A clinical trial of SCIB1, a DNA vaccine that targets dendritic cells *in vivo* in fully resected melanoma patients; continuing vaccination for up to two years maximises T cell reponses.

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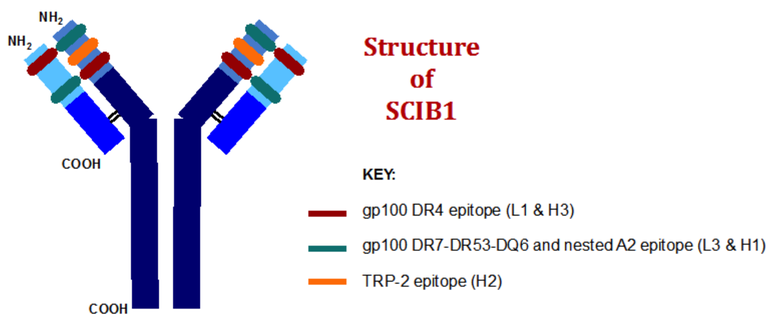
Introduction:

• SCIB1 is a DNA vaccine (ImmunoBody®) that encodes for a human IgG1 antibody containing 4 epitopes from 2 melanoma antigens (TRP2 and gp100).

•SCIB1 stimulates both CD8 (TRP2/A2) and CD4 (DR4/DR7) T cells.



• SCIB1 targets dendritic cells *in vivo* via the high affinity Fc receptor, CD64. By a combination of CROSS PRESENTATION and DIRECT PRESENTATION it stimulates the production of T cells that have:

• HIGH FREQUENCY
• HIGH AVIDITY
• POTENT ANTI-TUMOUR CAPABILITIES

Methods:

•20 patients with fully resected stage III (n=12) or stage IV (n=8) melanoma, were immunised with 2-4mg (n=16) or 8mg (n=4) of SCIB1 by intramuscular electroporation 3 times at 3 weekly intervals, then subsequently at 3 and 6 months.

•The 8mg cohort of patinets were recruited and started treatment later than the 2-4mg cohort of patients.

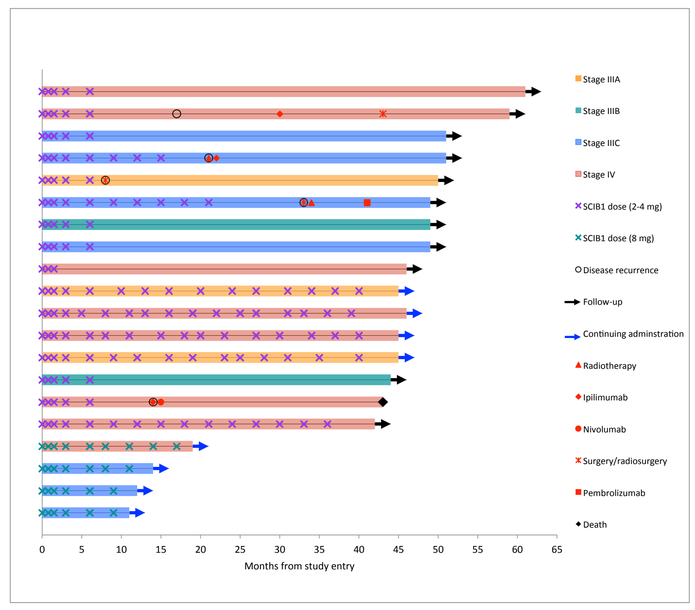
•11 patients tolerating treatment (7/16 receiving 4mg and 4/4 receiving 8mg) elected to continue treatment for up to 5 years receiving further vaccinations every 3 months.

•T cell responses were assayed pre and post vaccination by γIFN Elispot after *in-vitro* T-cell expansion.

•The frequency and diversity of the TCR V-J chain rearrangements was assayed from cryopreserved patient PBMCs by multiplex PCR (ImmunTrackerR®).

Clinical responses:

Fig 1: Swimmer plot showing disease staging, disease recurrence, treatment milestones and current trial status of fully resected patients (n=20).



