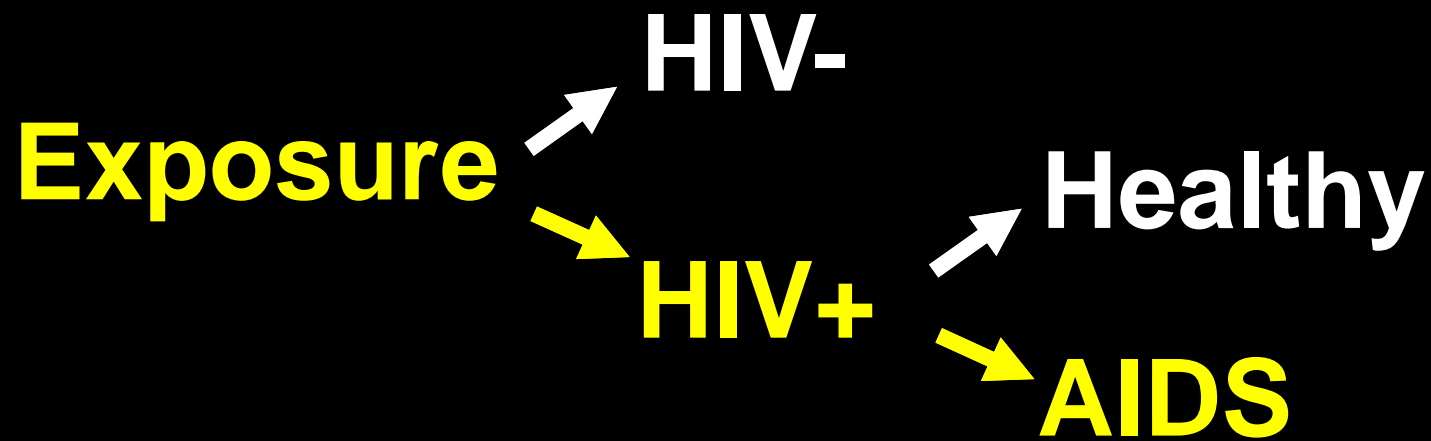
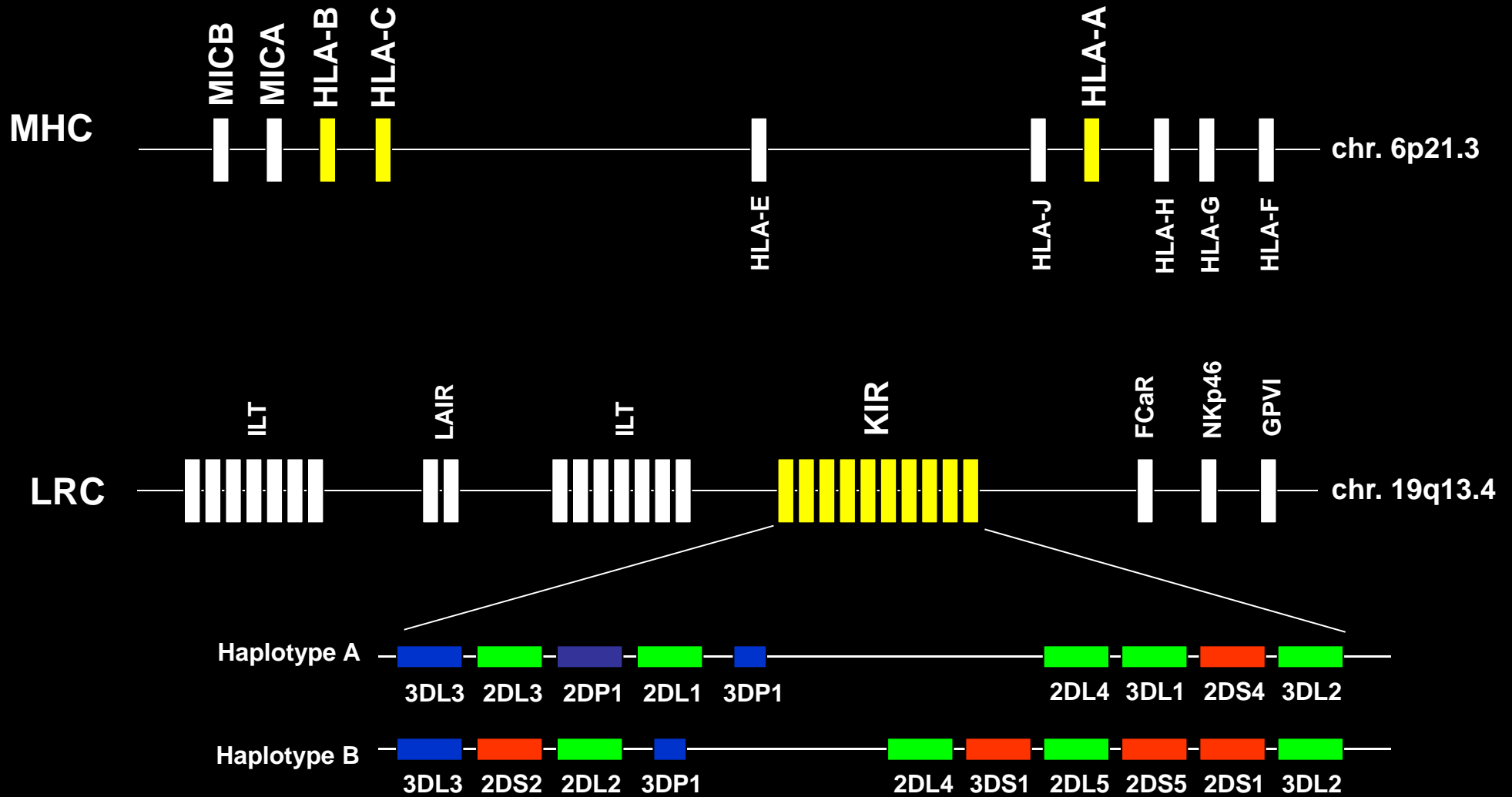


