patterning of silicon thin films that makes this work particularly exciting. Challenges do remain here: the physical properties of the liquid precursor, such as its viscosity, vapour pressure and surface tension, must be tuned to take full advantage of the printing tools available, while precisely controlling the post-baking thin-film morphology critical to semiconductor performance. Careful study of dilution effects is also needed. Finally, stricter control of the distribution of polysilane chain lengths within the precursor mixture would also probably help — a real test for polymer chemists.

It might be that, in the end, inkjet printing of 'liquid silicon' will not provide the resolution necessary to pattern a high-density integrated circuit and therefore make a computer chip. But what it will certainly allow is the remarkably straightforward generation of simple, cheap and flexible circuits for displays, as well as a range of other applications — solar cells, X-ray detectors and multi-analyte chemical sensors included. ■

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IMMUNOLOGY

The pick of the nibbled bits

Joel Swanson

How does the immune system avoid potentially damaging responses against the body's own molecules? The answer lies partly in the ability of dendritic cells to sample their surroundings selectively.

Animal tissues are groomed by phagocytes, migratory cells that routinely ingest moribund neighbouring cells, infecting microbes and particulate debris. In the immune system, specialized phagocytes called dendritic cells recycle the molecular fragments from ingested proteins, transporting the scraps to their plasma membranes for display on their external surface as antigens. If the fragments are derived from a microbe, then the dendritic cell adds indicators of the alien status of its meal onto its surface. The displayed antigens are recognized by circulating T lymphocytes, cells that can activate specific immune responses if they later find the same alien molecules presented elsewhere in the body[1]. The voracious appetites of phagocytes suggest a dilemma concerning mixed meals: phagocytosis of two particles, one that can trigger an immune response and another that cannot, could launch a misguided response against benign molecules.

On page 808 of this issue, Blander and Medzhitov[2] show that phagosomes, the intracellular organelles that contain ingested particles and antigenic proteins, can work independently of one another inside the same cell to determine the fate of their enclosed antigens. This subcellular regulation suggests a mechanism for focusing the immune response and provides clues for the rational design of vaccines.

Immature dendritic cells in peripheral tissues 'sample' their environment by phagocytosis, initiating specific immune responses when they sense microbes or tissue damage. Ingested material is usually degraded completely as phagosomes mature into phagolysosomes. The maturation, or 'differentiation', of dendritic cells can be stimulated in part by signalling through Toll-like receptors (TLRs), a family of cell-surface molecules that recognize molecular patterns common to microorganisms.

TLR4 recognizes lipopolysaccharide, a conserved and abundant surface molecule of Gram-negative bacteria such as *Escherichia coli*. Through TLR4, the lipopolysaccharide ligand stimulates dendritic-cell maturation and the re-routing of the cell's intracellular traffic, such that fragments of proteins generated in phagolysosomes are bound by 'MHC class II' proteins to make antigen-presentation complexes that move to the cell surface[3]. T lymphocytes capable of recognizing specific peptide antigens in MHC class II complexes continually scan surfaces of mature dendritic cells, and recognition of their cognate ligand typically leads to activation of an immune response specific to that antigen (Fig. 1).

Blander and Medzhitov[2] examined whether TLR4-mediated differentiation affects the fate of all phagosomes in the cell or only those containing the TLR4 ligand. They allowed dendritic cells from mice to ingest bacteria or dying (apoptotic) cells containing protein antigens, such that antigen processing could occur in the presence or absence of phagosome-restricted TLR4 signalling. They then compared the antigen-presentation responses when antigen and lipopolysaccharide were eaten together either on the same particle or in distinct particles inside the same cell.

Protein antigens delivered via *E. coli*, which would be expected to activate TLR4, were fully processed into peptide-loaded MHC class II complexes and were presented to antigen-specific T lymphocytes at the dendritic-cell surfaces. However, proteins delivered by phagocytosis of apoptotic cells, which lack TLR4 ligands, were not presented to T lymphocytes, even when those same dendritic