Results - immune responses - Elispot:

Figure 2: Melanoma antigen epitope recognition increases with the number of doses of SCIB1. A:Patients who receive <10 doses of SCIB1 respond to fewer epitopes than those receiving >10 doses (n=20). B: Of the 6 patients that received >10 doses of SCIB1 all showed a wider epitope recognition pattern at >10 doses than at 5 doses. The solid black line represents the median value. P values Mann Whitney test.

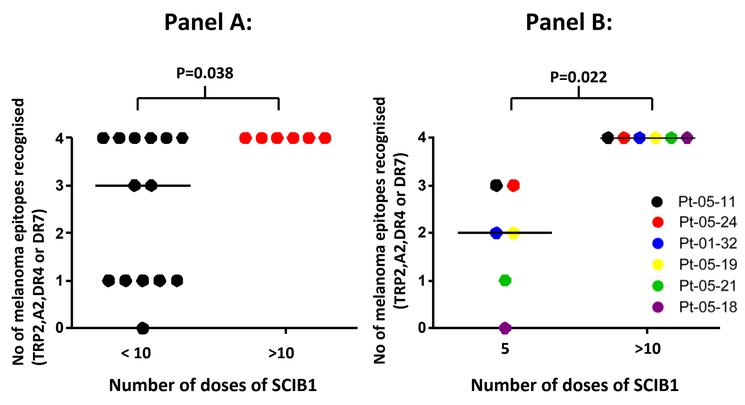
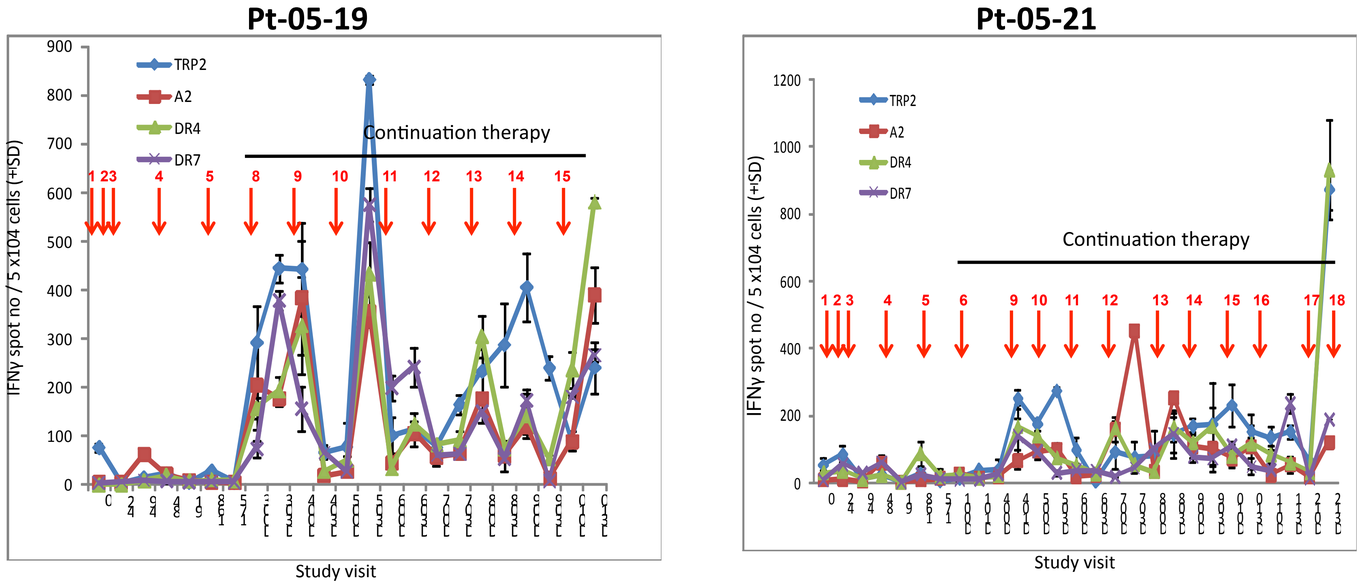


Figure 3: Two representative longitudinal studies of IFNγ generation by patient T cells following SCIB1 administration. Continued dosing with SCIB1 increases the number of melanoma epitopes recognised by T cells, the frequency of the response to epitopes and the magnitude of the response. Red arrows indicate the dosing of SCIB1.



Results - immune responses – TCR V-J gene rearrangements:

Figure 4: Two components of the immune repertoire diversity were mapped in all available samples.

