$\gamma\delta$ T-cells express the androgen receptor in a stage-selective fashion.

Shahan Mamoor, MS¹

¹Thomas Jefferson School of Law

San Diego, CA 92901

mamoorsk@tjssl.edu

In this study, we mined public datasets (1, 2) containing whole transcriptome information from $\gamma\delta$ T-cells to understand the most significant identifying features in the transcriptional landscape of $\gamma\delta$ T-cells. We found that the androgen receptor, AR, was one of the most differentially expressed genes between embryonic and adult $\gamma\delta$ T-cells. AR was expressed at significantly higher levels in $\gamma\delta$ T-cells from adult mice than in embryonic $\gamma\delta$ T-cells. Analysis of a separate dataset revealed that AR was among the genes most differentially expressed by $\gamma\delta$ T-cells transcriptome-wide when compared to immature, single positive T-cells (2). Androgen signaling downstream of AR may be important during $\gamma\delta$ T-cell development or for $\gamma\delta$ T-cell effector function.

Keywords: $\gamma\delta$ T-cells, $\gamma\delta$ T-cell development, AR, androgen receptor, hepatosplenic T-cell lymphoma, HSTCL, systems biology of the $\gamma\delta$ T-cell.

1 The blood is composed of white and red blood cells (3). One type of white cell is the
2 lymphocyte, which can be further classified by cell surface receptor expression and effector
3 function as a T- or B-cell (4). The earliest T-cell progenitor can differentiate into an $\alpha\beta$ T-cell or a
4 $\gamma\delta$ T-cell, defined by expression of an $\alpha\beta$ or $\gamma\delta$ T-cell receptor (TCR) (5). $\gamma\delta$ T-cells inhabit
5 tissues throughout the body and circulate in the periphery as part of the blood (6, 7). It has
6 become clear that immune defense by $\gamma\delta$ T-cells does not function through a rigid paradigm of
7 TCR-mediated recognition of antigen peptides displayed by antigen-presentation cells followed
8 by TCR gene rearrangements as immune defense in $\alpha\beta$ T-cells operates (8, 9). $\gamma\delta$ T-cells
9 respond to ligands that are diverse in chemical structure, like the phosphoantigens HMB-PP and
10 IPP (11, 12) and TCR rearrangement events are more limited than in $\alpha\beta$ T-cells (8). $\gamma\delta$ T-cells
11 exert their function by producing cytokines such as IFN γ (13), TNF- α (14) and IL-17 (15), by
12 producing chemokines such as RANTES (16), CXCL10 (17) and lymphotactin (18), and by
13 cytotoxicity of infected or transformed target cells in infection (19) or cancer (20, 21) (respectively)
14 using perforin (20) and granzyme (21). Thus, $\gamma\delta$ T cells are unique lymphocytes with both
15 innate and adaptive properties (22, 23). $\gamma\delta$ T-cells are important for resolution of infectious
16 diseases such as in *Toxoplasma gondii* through parasite clearance (24), and in cancer for tumor
17 surveillance (25) and tumor killing (26-28) but understanding of the transcriptional landscape of
18 $\gamma\delta$ T-cells (29, 30) in development and in relation to other cells of the T-lymphocyte lineage
19 remains incomplete.

20 To understand $\gamma\delta$ T-cell transcriptional behavior at the systems level and to assess how
21 gene expression in the $\gamma\delta$ T-cell changes most significantly through development, we compared
22 the adult $\gamma\delta$ T-cell transcriptome to that of the embryonic $\gamma\delta$ T-cell and to the immature single-

positive T-cell, the stage of lymphocyte development between double negative 4 (DN4) and double positive (DP), using two published microarray datasets (1, 2) . We found that the gene encoding the androgen receptor, AR, was among the genes whose expression changed most significantly in the adult $\gamma\delta$ T-cell, whether compared to embryonic $\gamma\delta$ T-cells or to immature single-positive T-cells. AR expression was significantly higher in adults versus in the embryo, and $\gamma\delta$ T-cells expressed significantly higher levels of AR than immature single-positive T-cells did. These findings establish that the gene encoding the androgen receptor is transcriptionally active in $\gamma\delta$ T-cells, that $\gamma\delta$ T-cells express higher levels of AR as compared to other lymphocytes, and suggest that androgen signaling might be important for $\gamma\delta$ T-cell effector function or development.

