IN THE NEWS

Mixed messages

There has been intense media interest in the AIDS epidemic recently, in light of the XIV International AIDS Conference in Barcelona (7–12 July). However, it is not clear whether the news is good or bad.

The authors of a United Nations report (3 July) and a study published in the *Lancet* (4 July) suggest that 40 million people are infected with HIV and that 70 million will die from AIDS over the next 20 years. Peter Piot, Executive Director of UNAIDS warns that, "we're only at the beginning of this epidemic" (*UN News Service*), and Stephen Lewis, special envoy of the Secretary General for HIV/AIDS in Africa, presented the worrying statistic that in sub-Saharan Africa, 67% of HIV$^+$ 15–24-year olds are female (UN Press Briefing).

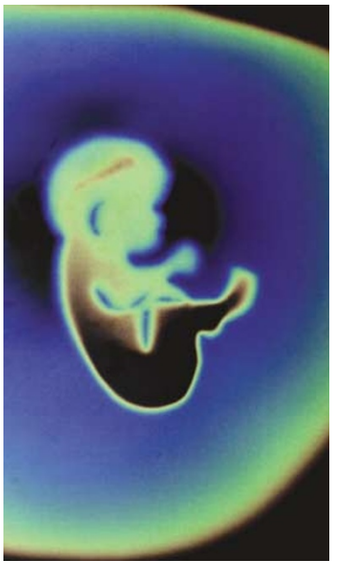
On a more optimistic note, the *Lancet* report proposes that 28 million new infections could be avoided by education programmes. The proposed introduction of an HIV$^+$ character to the South-African version of *Sesame Street* is one such initiative (*MediaGuardian*). The prevention of AIDS-related deaths will also require that anti-HIV drugs are more widely available. To this end, a court ruling in South Africa has ordered the government to stop denying nevirapine — which blocks mother-to-child transmission of HIV — to pregnant women (*Reuters*). Similarly, the world's largest HIV vaccine trial is awaiting final approval in Thailand. It is hoped that any success of the vaccine will not be confused with the recent controversy over V-1 Immunitor, a Thai food supplement made from the blood of HIV-infected individuals (*New Scientist*).

So, it seems that although the statistics are alarming and there is no room for complacency, preventive measures are having some impact and new developments look promising.

Kirsty Minton

REPRODUCTIVE IMMUNOLOGY

Placental presentation



Immunologists have never found it easy to explain why the semi-allogeneic fetus is not attacked in placental mammals by the maternal immune system. How is a response against paternal antigens avoided? Most researchers agree that local effects at the maternal–placental interface are important. Hobbs *et al.* suggest in *Cell* that the vertebrate-specific amino-terminal domain of the TATA-box-binding protein (TBP) regulates a placenta-specific β_2-microglobulin (β_2m)-dependent process that is used to evade a maternal rejection response.

The authors generated mice that have a modified *Tbp* allele ($Tbp^{\Delta N}$) that lacks the amino-terminal domain. More than 90% of $Tbp^{\Delta N/\Delta N}$ fetuses died in mid-gestation. Histopathology indicated that fetal death was the result of a placental insufficiency. Moreover, the physiology of mutant fetuses was normal, and the rare homozygous adults were healthy. This indicates that the mutation primarily affects a process that is required for placental, but not fetal, development.

Next, the authors showed that the defect could be complemented by an immunodeficient maternal environment. When the $Tbp^{\Delta N}$ mutation was bred into recombination-activating gene 1 ($Rag1$)$^{-/-}$ or severe combined immunodeficient (SCID) mice, most of the $Tbp^{\Delta N/\Delta N}$ fetuses survived, which indicates that the maternal immune response has an important role. This was confirmed by the observation that the defect can also be complemented by knockout of β_2m. As β_2m is required for the assembly and surface expression of MHC class I molecules, the defect

T-CELL SIGNALLING

Conformational change

We all know how T-cell receptors (TCRs) initiate antigen-induced signal transduction — right? Ligand-induced receptor clustering results in cross-phosphorylation of cytoplasmic immunoreceptor tyrosine-based activation (ITAM) motifs of associated CD3 chains, which recruit signalling molecules. But, what about the possibility of a ligand-induced conformational change in the TCR? G-protein-coupled receptors do it, and now in *Cell*, Gil *et al.* report that the TCR can do it too. They show that ligand engagement of TCR–CD3 induces a conformational change in CD3ε that recruits the adaptor protein NCK.

Using a yeast two-hybrid system, Gil and colleagues showed that non-ITAM regions of CD3ε interact with NCK after TCR–CD3 triggering. Precipitation experiments confirmed that CD3ε is the only CD3 subunit that interacts with NCK. NCK co-precipitates with TCR–CD3 from anti-CD3-stimulated, but not unstimulated, Jurkat T cells. This result was confirmed *in vivo*. It seems that the engagement of TCR–CD3 modifies this complex to recruit NCK to CD3ε. A cell-free assay was used to discount contributions from other cellular factors, and a monovalent Fab of anti-CD3 antibody was used to rule out receptor crosslinking, which indicates that a conformational change is responsible.

The authors went on to show that the amino-terminal SRC-homology 3 domain (SH3.1) of NCK binds to the proline-rich sequence (PRS) of CD3ε. Using deletion mutants of the CD3ε cytoplasmic tail, they showed that deletion of the PRS abolishes NCK binding. The expression of isolated domains of NCK was used to determine that only SH3.1 can bind CD3ε and that this binding is inducible.

How is NCK binding associated with TCR tyrosine phosphorylation? Surprisingly, the conformational change that allows NCK binding occurs independently of phosphorylation. Furthermore, after engagement of TCR–CD3, CD3ε can associate with NCK before the