary gland | B | ++ |  + |  ++ |  + |
| Pancreas | R | ++ |  + |  ++ |  + |
| Pancreas | R | +++ |  +++ |  + |  + |
| Pancreas | R | ++ |  ++ |  ++ |  ++ |
| Pancreas | R | ++ |  + |  +++ |  ++ |
| Renal | B | ++ | NS |  + |  + |
| Abdominal mucosa  | R | +++ |  ++ |  ++ |  ++ |
| **Inflammatory DC (n=5)** |
| Lymph node  | R | +++ |  ++ |  ++ |  + |
| Gall bladder | R | ++ |  + | 0 | 0 |
| Pancreas  | R | +++ |  +++ |  ++ |  + |
| Pancreas  | B | 0 | 0 | 0 | 0 |
| Bile duct | R | ++ |  + | 0 | 0 |
| **Non-Inflammatory DC (n=5)** |
| Lymph node  | R | + | 0 | 0 | 0 |
| Gall bladder | R | + | 0 | 0 | 0 |
| Pancreas  | R | 0 | 0 | 0 | 0 |
| Pancreas  | B | 0 | 0 | 0 | 0 |
| Bile duct | R | 0 | 0 | 0 | 0 |

Abbreviations: B: biopsy specimen; R: resection specimen; DC: disease control; N: number; NS: excessive background staining so unable to interpret. Absent (0); Few cells (+); Moderate cells (++); Abundant cells (+++).

**Table S4:** Quantitative histological staining for Tfh cells, activation and chemokine homing markers.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Quantity of positive stained cells** | **CD4** | **CXCR5** | **ICOS** | **CXCL13** |
| **IgG4-RD specimens n=12** |
| Absent cells | 0  | 0 (0) | 1 (8) | 1 (8) |
| Few cells, number (%) | 0  | 5 (42) | 5 (42) | 5 (42) |
| Moderate cells, number (%)  | 10 (83) | 4 (33) | 4 (33) | 4 (33) |
| Abundant cells, number (%) | 2 (17) | 1 (8) | 2 (17) | 2 (17) |
| **DC specimens n=10** |
| Absent cells | 4 (40) | 6 (60) | 6 (60) | 6 (60) |
| Few cells, number (%) | 2 (20) | 2 (20) | 0 (0) | 4 (40) |
| Moderate cells, number (%)  | 2 (20) | 1 (10) | 4 (40) | 0 (0) |
| Abundant cells, number (%) | 2 (20) | 1 (10) | 0 (0) | 0 (0) |