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Oral presentation

CD4+CD25high Regulatory T Cells in the Developing Human Immune System: Implications for Pediatric HIV Infection

Jakob Michaëlsson[†1], Jeff E Mold[†1], Joseph M McCune*[‡1,2,3] and Douglas F Nixon[1,2,3]

Address: [1]Gladstone Institute of Virology and Immunology, University of California, San Francisco, CA 94158, USA, [2]Department of Medicine, University of California, San Francisco, CA 94110 USA and [3]These authors are equal last authors

Email: Joseph M McCune* - mmccune@gladstone.ucsf.edu

* Corresponding author †Equal contributors‡Presenting author

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Background

Although human T cells enter the peripheral lymphoid tissues early during fetal development[1], the adaptive immune system in the fetus has largely been regarded as functionally immature and unresponsive to stimulation. In adults, CD4CD25high regulatory T cells (TReg) are critical for maintenance of peripheral T cell tolerance, but their role in the developing fetus is unknown. Here, we demonstrate that a large population of human fetal FOXP3CD4CD25high TReg cells, present from the earliest stages of T cell colonization of the periphery, efficiently suppresses fetal T cell responses.

Results

Depletion of $CD4^{+}CD25^{high}$ T_{Reg} cells from fetal lymph node cells, but not adult lymph nodes, resulted in the proliferation and acquisition of effector functions in the absence of exogenous stimulation by a large subpopulation of T cells identifiable by the expression of CD69 *in utero*. A large population of fetal $CD4^{+}CD25^{high}$ T_{Reg} cells also expressed CD69+ and displayed a memory/effector phenotype, as indicated by low expression of CD45RA and CCR7. However, the CD69+ and CD69- $CD4^{+}CD25^{high}$ T_{Reg} cells did not differ in their suppression of T cell responses in the absence of exogenous stimulation, indicating that the activation status of these cells do not correlate with their suppressive function.

Conclusion

These studies demonstrate that the fetal T cells are, in the absence $CD4^{+}CD25^{high}$ T_{Reg} cells, highly responsive to stimulation, indicating that human fetal T cells are active and functionally mature. Strong evidence has also been obtained for an important role for $CD4^{+}CD25^{high}$ T_{Reg} cells in controlling T cell responses *in utero*. The implications of these findings for pediatric HIV infection will be discussed.