Methods

Datasets GSE71637 and GSE86495 (1, 2) were utilized for this global differential gene expression profiling analysis using GEO2R. GSE86495 (2) was generated by Yang et al. using Affymetrix Mouse Gene 2.0 ST Array. GSE71637 (1) was generated by Muñoz-Ruiz et al. using Affymetrix Mouse Gene 2.1 ST Array technology. In the analysis using GSE86495, n=4 for immature single-positive T-cells and n=3 for gamma delta T-cells. In the analysis using GSE71637, n=2 for embryonic day 18 gamma delta T-cells and n=2 for adult gamma delta T-cells from mice 6 weeks of age. This includes mice of wild-type and CD3H-deficient genotypes (wild-type and CD3H-deficient for both embryonic and adults groups). For GSE86495, the “Benjamini and Hochberg” method of p-value adjustment was utilized, log-transformation of data was auto-detected and the submitter supplied category of platform annotation was chosen. For GSE71637, the “Bonferonni” method of p-value adjustment was utilized, log-transformation of data was auto-detected and the submitter supplied category of platform annotation was chosen. A statistical test was performed to evaluate the significance of difference in AR mRNA levels

1 between (a) embryonic and adult gamma delta T-cells, and (b) gamma delta T-cells and
2 immature single-positive T-cells, using PRISM (8.1.2)(227). For statistical tests involving
3 comparisons of groups with n=2 (1), a two-tailed, unpaired t-test was utilized. For statistical
4 tests involving comparisons of groups with n=3 or greater (2), the same two-tailed, unpaired t-
5 test was used but with Welch's correction. The results of these statistical tests are reported as a
6 p-value with values less than 0.05 considered significant.

8 **Results**

9
10 We performed global gene expression profiling of $\gamma\delta$ T-cells using published
11 transcriptome data to understand, in an unbiased and systematic manner, the most significant
12 changes in $\gamma\delta$ T-cell gene expression (a) across murine development, using transcriptome data
13 from $\gamma\delta$ T-cells from the embryo and the adult (1), and (b) between T-cells of the $\alpha\beta$ and $\gamma\delta$
14 lineage, using transcriptome data from immature single positive T-cells (2) as reference.

17 AR is differentially expressed in $\gamma\delta$ T-cells based on developmental stage

18
19 We compared the transcriptomes of embryonic and adult $\gamma\delta$ T-cells to identify the most
20 significant changes in the transcriptional landscape of $\gamma\delta$ T-cells across mammalian
21 development. We identified the gene encoding the androgen receptor, AR, as among the genes
22 whose expression was most different between $\gamma\delta$ T-cells from mice at embryonic day 18 and $\gamma\delta$
23 T-cells from adult mice at week 6 of life. AR was the 157th most differentially expressed gene
24 transcriptome-wide, counting 41345 total transcripts. This was statistically significant (Table 1;
25 p=1.25E-12).

1 AR is expressed at significantly higher levels in $\gamma\delta$ T-cells from mice 6 weeks of age when
2
3 compared to $\gamma\delta$ T-cells from mice at embryonic day 18 (E18)

4 After identifying AR as one of the genes whose expression changes most significantly
5 between embryonic and adult $\gamma\delta$ T-cells, we extracted mRNA expression values for AR in $\gamma\delta$ T-
6 cells from mice at embryonic stage (E18) and at adulthood (6 weeks). AR gene expression was
7 higher at 6 weeks than at embryonic day 18 (Figure 1). This difference was statistically
8 significant (Figure 1; $p=0.0222$).

11 AR is one of the genes whose expression is most different when comparing the transcriptomes
12 of immature, single-positive $\alpha\beta$ T-cells and $\gamma\delta$ T-cells

14 We analyzed a separate dataset (2) to assess what genes changed in expression the
15 most between $\gamma\delta$ T-cells, lymphocytes committed to the $\gamma\delta$ T-cell lineage, and immature single-
16 positive T-cells, lymphocytes that have completed lineage commitment to the $\alpha\beta$ T-cell fate.
18 Immature single-positive T-cells have past the double negative 4 (DN4) stage of lymphocyte
19 development but have not yet entered the double negative stage. Again, we identified AR as
20 among the genes most differentially expressed in the $\gamma\delta$ T-cell, here in reference to the
21 transcriptome of the immature single positive $\alpha\beta$ T-cell. AR was the third most differentially
22 expressed gene in the entire $\gamma\delta$ T-cell transcriptome (3rd out of 41345 total transcripts) when
23 compared to immature single positive $\alpha\beta$ T-cells. This was statistically significant (Table 2;
24 $p=0.00044102$).

