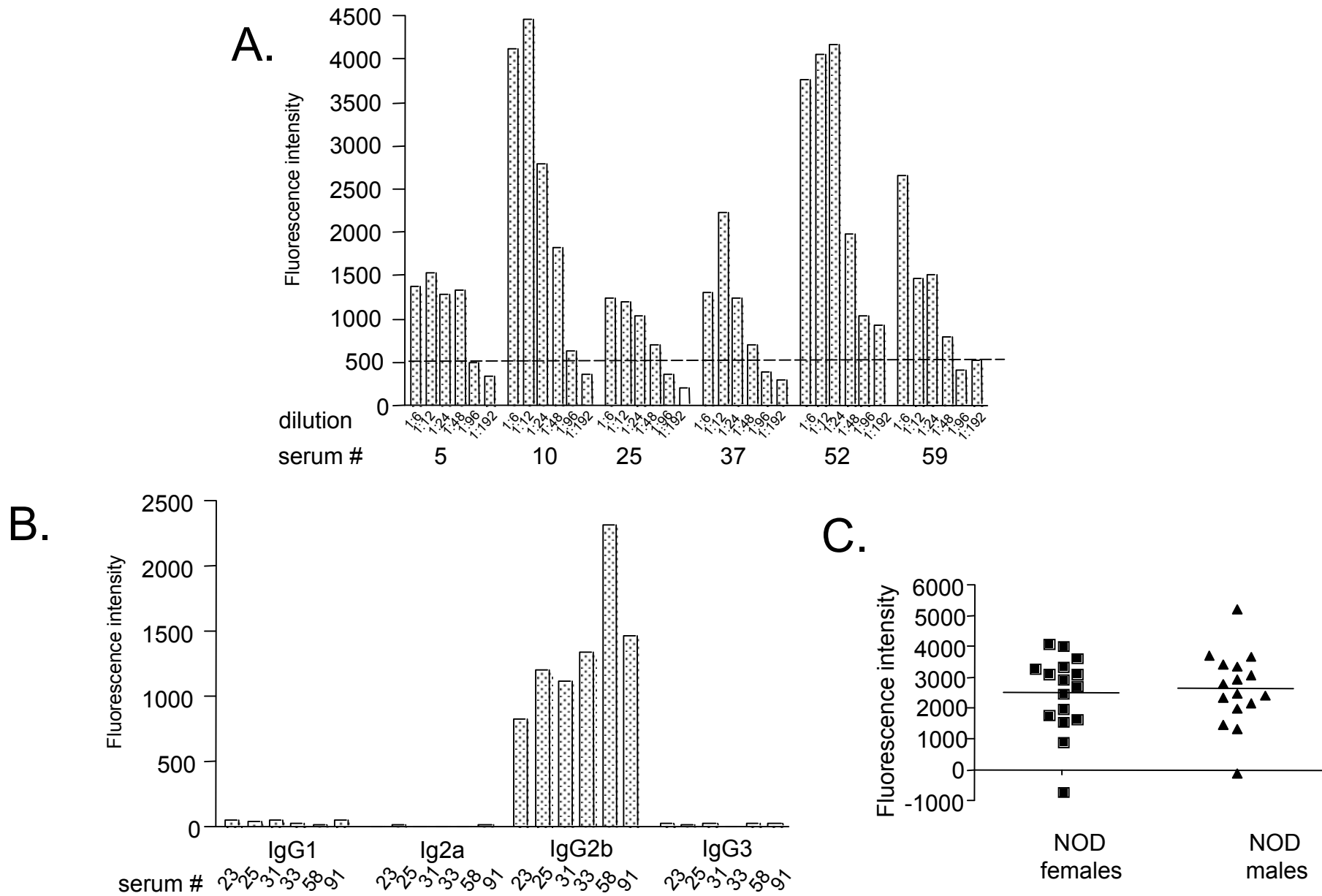


**Figure S1. Analysis of expression of serpinB13 in the pancreas.** Tissues isolated from 4-week old NOD female and 293 T cells transfected with serpinB13 (positive control) underwent Western blot in the order indicated. Staining of the nitrocellulose membranes shown on the right was preceded by preincubation of antibodies with soluble serpinB13 (10  $\mu\text{g}/\text{mL}$ ) at 4°C overnight.