•Diversity **richness** (X-Y axis)
Observed rearrangements between V and J gene families.

•Diversity **evenness** (Z axis)
Reflects the level of clonality of a repertoire.

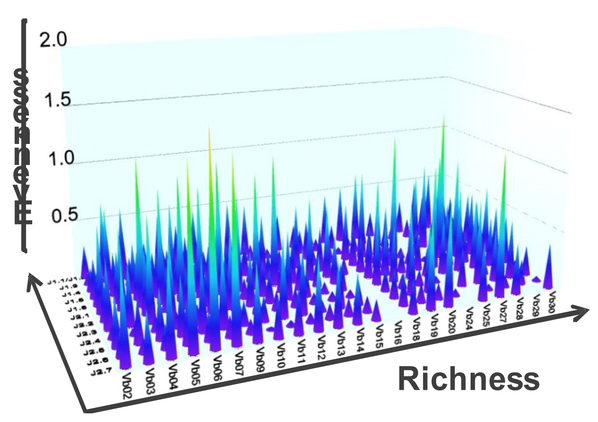


Figure 5: The diversity of evenness in patient PBMCs decreases with time.

Complete samples sets for days 0, 42, 84 and 91 were available from 9 samples.
Diversity evenness was significantly lower at day 84 and 91 with respect to day 0 (Wilcoxon Rank Sum Test).
Diversity of richness remained constant.

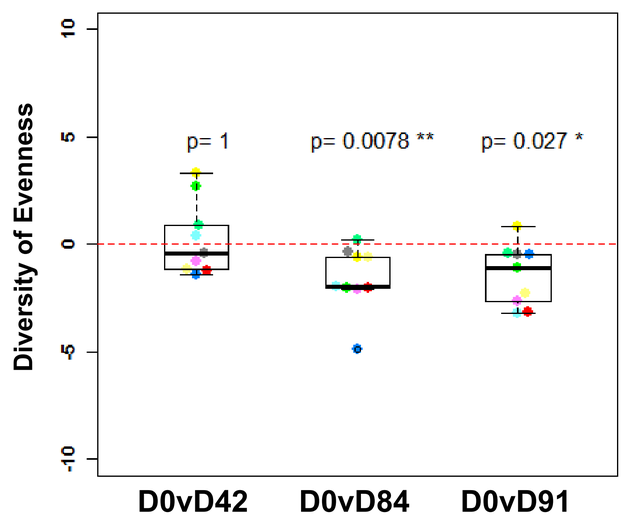
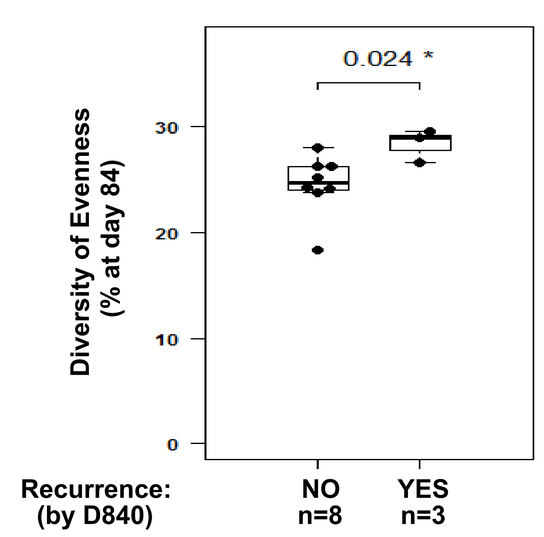


Figure 6: The diversity of evenness at day 84 may be an indicator of disease recurrence.

The immune map of 11 samples at day 84 was stratified into patents with no disease recurrence by day 840 (week 120) (n=8) and those with recurrence (n=3).
A high diversity of evenness at day 84 is associated with disease recurrence by day 840 (week 120) (Wilcoxon Rank Sum Test) .



Conclusion

These results suggest that SCIB1 is an active drug in fully resected metastatic melanoma. Continued treatment of patients every 3-6 months for up to 2 years appears to generate maximal T-cell responses. Disease recurrence in patients may be associated with a loss of clonality of the TCR and this may be predicted using ImmunoTraCkeR®.