1 AR is expressed at significantly higher levels in gamma-delta T-cells when compared to
2 immature, single-positive T-cells

3 We then extracted mRNA expression values for AR in $\gamma\delta$ T-cells and from immature
4 single positive $\alpha\beta$ T-cells. $\gamma\delta$ T-cells expressed higher amounts of AR than immature single
5 positive $\alpha\beta$ T-cells did (Figure 2). This difference in AR gene expression was statistically
6 significant (Figure 2; $p < 0.0001$).
7
8

9
10 Thus, we identified AR as one of the most differentially expressed genes in the $\gamma\delta$ T-cells
11 when compared to embryonic $\gamma\delta$ T-cells and to immature single positive $\alpha\beta$ T-cells, and found
12 that AR was expressed at significantly higher levels in adult $\gamma\delta$ T-cells than in embryonic $\gamma\delta$ T-
13 cells or immature single positive $\alpha\beta$ T-cells.
14
15

16 Discussion

17
18 We performed whole transcriptome profiling of $\gamma\delta$ T-cell to study $\gamma\delta$ T-cell transcriptional
19 behavior, by comparison across cell type and development by reference to the transcriptomes of
20 immature single positive T-cells and to embryonic gamma delta T-cells, respectively, using
21 separate published datasets (1, 2). We identified the androgen receptor, AR, as one of the most
22 differentially expressed genes in the $\gamma\delta$ T-cell.
23
24

25 This is the first report of differential expression of the AR gene in murine $\gamma\delta$ T-cells. A
26 previous study of $\gamma\delta$ T-cells in chickens demonstrated that an expansion in the number of
27 circulating $\gamma\delta$ T-cells occurs in chicken in male but not female chicken, coinciding with sexual
28

1 maturity. Administration of testosterone to female chicken resulted in an equivalent $\gamma\delta$ T-cell
2 expansion to that seems in males (31), demonstrating that male but not female chicken expand
3 their population of $\gamma\delta$ T-cells in response to developmentally-programmed hormone release
4 occurring at sexual maturity (31).
5

6 These findings may be of pertinence to the biology of hepatosplenic T-cell lymphoma
7 (HSTCL), a rare peripheral T-cell lymphoma that arises from $\gamma\delta$ T-cells of the blood and that in
8 recent decades, has affected a specific population of adolescent males with inflammatory bowel
9 disease (IBD) co-treated with TNF inhibitors like infliximab and mercaptopurine (32-38). The
10 risk in this population has been deemed serious enough to merit an FDA black box warning
11 regarding the potential for HSTCL and non-Hodgkin's lymphoma development after treatment
12 with TNF inhibitors (38). Though combined immunosuppression in the context of a viral
13 infection or some other immune trigger like the chronic disease process seen in IBD has been
14 suggested to contribute to HSTCL development in this population (39), it is not understood why
15 adolescent males are specifically affected.
16
17

18 Together with published data from chickens demonstrating that the growth of $\gamma\delta$ T-cells
19 is sensitive to androgen signaling, and that male chickens but not female chickens undergo
20 expansion of $\gamma\delta$ T-cells in response to a developmentally programed release of testosterone
21 during sexual maturity (31), we suggest that the reason young males are at highest risk for
22 HSTCL development is developmental androgen release during puberty. It should be evaluated
23 whether androgens contribute to tumor initiation in HSTCL.
24
25

26 We identified AR as one of the most differentially expressed genes in the $\gamma\delta$ T-cell and
27 found that it was expressed at significantly higher levels in adults than in embryos, as well in $\gamma\delta$
28 T-cells than in the immature single-positive T-cell. The impact of hormone-induced signaling
downstream of AR in $\gamma\delta$ T-cells on $\gamma\delta$ T-cell development and effector function should be

1 explored in AR-deficient mice *in vivo* and with androgen deprivation *in vitro*. $\gamma\delta$ T-cells are
2
3 important for clearance of infections and cancers (25-29) and androgen signaling in $\gamma\delta$ T-cells
4 could be important for the biology of hepatosplenic T-cell lymphomas, a cancer of the $\gamma\delta$ T-cell.
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28