**Figure S2. The titer (A) and IgG subclass (B), and gender specificity (C) of anti-serpinB13 autoantibodies in NOD mice.** Luminex-based methodology was used to detect antibodies, exactly as described in Figure 3. In (B), serum samples were tested at the final dilution of 1:12. Mice were bled at 4 weeks of age.

**Supplemental Table 1. Frequency of strong secretors of anti-serpinB13 autoantibodies in NOD mouse cohort.**

| Strong secretors (>3000 FI) at 4 weeks of age by group |                                  |              |              |            |               |        |
|--------------------------------------------------------|----------------------------------|--------------|--------------|------------|---------------|--------|
| Strong secretors                                       | Group (by age of diabetes onset) |              |              |            |               |        |
| Frequency<br>Percent<br>Row Pct<br>Col Pct             | <16<br>wks                       | 16-20<br>wks | 20-24<br>wks | >24<br>wks | Diab.<br>free | Total  |
| <b>No</b>                                              | 21                               | 26           | 13           | 8          | 14            | 82     |
|                                                        | 21.43                            | 26.53        | 13.27        | 8.16       | 14.29         | 83.67  |
|                                                        | 25.61                            | 31.71        | 15.85        | 9.76       | 17.07         |        |
|                                                        | 100.00                           | 83.87        | 81.25        | 57.14      | 87.50         |        |
| <b>Yes</b>                                             | 0                                | 5            | 3            | 6          | 2             | 16     |
|                                                        | 0.00                             | 5.10         | 3.06         | 6.12       | 2.04          | 16.33  |
|                                                        | 0.00                             | 31.25        | 18.75        | 37.50      | 12.50         |        |
|                                                        | 0.00                             | 16.13        | 18.75        | 42.86      | 12.50         |        |
| <b>Total</b>                                           | 21                               | 31           | 16           | 14         | 16            | 98     |
|                                                        | 21.43                            | 31.63        | 16.33        | 14.29      | 16.33         | 100.00 |

**Note:** Examination of the output of anti-serpinB13 autoantibodies was performed using luminex assay, exactly as described in the legend to Figure 3. All mice (n=98) were screened at 4 weeks of age and monitored once a week for diabetes onset.

