**Supplementary Table 1**

**Demographics and disease characteristics of HNT patients.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Patient No. | Age / Gender | Stagea | The frequency  of peptides vaccine received | The duration of survival (week)b | Clinical  responsec |
| 1f | 58 / F | Ⅳ | 48 | - | CR |
|  | 59 / F | Ⅳ | 54 | - | CR |
|  | 59 / F | Ⅳ | 56 | - | CR |
|  | 60 / F | Ⅳ | 60 | - | CR |
|  | 60 / F | Ⅳ | 64 | 321 | CR |
| 2f | 63 / F | Ⅳ | 28 | - | SD |
|  | 66 / F | Ⅳ | 40 | - | SD |
|  | 67 / F | Ⅳ | 44 | 269 | SD |
| 3f | 52 / M | Ⅳ | 20 | - | SD |
|  | 52 / M | Ⅳ | 24 | - | SD |
|  | 52 / M | Ⅳ | 27 | - | SD |
|  | 53 / M | Ⅳ | 32 | 211 | SD |
| 4f | 82 / M | Ⅳ | 16 | 256 | PR |
| 5f | 83 / M | Ⅳ | 16 | - | SD |
|  | 84 / M | Ⅳ | 20 | 185 | SD |
| 6 | 70 / M | Ⅳ | 0 | 7 | PR |
| 7 | 64 / F | Ⅳ | 0 | - | SD |
|  | 64 / F | Ⅳ | 4 | - | SD |
|  | 64 / F | Ⅳ | 8 | 11 | SD |
| 8 | 85 / M | Ⅳ | 0 | - | PR |
|  | 85 / M | Ⅳ | 4 | 5 | PD |
| 9 | 65 / F | Ⅳ | 0 | - | PR |
|  | 65 / F | Ⅳ | 4 | - | SD |
|  | 65 / F | Ⅳ | 8 | - | SD |
|  | 66 / F | Ⅳ | 12 | 36 | SD |
| 10 | 81 / F | Ⅳ | 0 | - | PD |
|  | 81 / F | Ⅳ | 4 | - | SD |
|  | 81 / F | Ⅳ | 8 | 35 | SD |
| 11 | 31 / M | Ⅳ | 0 | - | PD |
|  | 31 / M | Ⅳ | 4 | - | PD |
|  | 31 / M | Ⅳ | 8 | 18 | PD |
| 12 | 70 / M | Ⅳ | 0 | - | NEd |
|  | 70 / M | Ⅳ | 4 | - | NEd |
|  | 70 / M | Ⅳ | 8 | 39 | NEd |
| 13 | 85 / F | Ⅳ | 0 | 9 | PD |
| 14 | 34 / M | Ⅳ | 0 | - | PD |
|  | 34 / M | Ⅳ | 4 | 65 | PD |
| 15 | 67 / M | Ⅳ | 36 | - | NEd |
|  | 67 / M | Ⅳ | 40 | - | NEd |
|  | 67 / M | Ⅳ | 44 | 228 | NEd |
| 16 | 43 / M | Ⅳ | 32 | 192 | PD |
| 17f | 73 / F | Ⅱ | 16 | - | PR |
|  | 74 / F | Ⅱ | 24 | 201 | PD |
| 18f | 68 / M | Ⅳ | 0 | - | NEe |
| 19f | 66 / M | Ⅳ | 0 | - | NEe |
| 20f | 69 / M | Ⅳ | 0 | - | NEe |
| 21f | 65 / M | Ⅱ | 0 | - | NEe |
| 22f | 60 / M | Ⅱ | 0 | - | NEe |

a Stage: staging was carried out according to the TNM classification for head and neck tumors (WHO).

b The duration of survival was defined as a survival time from the end of standard therapy for HNT to the date of death or December 20, 2016.

c Clinical responses of cancer patients with peptide vaccination or chemoradiotherapy were evaluated according to RECIST guidelines.

d The patients received the peptide vaccination as an adjuvant therapy after the surgery to remove the tumors. Blood sampling was performed before surgery.

e The patients given surgery to remove the tumors did not receive any chemoradiotherapy or peptide vaccination. Blood sampling was performed before surgery.

f The patients are alive as of the end of December, 2016.

M, male; F, female; CR, complete response; SD, stable disease; PR, partial response; PD, progressive disease; NE, not evaluable.