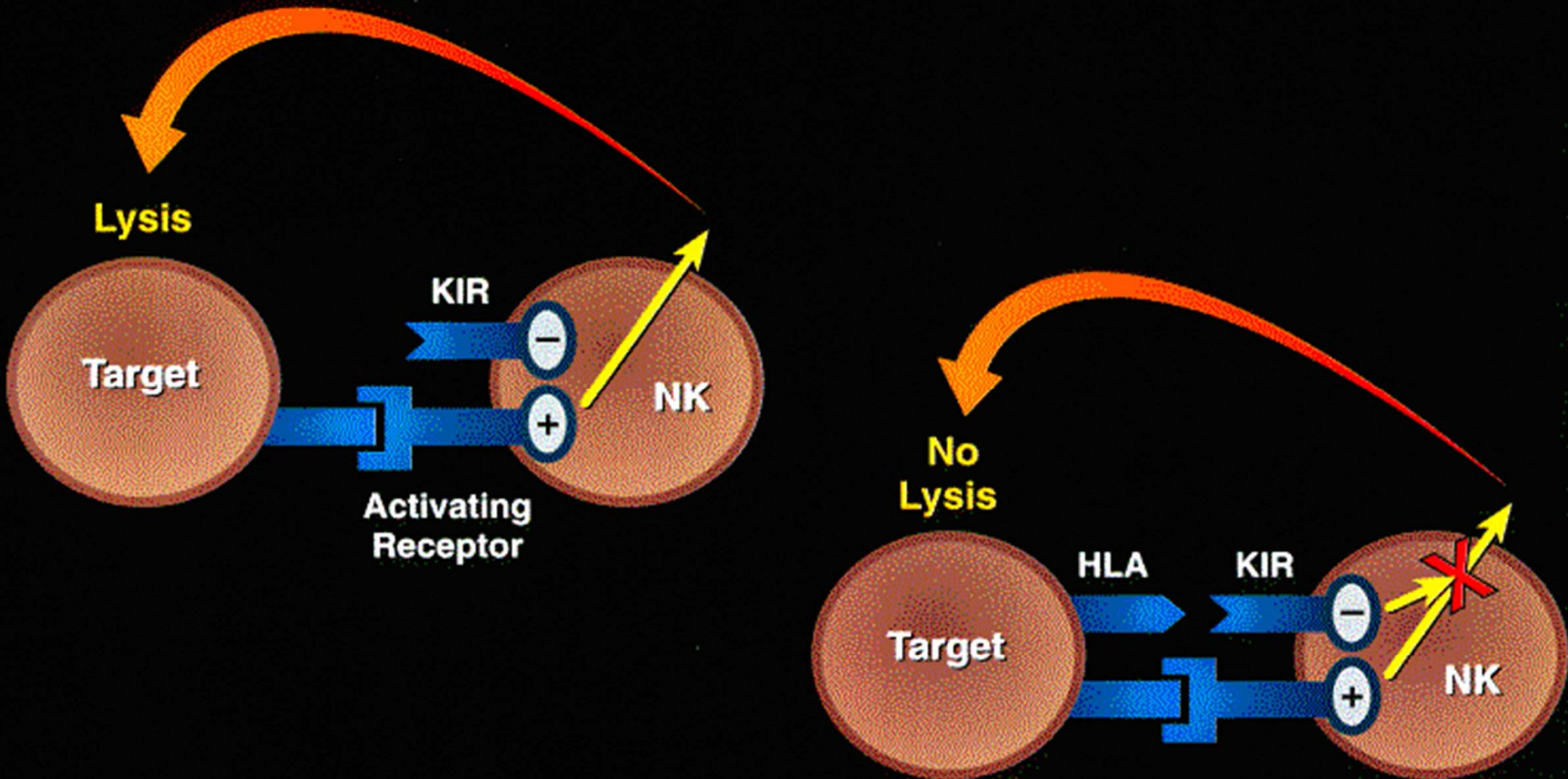
Influence of host genetics on HIV



HLA class I and KIR: functionally related gene clusters exhibiting extreme polymorphism

