Supplementary Table 1

Lymphocyte activation				Activation of immune response				Cell adhesion			
Rank	Gene	p-value	Fold change	Rank	Gene	p-value	Fold change	Rank	Gene	p-value	Fold change
1	BATF	0.00001	6.31564	1	DUSP6	0.00002	6.39359	1	IL21	0.00014	8.20000
2	MIF	0.00007	2.68925	2	TANK	0.00020	1.69235	2	IL2RA	0.00037	7.70668
3	NFATC2	0.00008	0.40405	3	IRAK1	0.00057	1.63217	3	C1QBP	0.00039	3.79258
4	INPP5D	0.00028	0.31780	4	CHUK	0.00080	1.59486	4	CCL28	0.00010	2.43756
5	TNFSF12	0.00002	0.30456	5	HRAS	0.00004	1.58111	5	BCL10	0.00036	0.62896
6	CASP8	0.00001	0.23611	6	CREB1	0.00037	0.58528	6	IRF1	0.00027	0.62762
7	SMAD3	0.00002	0.23043	7	CD3E	0.00023	0.49823	7	CD46	0.00033	0.52342
8	RORA	0.00001	0.14902	8	ZAP70	0.00068	0.46392	8	SPN	0.00022	0.48806
				9	CTSS	0.00024	0.30270	9	JAK2	0.00086	0.45576
				10	PLA2G6	0.00002	0.22338	10	TGFB1	0.00006	0.44888
				11	TLR3	0.00045	0.13067	11	IL12RB1	0.00021	0.39881
								12	ITGA4	0.00098	0.37128
								13	ITGAL	0.00013	0.32985
								14	CCR2	0.00049	0.29760
								15	CD44	0.00097	0.21387

Supplementary Table 1. Differentially expressed genes (p<0.05) in CAR compared to delta CAR T cells. The table displays the p-values and fold changes of genes that are differentially regulated in CAR T cells compared to the truncated CAR (ΔCAR) control T cells collected 24 hours post-stimulation with PSCA. Genes were grouped based on their associated functions determined from string db analysis tool (n=3) (p<0.05).

Supplementary Table 2

NF-kappaB signaling				Regulation of TNFSF				Cellular metabolic process			
Rank	Gene	p-value	Fold change	Rank	Gene	p-value	Fold change	Rank	Gene	p-value	Fold change
1	NLRP3	0.01166	1.69284	1	SPN	0.00905	1.28560	1	CMKLR1	0.04847	1.75794
2	CASP1	0.04651	0.83313	2	LTF	0.00255	0.74510	2	DUSP4	0.00980	1.34147
3	STAT1	0.02229	0.78497	3	CD86	0.03931	0.71570	3	BCL2	0.01526	1.26568
4	BST2	0.01404	0.77540	4	CCL3	0.03233	0.69981	4	STAT5B	0.04845	1.20929
				5	CCR2	0.00023	0.52036	5	PSMB7	0.04310	0.89055
								6	G6PD	0.01572	0.89041
								7	PSMD7	0.02141	0.89006
								8	ATG5	0.04347	0.87810
								9	PBK	0.04691	0.83074
								10	TP53	0.01337	0.83038
								11	C1QBP	0.00566	0.75221
								12	CCL4	0.00636	0.74713
								13	IFNA8	0.01686	0.61924
								14	IFIT1	0.04117	0.53138

Supplementary Table 2. Differentially expressed genes ($p<0.05$) in TBBR compared to delta TGFβRII modified T cells. The table lists differential expressed genes (DEGs) between TBBR and ΔTGFβRII modified T cells stimulated with OKT3 and TGFβ cytokine ($p<0.05$). The function associated signaling networks associated with the DEGs were determined using STRING database (db) (n=3).

Supplementary Table 3

JAK-STAT cascade				Lymphocyte proliferation				Cytokine production			
Rank	Gene	p-value	Fold change	Rank	Gene	p-value	Fold change	Rank	Gene	p-value	Fold change
1	IL19	0.04520	2.45052	1	ARG1	0.04753	2.16003	1	CXCL5	0.03693	1.36654
2	CSF2	0.01371	1.83445	2	PLA2G1B	0.01024	1.55416	2	IL22RA1	0.00526	1.26789
3	SOCS1	0.02039	1.67744	3	VEGFA	0.00599	1.49535	3	CXCR4	0.01259	1.19831
4	CSF1R	0.00816	1.53951	4	FLT3LG	0.03730	1.15909	4	MAPK14	0.01463	1.09217
5	CCL2	0.01770	1.21465	5	CDKN1A	0.03531	1.26588	5	STAT6	0.01977	0.93082
6	NOTCH1	0.04556	0.77239	6	CASP3	0.01407	1.18780	6	SPN	0.03023	0.87074
7	STAT1	0.00292	0.76702	7	BCL2L1	0.03732	1.16588	7	IL17RA	0.03528	0.85572
8	STAT4	0.00136	0.73604	8	ZNF143	0.04132	1.10166	8	CD86	0.03351	0.80072
								9	CASP1	0.01743	0.76780
								10	DDX58	0.01224	0.76092
								11	NLRC5	0.03423	0.62027
								12	NCAM1	0.02562	0.58143
								13	TLR3	0.03589	0.42504

Supplementary Table 3. Differentially expressed genes ($p<0.05$) in 4/7 ICR compared to delta IL4R modified T cells. Significance (p-value) and fold change of genes that are differentially expressed between 4/7 ICR and ΔIL4R modified T cells stimulated with OKT3 and IL4 cytokine. Genes have been grouped based on functional networks determined using STRING db analysis tool. (n=3) ($p<0.05$).