References

1. Muñoz-Ruiz, M., Ribot, J.C., Grosso, A.R., Gonçalves-Sousa, N., Pamplona, A., Pennington, D.J., Regueiro, J.R., Fernández-Malavé, E. and Silva-Santos, B., 2016. TCR signal strength controls thymic differentiation of discrete proinflammatory $\gamma\delta$ T cell subsets. *Nature immunology*, 17(6), p.721.
2. Yang, K., Blanco, D.B., Chen, X., Dash, P., Neale, G., Rosencrance, C., Easton, J., Chen, W., Cheng, C., Dhungana, Y. and Anil, K.C., 2018. Metabolic signaling directs the reciprocal lineage decisions of $\alpha\beta$ and $\gamma\delta$ T cells. *Science immunology*, 3(25), p.eaas9818.
3. Themeli, M., Kloss, C.C., Ciriello, G., Fedorov, V.D., Perna, F., Gonen, M. and Sadelain, M., 2013. Generation of tumor-targeted human T lymphocytes from induced pluripotent stem cells for cancer therapy. *Nature biotechnology*, 31(10), p.928.
4. Bøyum, A., 1964. Separation of white blood cells. *Nature*, 204(4960), pp.793-794.
5. Camara, N.O.S., Lepique, A.P. and Basso, A.S., 2012. Lymphocyte differentiation and effector functions. *Journal of Immunology Research*, 2012.
6. Saito TA, Hochstenbach FR, Marusic-Galesic SU, Kruisbeek AM, Brenner MI, Germain RN. Surface expression of only gamma delta and/or alpha beta T cell receptor heterodimers by cells with four (alpha, beta, gamma, delta) functional receptor chains. The Journal of experimental medicine. 1988 Sep 1;168(3):1003-20.
7. Hayday, A. and Tigelaar, R., 2003. Immunoregulation in the tissues by $\gamma\delta$ T cells. *Nature Reviews Immunology*, 3(3), pp.233-242.
8. Nielsen, M.M., Witherden, D.A. and Havran, W.L., 2017. $\gamma\delta$ T cells in homeostasis and host defence of epithelial barrier tissues. *Nature Reviews Immunology*, 17(12), p.733.
9. Carding, S.R. and Egan, P.J., 2002. $\gamma\delta$ T cells: functional plasticity and heterogeneity. *Nature reviews immunology*, 2(5), pp.336-345.
10. Tonegawa, S., Berns, A., Bonneville, M., Farr, A., Ishida, I., Ito, K., Itohara, S., Janeway, C.A., Kanagawa, O., Katsuki, M. and Kubo, R., 1989, January. Diversity, development, ligands, and probable functions of $\gamma\delta$ T cells. In *Cold Spring Harbor symposia on quantitative biology* (Vol. 54, pp. 31-44). Cold Spring Harbor Laboratory Press.
11. Hintz, M., Reichenberg, A., Altincicek, B., Bahr, U., Gschwind, R.M., Kollas, A.K., Beck, E., Wiesner, J., Eberl, M. and Jomaa, H., 2001. Identification of (E)-4-hydroxy-3-methyl-but-2-enyl pyrophosphate as a major activator for human $\gamma\delta$ T cells in Escherichia coli. *FEBS letters*, 509(2), pp.317-322.

12. Roelofs, A.J., Jauhainen, M., Mönkkönen, H., Rogers, M.J., Mönkkönen, J. and Thompson, K., 2009. Peripheral blood monocytes are responsible for $\gamma\delta$ T cell activation induced by zoledronic acid through accumulation of IPP/DMAPP. *British journal of haematology*, 144(2), pp.245-250.
13. Wang, T., Scully, E., Yin, Z., Kim, J.H., Wang, S., Yan, J., Mamula, M., Anderson, J.F., Craft, J. and Fikrig, E., 2003. IFN- γ -producing $\gamma\delta$ T cells help control murine West Nile virus infection. *The Journal of Immunology*, 171(5), pp.2524-2531.
14. Lafont, V., Liautard, J., Gross, A., Liautard, J.P. and Favero, J., 2000. Tumor necrosis factor- α production is differently regulated in $\gamma\delta$ and $\alpha\beta$ human T lymphocytes. *Journal of Biological Chemistry*, 275(25), pp.19282-19287.
15. Sutton, C.E., Lalor, S.J., Sweeney, C.M., Brereton, C.F., Lavelle, E.C. and Mills, K.H., 2009. Interleukin-1 and IL-23 induce innate IL-17 production from $\gamma\delta$ T cells, amplifying Th17 responses and autoimmunity. *Immunity*, 31(2), pp.331-341.
16. Hedges, J.F., Lubick, K.J. and Jutila, M.A., 2005. $\gamma\delta$ T cells respond directly to pathogen-associated molecular patterns. *The Journal of Immunology*, 174(10), pp.6045-6053.
17. Pociask, D.A., Chen, K., Choi, S.M., Oury, T.D., Steele, C. and Kolls, J.K., 2011. $\gamma\delta$ T cells attenuate bleomycin-induced fibrosis through the production of CXCL10. *The American journal of pathology*, 178(3), pp.1167-1176.
18. Middel, P., Thelen, P., Blaschke, S., Polzien, F., Reich, K., Blaschke, V., Wrede, A., Hummel, K.M., Gunawan, B. and Radzun, H.J., 2001. Expression of the T-cell chemoattractant chemokine lymphotactin in Crohn's disease. *The American journal of pathology*, 159(5), pp.1751-1761.
19. Passmore, J.S., Glashoff, R.H., Lukey, P.T. and Ress, S.R., 2001. Granule-dependent cytotoxicity of Mycobacterium tuberculosis-infected macrophages by human $\gamma\delta$ T cells has no effect on intracellular mycobacterial viability. *Clinical & Experimental Immunology*, 126(1), pp.76-83.
20. Narazaki, H., Watari, E., Shimizu, M., Owaki, A., Das, H., Fukunaga, Y., Takahashi, H. and Sugita, M., 2003. Perforin-dependent killing of tumor cells by V γ 1V δ 1-bearing T-cells. *Immunology letters*, 86(1), pp.113-119.
21. Mattarollo, S.R., Kenna, T., Nieda, M. and Nicol, A.J., 2007. Chemotherapy and zoledronate sensitize solid tumour cells to V γ 9V δ 2 T cell cytotoxicity. *Cancer immunology, immunotherapy*, 56(8), pp.1285-1297.

