

of transplants from donors who do not carry identical MHC alleles. Now, a report in *Nature* describes the isolation and characterization of the first known invertebrate histocompatibility gene.

When colonies of the sea squirt *Botryllus schlosseri* come into contact, they either fuse into a single colony or reject fusion. This was previously shown to be determined by histocompatibility reactions occurring at the periphery of each colony, the outcome of which depends on the alleles of the highly polymorphic locus FuHC (fusibility/histocompatibility) present in each colony. In this study, the authors mapped the FuHC locus and identified a candidate gene (*cFuHC*) that is highly polymorphic and encodes an immunoglobulin-superfamily member with no marked homology with MHC molecules. Polymorphisms in *cFuHC* were shown to segregate with histocompatibility, as determined

by fusion or rejection of pairs of colonies. Protein expression was also shown at sites of histocompatibility reactions.

Histocompatibility in vertebrates is thought to be a by-product of MHC-gene polymorphism. For *B. schlosseri*, however, histocompatibility reactions might restrict DNA exchange, allowing these organisms to maintain a diverse gene pool. So, this form of interaction might have preserved the genetic fitness of our ancestors. The dual function of MHC molecules in histocompatibility and immunity has long indicated that these processes are evolutionarily linked, and FuHC is the first structural link between vertebrate adaptive immunity and invertebrate histocompatibility.

Davina Dadley-Moore

**ORIGINAL RESEARCH PAPER** De Tomaso, A. W. *et al.* Isolation and characterization of a protochordate histocompatibility locus. *Nature* **438**, 454–459 (2005)

differences in activity were observed. By contrast, the IgG subclasses showed enhanced activity in mice lacking the inhibitory receptor FcγRIIB, and IgG subclasses with low A/I ratios were most profoundly affected. The link between A/I ratios and biological activity was further explored by altering the glycosylation pattern of the IgG constant regions to alter the A/I ratios, and again a correlation between A/I ratios and biological activity was noted.

These results support the idea that the differential biological activities of the IgG subclasses are dependent on their differential affinities for FcRs. Although there is no direct correlation between the mouse and human IgG subclasses, the principle established with this study might be applicable to human situations and might lead to better predictability of antibody performance and selection of the most appropriate isotype for therapeutic situations.

Elaine Bell

**ORIGINAL RESEARCH PAPER** Nimmerjahn, F. & Ravetch, J. V. Divergent immunoglobulin G subclass activity through selective Fc receptor binding. *Science* **310**, 1510–1512 (2005)

outcome, and IgG3, the subclass with the lowest ratio, had the poorest outcome, showing that A/I ratios correlate with *in vivo* activity. When these experiments were repeated in complement-deficient mice, no

## IN BRIEF

### DENDRITIC CELLS

Siglec-H is an IPC-specific receptor that modulates type I IFN secretion through DAP12.

Blasius, A. L. *et al.* *Blood* **17** Nov 2005 (doi:10.1182/blood-2005-09-3746)

Marco Colonna and colleagues previously generated an antibody (denoted 440c) specific for interferon (IFN)-producing cells (IPCs; also known as plasmacytoid dendritic cells). They now show that 440c binds a new member of the sialic-acid-binding immunoglobulin-like lectin (SIGLEC) family, SIGLEC-H. SIGLEC-H is unique because it binds the adaptor protein DAP12 (DNAX activation protein 12). Stimulation with 440c has been shown to inhibit IPC production of IFN $\alpha$  that is induced by CpG-containing DNA (a Toll-like receptor 9 (TLR9) ligand), and low concentrations of CpG-containing DNA induce DAP12-deficient IPCs to produce more IFN $\alpha$  than wild-type cells. But high concentrations of CpG-containing DNA induce equivalent amounts of IFN $\alpha$ , leading the authors to suggest that low-level activation of DAP12 for example, by antibodies specific for associated receptors, sequesters signalling molecules and interferes with TLR signalling.

### PHAGOCYTOSIS

A role for mammalian Diaphanous-related formins in complement receptor (CR3)-mediated phagocytosis in macrophages.

Colucci-Guyon, E. *et al.* *Curr. Biol.* **15**, 2007–2012 (2005)

Phagocytosis is mediated by receptors such as Fc receptors (FcRs) and complement receptor 3 (CR3). Colucci-Guyon *et al.* show that Diaphanous homologue 1 (DIA1), which regulates actin remodelling in fibroblasts, colocalizes with polymerized actin at the site of CR3-mediated phagocytosis in the macrophage cell line RAW264.7. In RAW264.7 cells, mutated DIA2 proteins that can inhibit endogenous DIA1 and DIA2, as well as knockdown of *Dia1* expression by small interfering RNA, decreased CR3-mediated phagocytosis, but had no effect on FcR-mediated phagocytosis. In addition, both the DIA2 mutants and knockdown of *Dia1* expression decreased actin recruitment to the site of CR3-mediated phagocytosis, providing a molecular distinction between CR3- and FcR-mediated phagocytosis.

### AUTOIMMUNITY

Identification of autoantibody clusters that best predict lupus disease activity using glomerular proteome arrays.

Zhen, Q. L. *et al.* *J. Clin. Invest.* **115**, 3428–3439 (2005)

Systemic lupus erythematosus (SLE) is characterized by circulating autoantibodies, in particular autoantibodies specific for DNA or the glomerulus. Zhen *et al.* developed a 'glomerular-proteome array' to analyse the fine specificity of these autoantibodies and screened numerous glomerular, glomerular basement membrane and DNA antigens using this approach. IgG in the sera of patients with SLE fell into five clusters of antigen reactivity, two of which were associated with higher disease activity. By contrast, the specificity of IgM autoantibodies fell into two clusters of antigen reactivity (DNA-reactive or seemingly polyreactive). Individuals with IgM in the DNA-reactive cluster had more severe disease, leading the authors to suggest that analysing autoantibody specificity on a glomerular-proteome array might provide a new means of screening patients with SLE.