



## 50 Years Ago

Professor Rankama has rightly drawn attention to the prevailing disorder in geochronological time-units and the abbreviations used for them, and his advocacy of “megayear” and “gigayear” is worthy of support. But the current international abbreviation for “year” ... is not “yr” but “a” and the appropriate abbreviations for megayear and gigayear are thus Ma and Ga. The admittedly incongruous appearance (for English-speaking readers) of the first may perhaps explain why it has not yet been generally adopted.

From *Nature* 1 July 1967

## 100 Years Ago

One day recently I went to look at a chaffinch's nest which I had known of for some time. I had just begun to climb up the hawthorn-tree in which the nest was placed when I heard the “pink, pink” of an alarmed chaffinch, and immediately about five cock chaffinches and more than half a dozen hens and young ones appeared from what seemed to me nowhere. These chaffinches flew all round the tree in a most agitated manner, and one cock actually got on top of my head and pulled my hair vigorously, while a hen, which ... I think was the mate of my assailant, flew on to the nest and pecked at me every time I tried to touch it. Their attack induced me to get down; and not until I was more than fifty paces from the tree did the other chaffinches go away. Not very long after this I was in the garden when I saw two cuckoos which were flying very low, and I could clearly perceive that one of them was carrying an egg in its beak ... I know that there has been much dispute as to whether cuckoos do or do not carry their eggs; but in this instance I can personally testify that a cuckoo was carrying what was obviously an egg.

From *Nature* 28 June 1917

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### IMMUNOLOGY

# Gut sensor halts viral attack

**Intestinal infection with rotavirus is a major cause of diarrhoea in infants, and can be fatal. The identification of immune sensor proteins that detect and restrict this viral infection now illuminates the body's defence system. [SEE LETTER P.667](#)**

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Intestinal cells can be infected by a type of virus known as a rotavirus, which is one of the leading causes of severe diarrhoea in infants and young children worldwide. Although effective rotavirus vaccines have been available since 2006, routine vaccination has been adopted in only a few developing countries, and it is estimated that the virus causes more than 200,000 childhood deaths annually<sup>1</sup>. There is only limited understanding of how intestinal cells sense rotavirus infection and mount an antiviral response. Now, on page 667, Zhu *et al.*<sup>2</sup> identify host proteins that are key components of this response.

Rotavirus is mainly spread by direct oral ingestion through contact with contaminated objects, or from water or food. Once ingested, the virus tends to infect epithelial cells that line the intestine, and this is where the virus, which contains double-stranded RNA, replicates. Zhu and colleagues investigated the host-defence response to the infection.

A key component of the response is the formation of a multiprotein complex called an inflammasome<sup>3</sup>. This complex contains core proteins, which are present in most inflammasomes, and sensor proteins that respond to specific types of pathogen and are present in only a subset of inflammasome complexes. Inflammasome activation usually promotes protective host defence and repair mechanisms. However, if activated in diseases such as chronic inflammatory disorders, these complexes can contribute to tissue damage and disease development<sup>4</sup>.

Inflammasome complexes mainly serve to recruit and engage the enzyme caspase-1.

When activated in response to specific pathogen- or host-derived cues, caspase-1 acts as ‘molecular scissors’, cleaving proteins containing certain sequences of amino acids that include aspartate. This cleavage activates key immune regulators, including signalling proteins known as cytokines, which convert biologically inert precursor proteins such as pro-interleukin-1 $\beta$  (pro-IL-1 $\beta$ ) and pro-IL-18 into the pro-inflammatory proteins IL-1 $\beta$  and IL-18, respectively<sup>3</sup>. Caspase-1 can also cleave the gasdermin D protein, releasing its amino-terminal fragment. This fragment can generate pores in cellular membranes and cause a type of cell death called pyroptosis, which occurs through cellular rupture<sup>5–9</sup>.

Zhu and colleagues investigated whether inflammasomes might be involved in host defence against the virus. They observed that, compared with wild-type mice, animals lacking a functional copy of the core inflammasome proteins Asc or caspase-1 were more susceptible to rotavirus infection. By contrast, animals lacking known inflammasome sensor proteins were not more susceptible. This prompted the authors to search for other sensor proteins that might detect rotaviral infection and engage a protective inflammasome response.

The authors focused on the evolutionarily conserved family of nucleotide binding domain and leucine-rich (NLR) proteins, which have diverse roles in immunity<sup>10</sup>. They investigated the protein Nlrp9b, a previously uncharacterized member of this family, because it is expressed mainly in intestinal epithelial cells. The authors used genetic engineering to produce mice that either lacked Nlrp9b throughout their bodies or lacked it only in intestinal epithelial cells. They found