Supplementary Table 4

CAR				TBBR				4/7 ICR			
Rank	Gene	p-value	Fold change	Rank	Gene	p-value	Fold change	Rank	Gene	p-value	Fold change
1	IL2RA	0.01477	13.32763	1	CCL3	0.03181	15.79317	1	CSF2	0.03940	16.99487
2	DUSP6	0.00778	9.57425	2	CCL4	0.01903	6.39590	2	CCL2	0.01253	10.85138
3	BATF	0.04896	4.72133	3	CCR2	0.05831	3.84391	3	SOCS1	0.00713	5.13013
4	IL21	0.04677	3.33443	4	BCL2	0.00447	1.76164	4	CDKN1A	5.05E-7	4.13059
5	MIF	0.03236	2.20167	5	TP53	0.01122	1.49902	5	BCL2L1	0.00979	2.17212
6	TANK	0.02974	1.99637	6	LTF	0.03867	1.46036	6	ARG1	0.03461	2.08442
7	HRAS	0.00047	1.70011	7	DUSP4	0.00360	1.45452	7	DDX58	0.02432	2.04402
8	CHUK	0.00801	1.41085	8	CMKLR1	0.19400	1.38347	8	TLR3	0.19625	2.01499
9	IRAK1	0.43088	0.99306	9	PSMD7	0.01098	1.28820	9	CASP3	0.00031	1.98805
10	TGFB1	0.12229	0.86157	10	PSMB7	0.06284	1.17150	10	NLRC5	0.08879	1.30742
11	BCL10	0.04982	0.75627	11	PBK	0.16090	1.13191	11	NOTCH1	0.04014	1.22677
12	IRF1	0.00014	0.74149	12	CASP1	0.27511	1.09822	12	ZNF143	0.04066	1.21487
13	TNFSF12	0.00230	0.70405	13	ATG5	0.07984	0.90254	13	MAPK14	0.25013	1.07945
14	CD3E	0.03022	0.66686	14	SPN	0.03377	0.80330	14	STAT4	0.43740	0.98766
15	CD44	0.00481	0.65741	15	G6PD	0.02245	0.78725	15	STAT6	0.21784	0.90802
16	CD46	0.00109	0.60341	16	C1QB	0.16813	0.78088	16	IL17RA	0.18260	0.89115
17	JAK2	0.00199	0.52032	17	STAT5B	0.00479	0.59476	17	VEGFA	0.22705	0.85792
18	IL12RB1	0.02097	0.45613	18	STAT1	0.01211	0.57119	18	CXCR4	0.16216	0.81951
19	ZAP70	0.00145	0.39058								
20	ITGAL	0.00018	0.36587								
21	CTSS	0.00060	0.35997								
22	INPP5D	0.00024	0.34951								
23	ITGA4	0.00155	0.25875								
24	PLA2G6	0.00001	0.22654								
25	RORA	0.00609	0.20701								
26	CASP8	0.00001	0.20290								
27	SMAD3	0.00002	0.19891								

Supplementary Table 4. Differentially expressed genes in SmarT-cells derived from CAR, TBBR and 4/7 ICR. The table lists the p-values and fold changes of differentially expressed genes detected in SmarT-cells compared to T cells expressing delta constructs (ΔCAR, ΔTGFβRII, ΔIL4R) after exposure to tumor milieu conditions (24 hours) that can be assigned to CAR, TBBR or 4/7 ICR transgenic modifications (n=3) ($p<0.05$).

Supplementary Table 5.

