In the news

COLD–CANCER LINK

Common infections that affect mothers and babies might trigger certain types of childhood cancer, according to a report in the December issue of the *European Journal of Cancer*.

A team led by Richard McNally (University of Newcastle upon Tyne, UK) analysed more than 3,000 childhood cancer cases, in individuals of 0–14 years of age, that occurred over a 45-year period. They found unusual clusters of brain tumours and leukaemia that were typical of infection-related diseases (*BBC News*, 12 December 2005).

"We found that place of birth was particularly significant, which suggests that an infection in the mother while she is carrying her baby, or in a child's early years, could be a trigger factor in cancer … these could be minor common illnesses, such as a cold, mild flu or respiratory infection", said McNally (*Reuters*, 12 December 2005).

However, the researchers stressed that people could not 'catch cancer' from a cold, as only a small number of children that are already susceptible to the disease will be affected. "It is important to stress that it doesn't look as if it is any particular infection that is involved: rather it is the response of the body to a number of different infections", said Tim Eden, Cancer Research UK Professor of Paediatric Oncology at the University of Manchester (*Manchester Evening News*, 13 December 2005).

Analysis of patterns of childhood leukaemia and brain tumours suggested that 8% of cases were probably linked to the spread of infectious diseases. These findings support previous research that showed that young children who are socially active, such as those who attend nurseries, are less at risk than those who are more sheltered, because they develop stronger immune systems (*Telegraph*, 12 December 2005).

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EVOLUTION

Evidence stacks up for evolutionary link

Although the ability to distinguish between self and non-self (that is, histocompatibility) is common among metazoans, the genetic basis of this process has only been well described for vertebrates. In vertebrates, this process is mediated by molecules that are encoded by the highly polymorphic MHC locus and results in the rejection

ANTIBODIES

IgG effector function: a question of balance

There are four subclasses of IgG antibodies, in both humans and mice, whose Fc regions differ in their ability to activate effector responses. Two theories have been proposed to explain these differences; first, that the differences are due to varying abilities to activate complement components in serum, and second, that the differences are due to differential binding to Fc receptors (FcRs). Now, in a study reported in *Science*, Falk Nimmerjahn and Jeffrey Ravetch show that the *in vivo* activity of IgG antibodies correlates with their interactions with FcRs and not with complement components.

FcRs can either activate or inhibit immune responses. A single inhibitory FcR, FcγRIIB, is present in both humans and mice, and the cellular response is determined by the balance between activating and inhibitory signals through FcRs on a cell. Each IgG subclass has a different affinity for different FcRs. In previous work, the authors developed the idea of an activating-to-inhibitory ratio (the A/I ratio, calculated by dividing the affinity of a specific IgG subclass for an activating receptor by the affinity for the inhibitory receptor) and found that these ratios varied between IgG subclasses. In the current study, an *in vivo* system was established to address whether A/I ratios correlated with the variation in subclass activity. The IgG2a subclass had the highest A/I ratio (~70) and the IgG1 subclass had the lowest ratio.

> "the differential biological activities of the IgG subclasses are dependent on their differential affinities for FcRs"

Two series of soluble IgG antibodies were generated, one specific for the melanoma antigen gp75 (TA99) and the other for the platelet integrin antigen 6A6, which allowed the authors to test whether A/I ratios correlated with the biological outcome. The antibodies were assessed for their ability to clear lung metastases in mice that were injected with tumour cells, or to clear integrin-expressing platelets. In both model systems, IgG2a, the IgG antibody subclass with the highest A/I ratio, displayed the best biological