22. Born, W.K., Reardon, C.L. and O'Brien, R.L., 2006. The function of $\gamma\delta$ T cells in innate immunity. *Current opinion in immunology*, 18(1), pp.31-38.
23. Bonneville, M., O'Brien, R.L. and Born, W.K., 2010. $\gamma\delta$ T cell effector functions: a blend of innate programming and acquired plasticity. *Nature Reviews Immunology*, 10(7), pp.467-478.
24. Egan, C.E., Dalton, J.E., Andrew, E.M., Smith, J.E., Gubbels, M.J., Striepen, B. and Carding, S.R., 2005. A requirement for the V γ 1+ subset of peripheral $\gamma\delta$ T cells in the control of the systemic growth of *Toxoplasma gondii* and infection-induced pathology. *The Journal of Immunology*, 175(12), pp.8191-8199.
25. Ebert, L.M., Meuter, S. and Moser, B., 2006. Homing and function of human skin $\gamma\delta$ T cells and NK cells: relevance for tumor surveillance. *The journal of immunology*, 176(7), pp. 4331-4336.
26. Wei, Y.Q., Zhao, X., Kariya, Y., Fukata, H., Teshigawara, K. and Uchida, A., 1996. Induction of autologous tumor killing by heat treatment of fresh human tumor cells: involvement of $\gamma\delta$ T cells and heat shock protein 70. *Cancer research*, 56(5), pp.1104-1110.
27. Viey, E., Fromont, G., Escudier, B., Morel, Y., Da Rocha, S., Chouaib, S. and Caignard, A., 2005. Phosphostim-activated $\gamma\delta$ T cells kill autologous metastatic renal cell carcinoma. *The Journal of Immunology*, 174(3), pp.1338-1347.
28. Todaro, M., D'Asaro, M., Caccamo, N., Iovino, F., Francipane, M.G., Meraviglia, S., Orlando, V., La Mendola, C., Gulotta, G., Salerno, A. and Dieli, F., 2009. Efficient killing of human colon cancer stem cells by $\gamma\delta$ T lymphocytes. *The Journal of Immunology*, 182(11), pp.7287-7296.
29. Graff, J.C., Behnke, M., Radke, J., White, M. and Jutila, M.A., 2006. A comprehensive SAGE database for the analysis of $\gamma\delta$ T cells. *International immunology*, 18(4), pp.613-626.
30. Narayan, K., Sylvia, K.E., Malhotra, N., Yin, C.C., Martens, G., Vallerskog, T., Kornfeld, H., Xiong, N., Cohen, N.R., Brenner, M.B. and Berg, L.J., 2012. Intrathymic programming of effector fates in three molecularly distinct $\gamma\delta$ T cell subtypes. *Nature immunology*, 13(5), p. 511.
31. Arstila, T.P. and Lassila, O., 1993. Androgen-induced expression of the peripheral blood gamma delta T cell population in the chicken. *The Journal of Immunology*, 151(12), pp. 6627-6633.
32. Vega, F., Medeiros, L.J. and Gaulard, P., 2007. Hepatosplenic and other $\gamma\delta$ T-cell lymphomas. *American journal of clinical pathology*, 127(6), pp.869-880.

