Supplementary Figure 1. Schedule of treatment and monitoring.

Patients received 3 vaccinations a biweekly interval, followed a delayed type hypersensitivity (DTH) skin test. After completing one cycle and if no progression of disease was confirmed on CT-scan, patients were eligible to receive a maximum of two more cycles and were followed up to 5 years. Abbreviations: Vx = visit x; M = month, D = day, W = week, Y = year, vacx = vaccination x; FU = follow-up; * follow-up visits were planned every 3 months; # CT-scans were planned every 6 months.

Supplementary Figure 2. Definition of criteria for SKIL culture evaluation.

Three examples are shown to illustrate the definition of SKIL culture criteria. **(A)** Criterion III, one patient (IV-B-16-St) with a clear population of TAA-specific $CD8^+$ T cells in SKIL cultures, which produce high levels of IFNg upon encounter of both the defined gp100 peptides and naturally processed gp100 presented by a HLA-A*02:01 positive melanoma cell line (Mel624). Moderate amounts of IL-2 are produced and minimal production of IL-5, representing a clear IFNg dominant cytokine profile. **(B)** Criterion II, a patient (IV-B-11-Ro) with TAA-specific $CD8^+$ T cells in SKIL cultures which produce high levels of IFNg and IL-2 upon encounter of the gp100 peptide, but fail to recognize the naturally processed gp100. **(C)** Criterion I, a patient (IV-A-07-Th) with a population of TAA-specific $CD8^+$ T cells in SKIL cultures, recognizing the g100-154 peptide, but not the naturally processed gp100. Furthermore, those TAA-specific $CD8^+$ T cells do not produce IFNg but produce elevated levels of IL-5 instead, indicating that the immune system is skewed towards tumor tolerance.

Supplementary Figure 3. KLH-specific T cell responses according to SKIL classification.

Regardless of the number of epitopes or the increasingly stringent criteria for TAA-specific immune responses; the levels of KLH-specific T cell responses were similar and highly variable between individuals. One-way ANOVA was used for comparison of KLH-specific T cell responses in groups of patients with increasing breadth of TAA-specific $CD8^+$ T cell responses. Student t-test was used for comparison of KLH-specific T cell responses in groups of patients as defined by different SKIL criteria.

Supplementary Figure 4. Levels of induration according to SKIL classification.

Regardless of the number of epitopes or the increasingly stringent criteria for TAA-specific immune responses; the maximum induration at the injection site was similar in all groups. One-way ANOVA was used for comparison of induration in groups of patients with increasing breadth of TAA-specific $CD8^+$ T cell responses. Student t-test was used for comparison of induration in groups of patients as defined by different SKIL criteria.

Supplementary Figure 5. Patient selection based on SKIL criteria.

SKIL criteria are applied to select patients with immune responses meeting increasingly stringent criteria.