IN BRIEF

INNATE IMMUNITY

Cutting edge: mast cell antimicrobial activity is mediated by expression of cathelicidin antimicrobial peptide.

Di Nardo, A. *et al. J. Immunol.* **170**, 2274–2278 (2003)

Cathelicidins are antimicrobial peptides that kill various micro-organisms. The microbicidal activity of mast cells (MCs), together with the recent detection of cathelicidins in fish MCs, prompted Di Nardo *et al.* to investigate whether MCs in mice and humans contain cathelicidins. Human cathelicidin LL-37 was detected in skin MCs. Mice also have a single cathelicidin — CRAMP (cathelin-related antimicrobial peptide) — and this was detected in MCs. CRAMP expression was upregulated by mouse MCs following lipopolysaccharide stimulation. MCs from CRAMP-deficient mice had a reduced ability to kill group A streptococci.

MHC MOLECULES

Functional expression of murine V2R pheromone receptors involves selective association with the M10 and M1 families of MHC class Ib molecules.

Loconto, J. *et al*. *Cell* **112**, 607–618 (2003)

Combinatorial coexpression of neural and immune multigene families in mouse vomeronasal sensory neurons.

Ishii, T. *et al*. *Curr. Biol.* **13**, 394–400 (2003)

Pheromones are chemical cues that trigger behaviours such as mating and territorial fighting. Two classes of pheromone receptor are expressed in the vomeronasal organ (VMO) — V1r in the apical layer and V2r in the basal layer. These studies show that V2r-expressing neurons in the basal layer also express non-classical MHC molecules (M1 and M10 families), and co-expression studies showed a correlation between the expression of a given V2r and a given M10 in a single cell. Immunoaffinity chromatography experiments showed that the V2r receptors are complexed with an M10 molecule plus β_2-microglobulin. The complexes might function to regulate cell-surface expression of pheromone receptors. So, pheromone detection might involve MHC molecules.

LYMPHOCYTE DEVELOPMENT

In vivo transposition mediated by V(D)J recombinase in human T lymphocytes.

Messier, T. L. *et al*. *EMBO J*. **22**, 1381–1388 (2003)

In addition to mediating the rearrangement of immunoglobulin and T-cell receptor (TCR) genes, the recombination-activating gene (RAG) proteins have been shown, at least *in vitro,* to mediate transposition reactions, which could potentially lead to oncogenic events. This study provides the first evidence of RAG-mediated transposition *in vivo*. Human T cells with mutations in the *HPRT* (hypoxanthine-guanine phosphoribosyl transferase) gene were selected by culture with a cytotoxic purine analogue. Sequence analysis of two mutants indicated that insertions of a TCRα coding segment had occurred in intron 1 of *HPRT*. Subsequent breakpoint analysis showed the presence of TCRα signal ends, which is indicative of RAG-mediated transposition.

HIV

REVealing HIV

Viruses, including HIV-1, encode proteins that help them to evade attack by the immune system. For example, HIV Nef promotes immune evasion by reducing the cell-surface expression of MHC class I molecules, so protecting infected cells from cytotoxic T lymphocyte (CTL)-mediated death. Now, Bobbitt and colleagues show for the first time that the activity of Rev, an HIV regulatory protein that is required for the expression of HIV late proteins, can also influence the susceptibility of infected cells to CTLs.

First, the authors tested whether cells infected with different HIV-1 clones differed with respect to their sensitivity to CTL recognition and cytotoxicity. Cells infected with the HIV clone NL-PI were less sensitive to CTL-mediated death than cells infected with another clone (HXB-PI). Further analysis showed that this protection against CTL attack resulted from a single amino-acid change (Leu60Phe) in the coding sequence of Rev in NL-PI.

As Rev is required for the synthesis of late gene products (including Gag, Pol and Env), Bobbitt *et al.* reasoned that this Rev mutation might reduce CTL-mediated killing by limiting the expression of Gag, so reducing Gag-epitope density on the surface of infected cells (required for Gag-specific CTL-mediated killing). Expression of the Phe60 form of Rev in transfected cell lines and infected primary T cells resulted in a 2–3-fold decrease in Gag protein levels and a small decrease in Env protein levels, but had no effect on the level of Nef in these cells.

So, mutated *Rev* alleles could protect infected cells from CTL attack in two ways: first, by decreasing the expression of viral proteins, including Gag, which are a source of antigens for recognition by CTLs; and second, by maintaining the expression of Nef, which promotes MHC class I downmodulation.

Finally, primary viral isolates from asymptomatic HIV-infected individuals and from patients with AIDS were screened. Viruses derived from asymptomatic individuals had lower Rev activity, and cells infected with these isolates had reduced levels of Gag proteins and were more resistant to Gag-specific CTL-mediated killing than cells from patients with AIDS. The authors conclude that, in contrast to those individuals with AIDS, immune pressure in asymptomatic individuals might result in the selection of active forms of viral genes, including mutated *Rev* alleles, that are involved in viral immune evasion.

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References and links

ORIGINAL RESEARCH PAPER Bobbitt, K. R. *et al.* Rev activity determines sensitivity of HIV-1-infected primary T cells to CTL killing. *Immunity* **18**, 289–299 (2003)

FURTHER READING Peterlin, B. M. & Trono, D. Hide, shield and strike back: how HIV-infected cells avoid immune eradication. *Nature Rev. Immunol.* **2**, 97–107 (2003)

WEB SITE

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