IN BRIEF

INNATE IMMUNITY

TLR3 — enhancing pluripotency

The induction of pluripotency in human somatic cells can be achieved by the overexpression of four transcription factors (namely, OCT4, SOX2, KLF4 and MYC). This overexpression can be mediated by retroviral vectors, but there are concerns regarding the safety of this approach. A protein-based approach using purified recombinant proteins, termed cell-permeant proteins (CPPs), or cell extracts containing these proteins has overcome these concerns. But this approach is very inefficient compared with retroviral overexpression. Lee *et al.* examined target gene expression patterns induced by these two approaches. They found that the virus particles accelerate and augment the expression of the target pluripotency factor genes through Toll-like receptor 3 (TLR3). TLR3 activation caused rapid changes in the expression of epigenetic modifiers to enhance chromatin remodelling and early transcriptional activation. Importantly, the efficacy of CPP-induced pluripotency was greatly enhanced by the inclusion of retrovirus particles or the TLR3 agonist polyI:C.

ORIGINAL RESEARCH PAPER Lee, J. *et al.* Activation of innate immunity is required for efficient nuclear reprogramming. *Cell* **151**, 547–558 (2012)

AUTOIMMUNITY

Self DNAs can STING

Failure to clear self nucleic acids is thought to drive pathological inflammation in diseases such as systemic lupus erythematosus and polyarthritis. In support of this, *Dnase2*$^{-/-}$ mice (whose phagocytes cannot digest engulfed DNA) die during embryonic development owing to the overproduction of type I interferons (IFNs). In addition, although *Dnase2*$^{-/-}$ mice with defects in IFN signalling are viable, they develop severe arthritis. Ahn *et al.* show here that pathological inflammation in these mice is driven by activation of the cytoplasmic DNA sensor STING (stimulator of IFN genes). They found that DNA from necrotic or apoptotic cells induced pro-inflammatory cytokine production by myeloid cells in a STING-dependent manner. The authors next generated *Dnase2*$^{-/-}$*Sting*$^{-/-}$ mice; these animals survived birth, grew normally and did not develop polyarthritis. Similarly to *Dnase2*$^{-/-}$ macrophages, *Dnase2*$^{-/-}$*Sting*$^{-/-}$ macrophages could not digest engulfed nuclei from apoptotic thymocytes. So, potentially harmful self DNAs still accumulate in *Dnase2*$^{-/-}$*Sting*$^{-/-}$ mice, but they do not drive pathological inflammation.

ORIGINAL RESEARCH PAPER Ahn, J. *et al.* STING manifests self DNA-dependent inflammatory disease. *Proc. Natl Acad. Sci. USA* 6 Nov 2012 (doi:10.1073/pnas.1215006109)

INNATE IMMUNITY

X factor shows that the old ways still work

The coagulation system is important for immune defence in 'living fossils', such as the horseshoe crab, but it is not clear whether it contributes to immunity in higher organisms. This study shows that human coagulation factor X can bind to human adenovirus C (HAdv-C), thereby forming a complex that serves as a pathogen-associated molecular pattern for the activation of innate immune pathways. A mutant form of HAdv-C that could not complex with factor X did not induce the NF-κB-dependent pro-inflammatory responses that are normally associated with HAdv-C infection. Further analyses showed that Toll-like receptor 4- and TRAF6-mediated signalling are also required for a full-scale inflammatory response to HAdv-C.

ORIGINAL RESEARCH PAPER Doronin, K. *et al.* Coagulation factor X activates innate immunity to human species C adenovirus. *Science* 9 Nov 2012 (doi:10.1126/science.1226625)