- 33.Shale, M., Kanfer, E., Panaccione, R. and Ghosh, S., 2008. Hepatosplenic T cell lymphoma in inflammatory bowel disease. *Gut*, 57(12), pp.1639-1641.
- 34.Mackey, A.C., Green, L., Liang, L.C., Dinndorf, P. and Avigan, M., 2007. Hepatosplenic T cell lymphoma associated with infliximab use in young patients treated for inflammatory bowel disease. *Journal of pediatric gastroenterology and nutrition*, 44(2), pp.265-267.
- 35.Ochenrider, M.G., Patterson, D.J. and Aboulafia, D.M., 2010. Hepatosplenic T-cell lymphoma in a young man with Crohn's disease: case report and literature review. *Clinical Lymphoma Myeloma and Leukemia*, 10(2), pp.144-148.
- 36.Leptak, C. and Avigan, M., 2009. Hepatosplenic T cell lymphoma associated with infliximab use in young patients treated for inflammatory bowel disease: update. *Journal of pediatric gastroenterology and nutrition*, 48(3), pp.386-388.
- 37.Parakkal, D., Sifuentes, H., Semer, R. and Ehrenpreis, E.D., 2011. Hepatosplenic T-cell lymphoma in patients receiving TNF- α inhibitor therapy: expanding the groups at risk. *European journal of gastroenterology & hepatology*, 23(12), pp.1150-1156.
- 38.Kotlyar, D.S., Osterman, M.T., Diamond, R.H., Porter, D., Blonski, W.C., Wasik, M., Sampat, S., Mendizabal, M., Lin, M.V. and Lichtenstein, G.R., 2011. A systematic review of factors that contribute to hepatosplenic T-cell lymphoma in patients with inflammatory bowel disease. *Clinical Gastroenterology and Hepatology*, 9(1), pp.36-41.
- 39.Subramaniam, K., Yeung, D., Grimpen, F., Joseph, J., Fay, K., Buckland, M., Talaulikar, D., Elijah, J., Clarke, A.C., Pavli, P. and Moore, J., 2014. Hepatosplenic T-cell lymphoma, immunosuppressive agents and biologicals: what are the risks?. *Internal medicine journal*, 44(3), pp.287-290.

Rank	ID	p-value	t	B	Gene
157	17536436	0.00044102	9.304763	0.79692	AR

Table 1: AR is differentially expressed in $\gamma\delta$ T-cells based on developmental stage.

The rank of global differential gene expression for the androgen receptor (AR) mRNA message (out of 41345 total mRNA transcripts compared)), the p-value with respect to global differential expression, t, a moderated t-statistic, B, the log-odds of differential expressed between the two groups compared, the gene symbol and gene name are shown in this chart (obtained from GEO2R).

Figure 1: AR expression is significantly higher in adult $\gamma\delta$ T-cells compared to embryonic $\gamma\delta$ T-cells.

The mRNA expression level of the AR gene in $\gamma\delta$ T-cells from embryonic day 18 (green) and in $\gamma\delta$ T-cells from adult mice at 6 weeks (red) is graphically represented in bar format with the error bars denoting the standard error of the mean. The results of a statistical test evaluating the difference in expression between embryonic and adult groups, a p-value, is listed on the graph.

Rank	ID	p-value	t	B	Gene
3	17536436	1.25E-12	99.05987	18.868846	AR

Table 2: AR is one of the genes whose expression changes most significantly between $\gamma\delta$ T-cells and immature single positive T-cells.

The rank of global differential gene expression for the androgen receptor (AR) mRNA message (out of 41345 total mRNA transcripts compared)), the p-value with respect to global differential expression, t, a moderated t-statistic, B, the log-odds of differential expressed between the two groups compared, the gene symbol and gene name are shown in this chart (obtained from GEO2R).

Figure 2: AR is expressed at significantly higher levels in $\gamma\delta$ T-cells than in immature single positive T-cells.

The mRNA expression level of the AR gene in immature single-positive T-cells (green) and in $\gamma\delta$ T-cells (red) is graphically represented in bar format with the error bars denoting the standard error of the mean. The results of a statistical test evaluating the difference in expression between embryonic and adult groups, a p-value, is listed on the graph.