A Gleam of Hope

Long-term non-progressors
HIV-exposed non-seroconverters

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Background

- Rapid Progressors, ~10%, 2-3 years
- Typical Progressors, ~80%, <10 years
- Long-term non-progressors, >10 years
  - Varying definitions of LTNP: ~0.8%-10%
- HIV-exposed non-seroconverters
  - Impossible to measure the frequency
Hypothesis

- What is learned through the study of LTNPs and non-converters may lead to advances extending the life expectancy of HIV-positive people or preventing seroconversion entirely by inducing a similar immunity to that naturally possessed by non-seroconverters.
Methods

- Medical Literature
- Press Releases, current and past
- AIDS research organization publications
- Clinical trial data
- Biochemical test data
- Anecdotal evidence
Factors Influencing Infection and Progression

- Route of exposure and quantity of virus
- Phenotype (virulence) of virus
- Host polymorphism in coreceptors
- Capacity of host immune system
- Other genetic factors affecting host immunity
- A *combination* of these factors
Long-term non-progressors

- Less virulent HIV virus
- Mutant form of HIV virus
- “Superman” immune system hypothesis
  - Cytotoxic T Lymphocyte activity
  - CD-8 cells and alpha-defensins -1, -2, -3
  - HLA B*5701
HLA B*5701

- Human Leukocyte Antigen
- HLA proteins attach to virus fragments in infected cells, bring to cell surface and present to CD-8 cells (cytotoxic T lymphocytes) that destroy the infected cell
- Present in 85% of LTNPs
  - Only true for a very strict definition of LTNPs
HIV-exposed non-converters

- Discordant Partners (HIV-/HIV+)
- HIV- infants from HIV+ mothers
- Exposed health workers
- Exposed sex workers, extremely high risk
  - Women from Nairobi, Kenya among the first discovered: 25% - 95% of clients infected. Similar cases found in Gambian women.
Cytotoxic T Lymphocytes

- Recognize infected cells and destroy them before HIV buds from cell and infects others
- Discordant partner trials: HIV- partner had CTL response against partner’s HIV virus, but did not seroconvert (41-45% of cases)
- Virus exposure induces HIV-immunity without infection
CCR-5

- HIV-coreceptor on surface of CD-4 cell
- CCR-5 mutant gene causes 32bp deletion
- Causes no phenotypic abnormality
- HIV cannot enter cells of individuals who are homozygous for the CCR-5 mutation
- Rare: 1% Caucasians homozygous mutant
Potential Solutions and Conclusions

- Analysis of how LTNPs and non-seroconverters effectively control the HIV virus may lead to therapeutic interventions

- Cell-mediated vs. antibody response
  - Determined by genetics, dose of virus and route of infection
  - Engineer a prophylactic vaccine to promote response