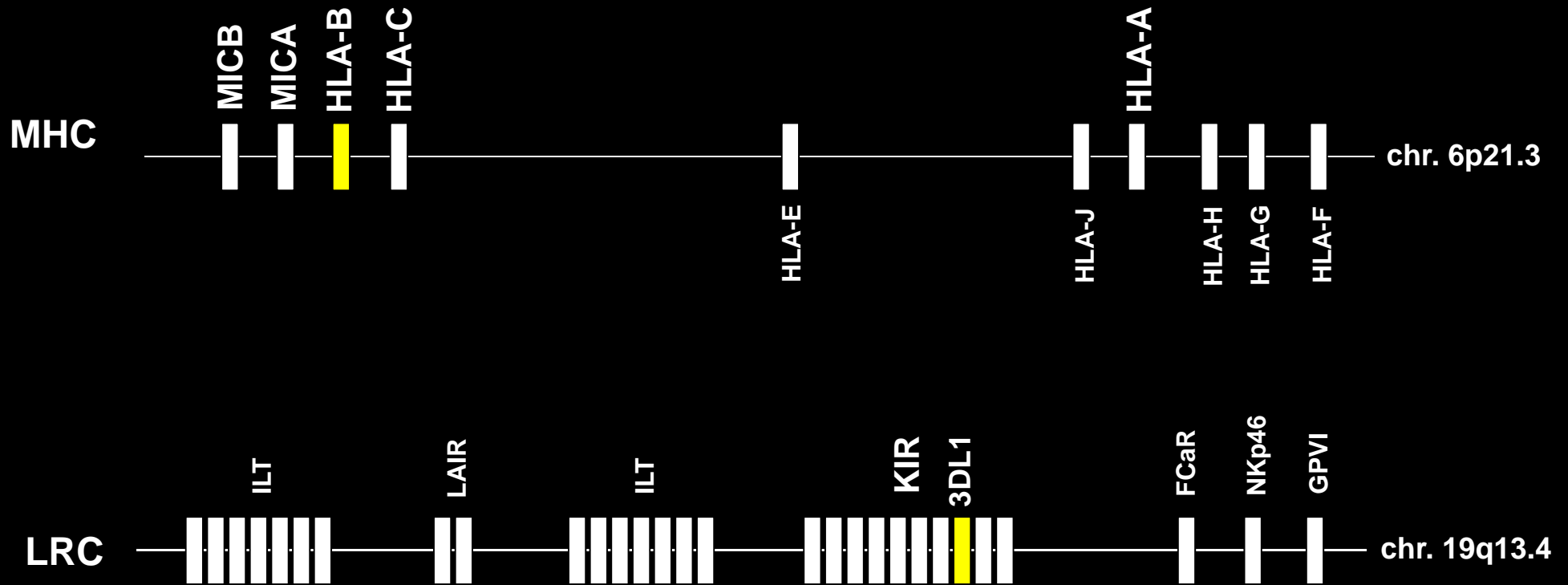


KIR regulate natural killer cell activity



NK cells kill targets that do not express HLA class I in the “normal” context

HLA-B + KIR3DL1: Multiplicity