**Supplementary Table 2**

**Healthy donor information.**

|  |  |
| --- | --- |
| HD No. | Age / Gender |
| 1 | 63 / M |
| 2 | 53 / M |
| 3 | 52 / M |
| 4 | 39 / M |
| 5 | 38 / M |
| 6 | 33 / M |
| 7 | 30 / M |
| 8 | 34 / M |
| 9 | 32 / M |
| 10 | 27 / F |
| 11 | 32 / M |
| 12 | 39 / F |
| 13 | 35 / F |
| 14 | 37 / F |
| 15 | 32 / M |
| 16 | 30 / F |
| 17 | 54 / M |
| 18 | 53 / F |
| 19 | 57 / F |
| 20 | 59 / M |
| 21 | 58 / M |
| 22 | 58 / F |
| 23 | 66 / M |
| 24 | 62 / F |
| 25 | 62 / F |

HD, healthy donors; M, male;

F, female

**Supplementary Table 3**

**The comparison of pathway parameters without covariates between HD and HNT.**

**(Related to Fig. 6D)**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Endogenous variable** | | **Exogenous variable** | **Estimate** | **SE** | **Z** | ***p* value** | **95% CI** |
| HD vs HNT | | | | | | | |
| % IL-6Rlow  CD14+CD16- | Log (sIL-6R) | | 0.006 | 0.028 | 0.23 | 0.821 | (-0.049, 0.062) |
| Log (sIL-6R) | Log (IL-6) | | 0.557 | 0.576 | 0.98 | 0.326 | (-0.563, 1.696) |
| Log (IL-6) | Log (CD4+) | | -0.24 | 0.241 | -1.00 | 0.319 | (-0.713, 0.232) |
| Log (CD4+) | % c-Maf+ | | 5.917 | 1.939 | 3.05 | 0.002 | (2.117, 9.718) |

HD: healthy donor, HNT: head and neck malignant tumor patients, SE: standard error; CI: confidence interval.

**Supplementary Table 4**

**Result of multilevel linear models with covariates. (Related to Supplemental Fig. 4)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Endogenous variable** | **Exogenous variable** | **Estimate** | **SE** | **Z** | ***p* value** | **95% CI** |
| **HD (n = 25)** |  |  |  |  |  |  |
| Log (sIL-6R) | Intercept | 5.547 | 0.272 | 20.42 | < 0.001 | (5.016, 6.081) |
|  | % IL-6Rlow  CD14+CD16- | 0.027 | 0.033 | 0.81 | 0.416 | (-0.038, 0.092) |
|  | Age | 0.001 | 0. 005 | 0.23 | 0.816 | (-0.009, 0.011) |
|  | Vaccination | constrained |  |  |  |  |
| Log (IL-6) | Intercept | -2.499 | 1.704 | -1.47 | 0.143 | (-5.84, 0.841) |
|  | Log (sIL-6R) | 0.274 | 0.301 | 0.91 | 0.363 | (-0.316, 0.864) |
|  | Age | 0.026 | 0.005 | 5.06 | < 0.001 | (0.016, 0.035) |
|  | Vaccination | constrained |  |  |  |  |
| Log (CD4) | Intercept | 2.509 | 0.355 | 7.06 | < 0.001 | (1.813, 3.205) |
|  | Log (IL-6) | -0.056 | 0.235 | -0.24 | 0.813 | (-0.517, 0.405) |
|  | Age | 0.015 | 0.009 | 1.66 | 0.097 | (-0.003, 0.032) |
| % c-Maf+ | Intercept | 28.54 | 5.419 | 5.27 | < 0.001 | (17.92, 39.16) |
|  | Log (CD4) | -5.908 | 1.617 | -3.65 | < 0.001 | (-9.077, -2.74) |
| **HNT (n = 44)a** |  |  |  |  |  |  |
| Log (sIL-6R) | Intercept | 6.227 | 0.171 | 36.42 | < 0.001 | (5.892, 6.562) |
|  | % IL-6Rlow  CD14+CD16- | 0.028 | 0.008 | 3.46 | 0.001 | (0.012, 0.436) |
|  | Age | -0.004 | 0.003 | -1.5 | 0.134 | (-0.009, -0.001) |
|  | Vaccination | -0.004 | 0.002 | -1.99 | 0.047 | (-0.007, -0.001) |
| Log (IL-6) | Intercept | -2.649 | 1.648 | -1.61 | 0.108 | (-5.879, 0.582) |
|  | Log (sIL-6R) | 0.599 | 0.264 | 2.27 | 0.023 | (0.083, 1.116) |
|  | Age | 0.006 | 0.006 | 1.18 | 0. 239 | (-0.004, 0.017) |
|  | Vaccination | -0.017 | 0.004 | -4.53 | < 0.001 | (-0.024, -0.009) |
| Log (CD4) | Intercept | 2.414 | 0.679 | 3.56 | < 0.001 | (1.083, 3.744) |
|  | Log (IL-6) | 0.002 | 0.218 | 0.01 | 0.994 | (-0.426, 0.43) |
|  | Age | -0.002 | 0.01 | -0.24 | 0.813 | (-0.021, 0.017) |
| % c-Maf+ | Intercept | 12.02 | 2.683 | 4.48 | < 0.001 | (6.756, 17.27) |
|  | Log (CD4) | 0.009 | 1.07 | 0.01 | 0.994 | (-2.089, 2.107) |

a Forty-eight samples were collected from 22 HNT patients before and after peptide vaccination. In some cases, sample collection was performed several times along with the vaccination.

HD: healthy donors, HNT: head and neck malignant tumor patients, SE: standard error; CI: confidence interval.