**Supplemental Table 2A. Secretion of anti-serpinB13 antibodies in healthy population.**

| <b>Controls 1-20 years (n=53)</b> |              |                                |                                    |                |               |
|-----------------------------------|--------------|--------------------------------|------------------------------------|----------------|---------------|
| <b>Age</b>                        | <b>I. D.</b> | <b><math>\Delta 8^*</math></b> | <b><math>\Delta 13^{**}</math></b> | <b>Inh.***</b> | <b>Result</b> |
| 3                                 | II-60        | 454                            | 166                                | 63%            | ++            |
| 4                                 | II-51        | 762                            | 502                                | 34%            | +             |
| 4                                 | II-52        | 262                            | 114                                | 56%            | ++            |
| 5                                 | I-55         | 475                            | 266                                | 44%            | +             |
| 5                                 | I-64         | -64                            | 8.75                               | X              | Neg.          |
| 5                                 | II-53        | -367                           | -500                               | X              | Neg.          |
| 5                                 | II-54        | 200                            | -141                               | 100%           | ++            |
| 6                                 | I-52         | 583                            | 404                                | 31%            | +             |
| 6                                 | I-61         | -2335                          | 100                                | X              | Neg.          |
| 6                                 | II-55        | 682                            | 916                                | X              | Neg.          |
| 6                                 | II-56        | 2495                           | -605                               | 100%           | ++            |
| 7                                 | I-56         | 60                             | -33                                | X              | Neg.          |
| 7                                 | II-57        | 500                            | 547                                | X              | Neg.          |
| 7                                 | II-58        | 263                            | 217                                | 17%            | Neg.          |
| 7                                 | II-59        | 128                            | 572                                | X              | Neg.          |
| 8                                 | I-59         | 791                            | -411                               | 100%           | ++            |
| 8                                 | II-61        | 815                            | 609                                | 25%            | +             |
| 9                                 | I-57         | -1060                          | 2897                               | X              | Neg.          |
| 9                                 | I-60         | -1896                          | 1007                               | X              | Neg.          |
| 9                                 | I-69         | 1081                           | 269                                | 75%            | ++            |
| 9                                 | II-63        | 388                            | 1033                               | X              | Neg.          |
| 10                                | I-66         | -136                           | 400                                | X              | Neg.          |
| 10                                | I-67         | 61                             | 1981                               | X              | Neg.          |
| 10                                | II-62        | 814                            | 126                                | 84%            | ++            |
| 10                                | II-64        | 523                            | 294                                | 44%            | +             |
| 10                                | II-65        | 219                            | 641                                | X              | Neg.          |
| 11                                | I-65         | 2.25                           | 126                                | X              | Neg.          |
| 11                                | I-68         | 2554                           | 1092                               | 56%            | ++            |
| 11                                | II-66        | 85                             | 382                                | X              | Neg.          |
| 12                                | I-62         | -85                            | -370                               | X              | Neg.          |
| 12                                | I-70         | 258                            | 72                                 | 72%            | ++            |
| 14                                | I-71         | -32                            | -203                               | X              | Neg.          |
| 14                                | II-67        | 904                            | -101                               | 100%           | ++            |
| 15                                | I-63         | 174                            | 672                                | X              | Neg.          |
| 15                                | II-68        | 297                            | 306                                | X              | Neg.          |
| 16                                | I-53         | 176                            | 260                                | X              | Neg.          |
| 16                                | I-54         | 70                             | 107                                | X              | Neg.          |
| 17                                | I-51         | -805                           | -312                               | X              | Neg.          |
| 17                                | II-69        | -36                            | 758                                | X              | Neg.          |
| 17                                | II-70        | 317                            | 280                                | 12%            | Neg.          |
| 17                                | II-71        | -331                           | -280                               | X              | Neg.          |
| 17                                | II-72        | -501                           | -160                               | X              | Neg.          |
| 18                                | I-58         | 635                            | -392                               | 100%           | ++            |
| 18                                | I-97         | 294                            | 780                                | X              | Neg.          |
| 18                                | II-73        | 260                            | 1675                               | X              | Neg.          |
| 19                                | I-94         | 309                            | 184                                | 40%            | +             |
| 19                                | I-96         | -1542                          | 798                                | X              | Neg.          |
| 19                                | II-74        | -16                            | -56                                | X              | Neg.          |
| 19                                | II-75        | 11                             | -91                                | X              | Neg.          |
| 19                                | II-76        | 375                            | 684                                | X              | Neg.          |
| 20                                | I-80         | -696                           | -169                               | X              | Neg.          |
| 20                                | I-98         | 320                            | -120                               | 100%           | ++            |
| 20                                | II-77        | 325                            | 126                                | 61%            | ++            |