of synergistic interactions



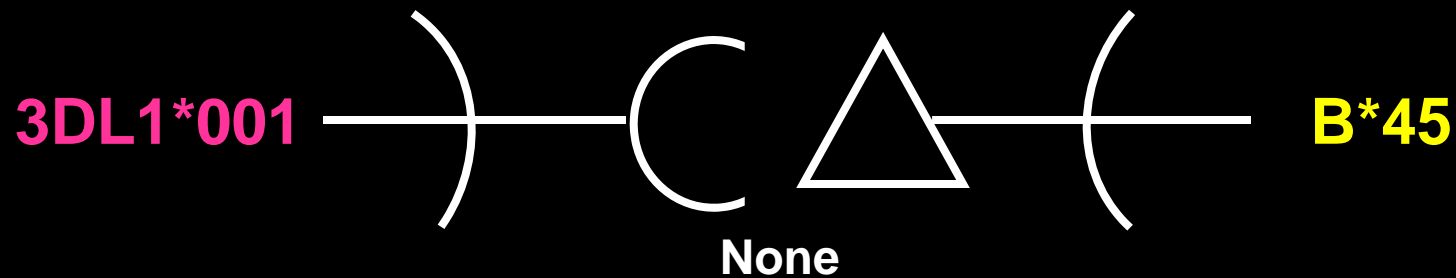
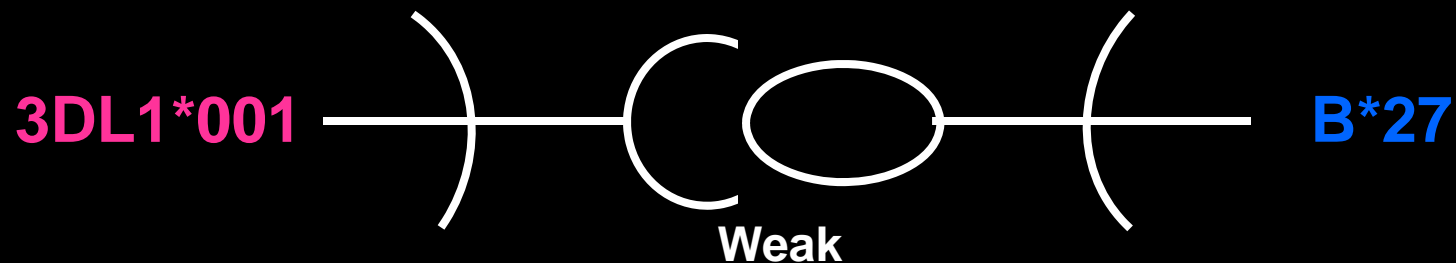
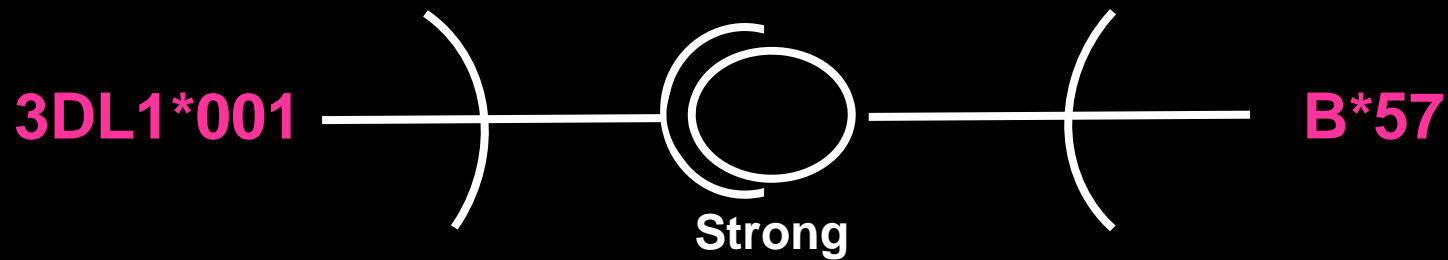
HLA-B: >500 alleles
KIR3DL1: >20 alleles

