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P02-05. All-*trans* retinoic acid during vaccination increases Ag-specific CD8 T cell homing to mucosal sites and improves recall responses to vaginal challenge

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Background

Vaccine-induced memory T cells present in mucosal surfaces may provide a potent barrier to infection with HIV, could reduce HIV transmission, and/or ameliorate progression to AIDS. All-trans retinoic acid (ATRA) has been shown to induce the expression of gut-homing receptors on T cells during activation *in vitro*.

Methods

We investigated the use of ATRA (300 μg. intraperitoneal) as an *in vivo* adjuvant during vaccination of mice with adenovirus expressing the LCMV glycoprotein (gp) as a model antigen (Ad5 gp, 5×10^8 pfu, intramuscular) on the formation and migration of antigen-specific T cells to mucosal sites. To have a definable population for tracking T cell responses, we adoptively transferred 10^3 congenically marked P14 TCR-transgenic CD8 T cells, which are specific for the gp33-41 epitope, prior to immunization.

Results

ATRA treatment during priming with Ad5gp did not systemically alter the activation or magnitude of the primary gp33-41 specific CD8 T response, but did increase the number of effector and (and subsequently memory) T cells that localized to mucosal associated tissues. However, ATRA during priming did result in a higher proportion of systemic central-memory phenotype T cells. T cells primed in the presence of ATRA proliferated more during heterologous boosting with modified vaccinia Ankara expressing gp (MVAgp, 10^7 pfu, intraperitoneal) and exhibited increased gut homing. Mice receiving ATRA during vaccination were also more resistant to vaginal mucosa challenge with vaccinia virus (VVgp, 6×10^6 pfu) and this correlated with increased gp33–41 specific T cell responses at these sites.

Conclusion

ATRA administration during priming in this mouse model resulted in increased mucosal and central memory T cells that were able to better control virus challenge. Thus, ATRA may be an ideal adjuvant for inclusion into vaccination strategies for humans against mucosally transmitted pathogens such as HIV. This study is supported by the Bill & Melinda Gates Foundation.

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