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A single amino acid in HLA can alter AIDS progression

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The strongest susceptibility to progression from HIV-1 infection to AIDS is conferred by the major-histocompatibility-complex (MHC) class I type HLA-B*35,Cw*04 allele. In the May 31 [New England Journal of Medicine](#), Xiaojiang Gao and colleagues from [Johns Hopkins School of Medicine](#), Baltimore shows that a single amino-acid change in HLA molecules has a substantial effect on the rate of progression to AIDS.

Gao *et al.* genotyped HLA class I loci for 850 patients who seroconverted and had known dates of HIV-1 infection. HLA-B*35 subtypes were divided into two groups according to peptide-binding specificity: the HLA-B*35-PY group, which consists primarily of HLA-B*3501 and binds epitopes with proline in position 2 and tyrosine in position 9; and the more broadly reactive HLA-B*35-Px group, which also binds epitopes with proline in position 2 but can bind several different amino acids (excluding tyrosine) in position 9. Survival analyses showed a rapid progression to AIDS in patients with HLA-B*35-Px alleles and a slower progression in patients with HLA-B*35-PY alleles, some of which differ from HLA-B*35-Px by only one amino acid residue (*NEJM* 2001, **344**:1668-1675).

The effect is probably attributable to an inappropriate cytotoxic-T-lymphocyte response in patients with HLA-B*35-Px, whereas a comparatively protective response occurs in patients with HLA-B*35-PY that corresponds with the slower progression to disease in these patients.

References

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2. Johns Hopkins School of Medicine, [<http://infonet.welch.jhu.edu/som/>]