Differential binding between KIR3DL1 and HLA-B

Receptor

Interaction

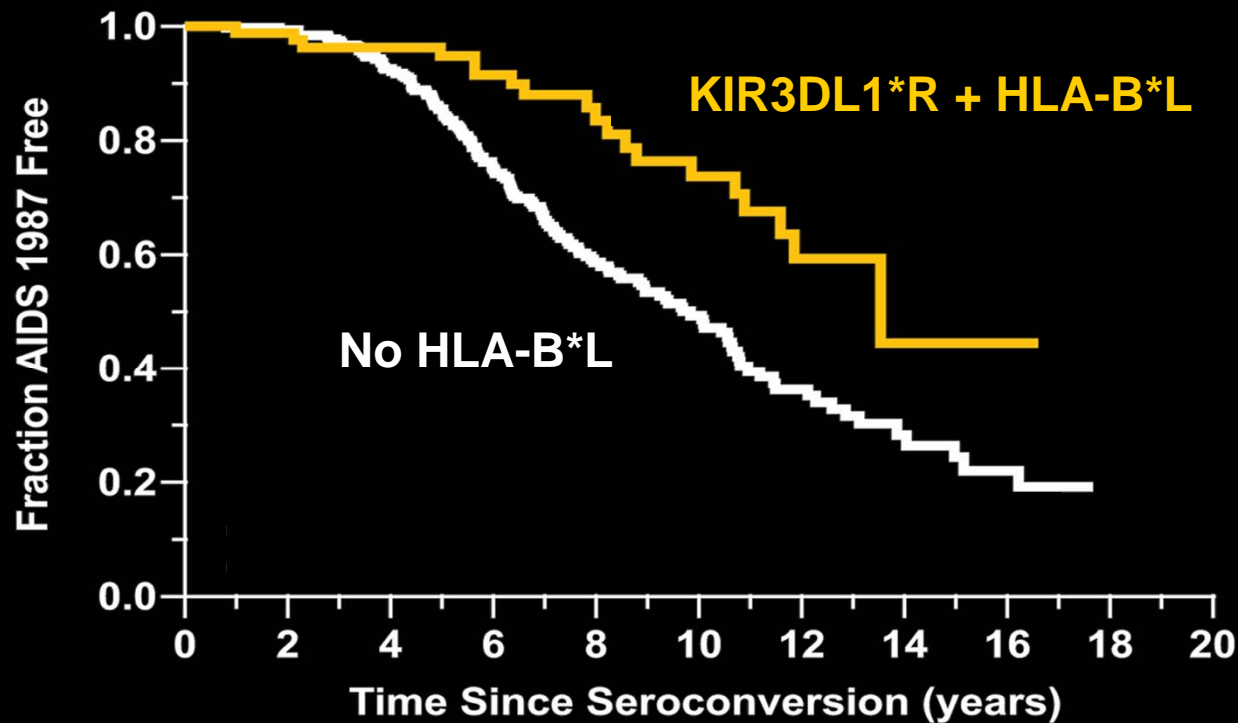
Class I Ligand



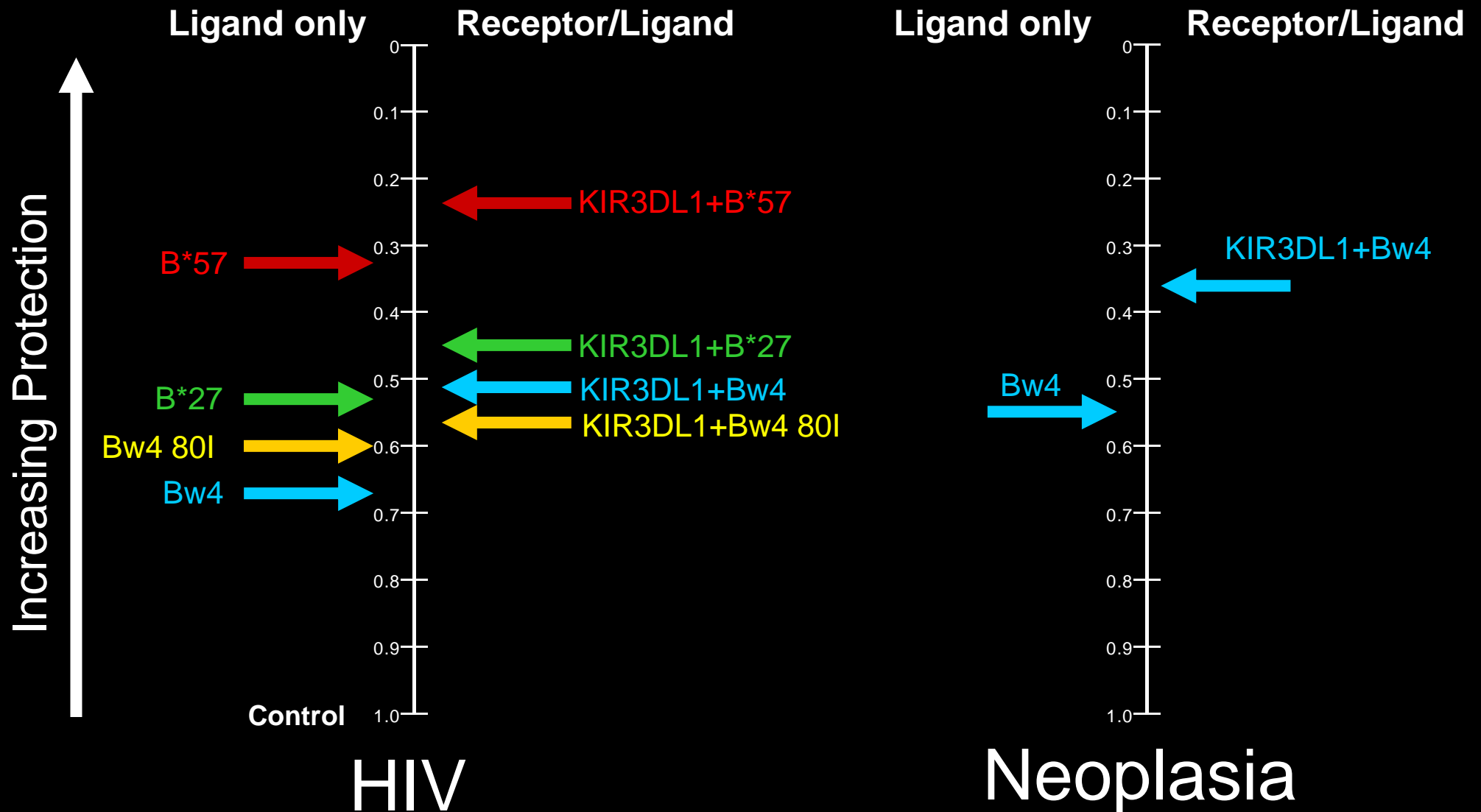
AIDS Cohorts

- **Multicenter Hemophilia Cohort Study (MHCS):**
Hemophilia, **DCEG, NCI**
- **Multicenter AIDS Cohort Study (MACS):** Gay men,
multiple U.S. sites (NIAID)
- **AIDS Linked to Intravenous Experience (ALIVE):** IV
drug users, **Johns Hopkins**
- **Hemophilia Growth and Development Study (HGDS):**
Hemophilia, **multiple U.S. sites**
- **San Francisco City Clinic Cohort (SFCCC):** Gay men,
SF Dept. of Health

Specific *KIR3DL1* + *HLA-B* combinations protect against AIDS progression



Multiple, distinct *KIR3DL1* + *HLA-B* compound genotypes protect against HIV (and cervical neoplasia?)



The complex, abundant epistatic effects observed for *KIR3DL1* and *Bw4* are unprecedented with regard to any pair of genetic loci in human disease, and underscore the primary role of *KIR3DL1*-*Bw4* interactions in controlling HIV-1.

Collaborators on KIR3DL1 studies

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AIDS Cohorts

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NCI, LGD

Many collaborators