**Supplemental Table 2B. Secretion of anti-serpinB13 antibodies in patients with recent-onset T1D.**

| <b>Type 1 diabetes patients 1-20 years (n=55)</b> |             |                              |                                 |                |               |
|---------------------------------------------------|-------------|------------------------------|---------------------------------|----------------|---------------|
| <b>Age</b>                                        | <b>I.D.</b> | <b><math>\Delta^8</math></b> | <b><math>\Delta^{13}</math></b> | <b>Inh.***</b> | <b>Result</b> |
| 4                                                 | II-7        | 200                          | 211                             | X              | Neg.          |
| 4                                                 | II-12       | -393                         | -561                            | X              | Neg.          |
| 4                                                 | II-25       | 867                          | 1044                            | X              | Neg.          |
| 5                                                 | I-12        | 139                          | -62                             | X              | Neg.          |
| 5                                                 | I-14        | 2424                         | 79                              | 97%            | ++            |
| 5                                                 | I-40        | -121                         | -294                            | X              | Neg.          |
| 6                                                 | I-32        | 1583                         | 1263                            | 20%            | Neg.          |
| 6                                                 | I-47        | -518                         | 232                             | X              | Neg.          |
| 6                                                 | II-30       | 39                           | 632                             | X              | Neg.          |
| 7                                                 | I-18        | 172                          | 464                             | X              | Neg.          |
| 7                                                 | I-41        | 2174                         | 382                             | 82%            | ++            |
| 7                                                 | II-2        | -452                         | -9                              | X              | Neg.          |
| 7                                                 | II-33       | 1361                         | 286                             | 79%            | ++            |
| 8                                                 | I-15        | 702                          | -845                            | 100%           | ++            |
| 8                                                 | I-48        | 941                          | 770                             | 18%            | Neg.          |
| 8                                                 | II-4        | -345                         | -136                            | X              | Neg.          |
| 8                                                 | II-16       | 1703                         | 861.75                          | 49%            | +             |
| 8                                                 | II-24       | -474                         | 782                             | X              | Neg.          |
| 8                                                 | II-37       | 565                          | 451                             | 20%            | Neg.          |
| 9                                                 | I-2         | -165                         | 147                             | X              | Neg.          |
| 9                                                 | I-26        | -816                         | 0                               | X              | Neg.          |
| 9                                                 | II-29       | -101                         | -288                            | X              | Neg.          |
| 9                                                 | II-32       | 532                          | 232                             | 56%            | ++            |
| 9                                                 | II-44       | 201                          | 222                             | X              | Neg.          |
| 10                                                | I-29        | -264                         | -365                            | X              | Neg.          |
| 10                                                | II-3        | -301                         | 529                             | X              | Neg.          |
| 10                                                | II-9        | -107                         | 816                             | X              | Neg.          |
| 11                                                | I-6         | 665                          | 381                             | 42%            | +             |
| 11                                                | I-11        | -2888                        | 1436                            | X              | Neg.          |
| 11                                                | I-23        | -303                         | 26                              | X              | Neg.          |
| 11                                                | I-38        | -198                         | 390                             | X              | Neg.          |
| 11                                                | II-11       | 64                           | -112                            | X              | Neg.          |
| 11                                                | II-15       | 88                           | 8.5                             | X              | Neg.          |
| 12                                                | I-9         | 97                           | -39                             | X              | Neg.          |
| 12                                                | I-25        | -1339                        | -18                             | X              | Neg.          |
| 13                                                | II-13       | -1803                        | -207                            | X              | Neg.          |
| 13                                                | II-22       | 222                          | 106                             | 52%            | ++            |
| 14                                                | I-4         | -348                         | -399                            | X              | Neg.          |
| 14                                                | I-7         | 503                          | 251                             | 50%            | ++            |
| 14                                                | I-28        | 985                          | 335                             | 66%            | ++            |
| 14                                                | II-14       | 502                          | 48                              | 90%            | ++            |
| 14                                                | II-28       | 1083                         | 518                             | 52%            | ++            |
| 14                                                | II-41       | 368                          | 3.5                             | 99%            | ++            |
| 16                                                | I-1         | -558                         | -77                             | X              | Neg.          |
| 16                                                | II-17       | 633                          | 635                             | X              | Neg.          |
| 17                                                | II-31       | 701                          | 615                             | 12%            | Neg.          |
| 18                                                | I-5         | 582                          | -483                            | 100%           | ++            |
| 18                                                | II-1        | 3010                         | -35                             | 100%           | ++            |
| 18                                                | II-27       | 701                          | 570                             | 18%            | Neg.          |
| 19                                                | I-10        | 210                          | -890                            | 100%           | ++            |
| 19                                                | I-21        | 399                          | 114                             | 71%            | ++            |
| 19                                                | II-19       | 802                          | 1182                            | X              | Neg.          |
| 19                                                | II-48       | 841                          | 492                             | 41%            | +             |
| 20                                                | I-20        | 538                          | 89                              | 83%            | ++            |

|    |       |     |     |     |      |
|----|-------|-----|-----|-----|------|
| 20 | II-36 | 382 | 334 | 13% | Neg. |
|----|-------|-----|-----|-----|------|

Legend to Table S2:

\* $\Delta^8$ : serum-binding activity for serpinB13 conjugated to beads minus serum-binding activity for beads conjugated to control antigens (secretagoin [Scgn] and GFP) in the presence of soluble serpinB8.

\*\* $\Delta^{13}$ : serum-binding activity for serpinB13 conjugated to beads minus serum-binding activity for beads conjugated to control antigens (Scgn and GFP) in the presence of soluble serpinB13.

\*\*\*Serum samples, for which  $\Delta^8$  was less than 200 or  $\Delta^{13}$  was higher than  $\Delta^8$  (X), or for which the percent inhibition with soluble serpinB13 was less than 25%, were considered negative. Serum samples, for which inhibition with soluble serpinB13 was 25% to 49% or 50% to 100% were considered positive (+) and strong positive (++), respectively.