Upregulated genes								
Gene	p-value	Fold change	Gene	p-value	Fold change	Gene	p-value	Fold change
IL9	0.02412	8.40800	TNFSF13	0.01299	1.78735	FCGR2A	0.01908	1.47436
CCR2	0.04527	6.37143	IL32	0.02585	1.74563	IRF1	0.00444	1.47194
CCR1	0.04544	5.76865	IL12RB2	0.02558	1.74345	C1QA	0.03023	1.40849
IL21	0.03726	4.47172	IFITM2	0.01553	1.74328	IL22RA2	0.04904	1.37973
CCL2	0.01325	4.33887	CSF1	0.02374	1.73504	ENG	0.00847	1.35841
FOXP3	0.01929	4.29318	IFIH1	0.02680	1.72643	MAGEA3	0.04587	1.35342
LTA	0.01992	3.73705	TNFSF12	0.01129	1.70176	SYCP1	0.03548	1.33794
TXK	0.01727	3.15756	TLR2	0.00526	1.68688	TFRC	0.01879	1.32969
IL2RA	0.02202	2.72891	CASP1	0.02977	1.66851	CD47	0.02645	1.32499
C4BPA	0.04509	2.72515	STAT3	0.00356	1.63571	PSMB10	0.00150	1.31674
LAG3	0.03285	2.59591	TNFRSF10B	0.00302	1.63226	IRAK1	0.00386	1.27685
CCR7	0.02044	2.50383	ITGAM	0.00294	1.62514	ALCAM	0.02144	1.27375
CD80	0.00532	2.26825	CCND3	0.01708	1.62390	IL6ST	0.01208	1.25675
LTB	0.03077	2.23740	CEACAM6	0.04695	1.59298	IL11RA	0.02040	1.25605
SPANXB1	0.00023	2.11869	IFI35	0.04859	1.59226	MAP2K1	0.03751	1.23536
DPP4	0.01219	2.02176	CLEC7A	0.02934	1.57527	ITK	0.02702	1.20188
BCL2	0.00512	1.99821	JAK3	0.04295	1.57088	GPI	0.00974	1.19833
IL15RA	0.00345	1.99633	CTAGE1	0.04269	1.56144	CD164	0.03184	1.19528
SBNO2	0.03078	1.99203	TAP2	0.04911	1.56070	FADD	0.04633	1.17836
CD40	0.01499	1.91753	FCGR1A	0.00206	1.55637	TIRAP	0.01213	1.17157
CD7	0.03037	1.91666	SLAMF1	0.01188	1.55321	CD37	0.04890	1.17117
IL10	0.04308	1.91484	STAT2	0.01165	1.52294	ECSIT	0.02412	1.15736
TBX21	0.03397	1.90425	AIRE	0.04572	1.52124	ETS1	0.02932	1.14494
TNFSF15	0.04742	1.90325	CCL8	0.04059	1.50864	TRAF2	0.03612	1.13595
CD48	0.00654	1.87069	MASP1	0.00086	1.50668	MAPKAPK2	0.04509	1.13198
MAGEC1	0.04639	1.82597	TXNIP	0.04836	1.50616	MYD88	0.04173	1.13135
CDKN1A	0.00554	1.80615	TRAF6	0.04445	1.50479	ATG16L1	0.03780	1.12603
ANXA1	0.02267	1.79993	CCL7	0.02742	1.48915	TAPBP	0.02786	1.11212
CCL14	0.03035	1.79836	CYFIP2	0.04604	1.48239	EWSR1	0.03392	1.06884

Downregulated genes								
Gene	p-value	Fold change	Gene	p-value	Fold change	Gene	p-value	Fold change
ZAP70	0.00383	0.86366	TNFRSF18	0.02237	0.66279	RRAD	0.02794	0.46494
TOLLIP	0.01939	0.85707	DEFB1	0.03759	0.65637	NT5E	0.00887	0.46176
CDK1	0.04280	0.82742	GZMA	0.03634	0.65544	CYLD	0.00424	0.45922
SMAD2	0.01978	0.82346	CD276	0.04728	0.64833	SH2D1B	0.01851	0.45444
GTF3C1	0.00041	0.81933	SLAMF6	0.02414	0.62577	CCL1	0.03865	0.44846
REPS1	0.04963	0.81773	REL	0.00872	0.61835	CD84	0.00678	0.43102
HMGB1	0.00546	0.81019	POU2AF1	0.02950	0.61199	NOS2A	0.03355	0.41355
IFNAR2	0.01279	0.79173	ITGAE	0.03460	0.60903	BCL6	0.00690	0.40137
TTK	0.00289	0.78922	EGR2	0.01013	0.58633	CD9	0.00993	0.38489
LCP1	0.00403	0.75663	AMICA1	0.03696	0.58003	IRF8	0.04414	0.37857
NFKB1	0.02817	0.75643	ITGA1	0.01409	0.55799	PLAU	0.02134	0.37498
MERTK	0.02800	0.73912	XCL2	0.02238	0.54706	LAMP3	0.00002	0.28230
THBD	0.04863	0.71705	PRKCD	0.04153	0.54646	TNFSF11	0.02687	0.27282
NFATC3	0.00857	0.70715	CCR4	0.04100	0.54135	IL1RN	0.01390	0.23265
CKLF	0.01173	0.70221	C1S	0.02701	0.51653	IL17RB	0.01023	0.22728
CD97	0.01802	0.68297	CD83	0.00722	0.51124	RORC	0.00490	0.18600
TNFRSF9	0.01761	0.66643	S100A8	0.02188	0.49114	MFGE8	0.00136	0.17545
RUNX1	0.02796	0.66609	PECAM1	0.04728	0.47934	CXCL13	0.00357	0.05956

Supplementary Table 5. Differentially expressed genes in SmarT-cells compared to 1G.CAR T cells. List of genes detected in SmarT-cells vs 1G.CAR T cells collected 24 hours after stimulation with PSCA, TGFβ and IL4 (n=3) ($p<0.05$).