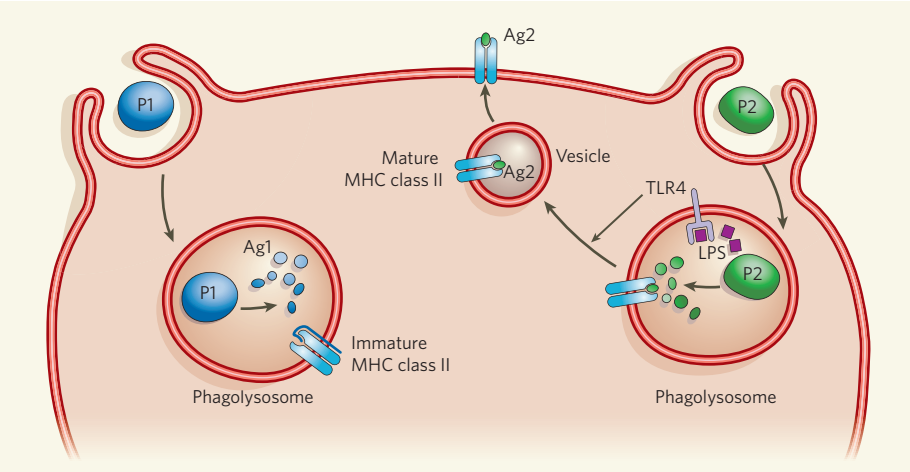

Figure 1 | Independence for phagosomes. Dendritic cells ingest detritus from their environment into organelles called phagosomes, where particle-associated proteins (P1 and P2) are partially degraded into antigenic fragments (Ag1 and Ag2). Phagosomes mature into phagolysosomes. If the antigens come from proteins that are alien to the body (P2), the antigens (Ag2) associate with MHC class II antigen-presenting complexes, and are then transported to the cell surface by membrane-bound 'vesicles'. In the case of proteins from invading bacteria, the lipopolysaccharide (LPS) secreted by Gram-negative bacteria is recognized by TLR4 molecules on dendritic cells, which then aids the formation and trafficking of the antigen-presenting complex. Once on the cell surface, the antigen can be recognized by circulating T lymphocyte cells, which initiate a full immune response against the alien molecule. So does a dendritic cell that has eaten particles containing LPS indiscriminately present antigens from all of its phagolysosomes? Blander and Medzhitov[2] found that phagosomes in the same cell process antigens independently of one another. Those that contain LPS along with the ingested proteins send antigens to the cell surface (Ag2) and those lacking LPS do not (Ag1).

cells contained lipopolysaccharide in other phagosomes. Antigen could be successfully processed from phagosomes containing apoptotic cells if those cells were given lipopolysaccharide before their ingestion. This indicated that activation of TLR4 in the phagosome resulted in selective loading of antigen from that phagosome.

To address possible confounding effects of comparing different kinds of cells as phagocytosed particles, the authors performed analogous experiments using protein antigens attached to synthetic microspheres, with or without added lipopolysaccharide. Antigens were fully processed and presented when the microspheres they were delivered on also contained lipopolysaccharide. By contrast, antigens associated with lipopolysaccharide-free particles did not reach the cell surface, even in cells that had lipopolysaccharide-labelled particles in other phagosomes. Characterization of isolated microparticle-containing phagosomes showed that all of them, with or without lipopolysaccharide, had matured into phagolysosomes. The essential difference was that the phagosomes with lipopolysaccharide particles contained stable MHC class II molecules and showed indications of the advanced stages of antigen processing (that is, proteolysed invariant chain proteins).

Therefore, the organizational unit for this information processing is not the entire cell but rather the individual organelle. Such phagosome autonomy was indicated by a study of antigen presentation by MHC class I proteins from phagosomes[4], although the independence of the phagosomes was not established as thoroughly as in Blander and Medzhitov's work[2]. The localized selection of antigens for presentation implies that TLR4 signals are generated inside the phagosome, at least with respect to directing the maturation of MHC class II complexes. It also suggests that TLR4 can direct traffic of the membrane organelles that transport protein cargoes from phagosomes to the cell surface. TLR4 signalling was reported to inhibit the trafficking that leads to formation of phagolysosomes[5], although this point remains controversial[6,7].

It is somewhat surprising that the contents of phagosomes remain isolated from each other inside the cells used by Blander and Medzhitov, as studies of other phagocytes have indicated that phagosomes and endocytic organelles readily merge together or exchange contents[8,9]. Perhaps TLR4 or other lipopolysaccharide-associated activities isolate lipopolysaccharide-rich phagosomes from other kinds of phagosomes.

Several questions emerge from this work, the answers to which could guide the understanding of immune recognition and the design of vaccines. Is the organizational unit smaller than one phagosome? Perhaps patches of phagosomal membranes are sufficient to organize TLR4-dependent MHC class II maturation and trafficking. How are TLR4-mediated signals that stimulate dendritic-cell maturation integrated with the local signals that drive antigen processing and presentation? Vaccines elicit immune responses using combinations of antigen, particles and TLR ligands, so might vaccine formulations be improved by ensuring the persistent association of these ingredients inside phagosomes? Finally, are there counteracting but as yet undetected signals coming from the apparently inert phagosomes? Maybe every nibbled bit affects the quality of the meal. ■

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SOLAR SYSTEM

When the dust unsettles

Gary R. Huss

Two attempts to measure the isotopic composition of oxygen in the Sun from particles trapped in lunar soils give very different results. A rethink of why the Solar System is as it is might be required.

On page 776 of this issue, Ireland *et al.*[1] report investigations of lunar soil from which they infer that, compared with other Solar System bodies, the Sun is depleted in the naturally most plentiful oxygen isotope, ^{16}O. Just a year ago, another study[2] of soils on the Moon concluded exactly the reverse. So who is right?

Oxygen is the third most abundant element in the Solar System (the Sun's huge stores of hydrogen and helium claim first and second place), and a principal constituent of the rocks, ices and atmospheres that make up the planets. Its three naturally occurring isotopes — ^{16}O, ^{17}O and ^{18}O — are found in relative abundances of about 2,700:1:5, although the physical and chemical processes occurring in different environments of the Solar System can cause shifts in these abundances of up to a few per cent.

Such deviations can be depicted on an oxygen three-isotope plot (Fig. 1, overleaf). Here, all samples from Earth fall along a single line with a slope of about 0.5, indicating that the ratio $^{18}O/^{16}O$ shifts by twice as much as the ratio $^{17}O/^{16}O$. This is mass-dependent behaviour, as the difference in mass between ^{18}O and ^{16}O is twice that between ^{17}O and ^{16}O. Oxygen from other planets or asteroids — represented on Earth by different classes of meteorite — show similar mass-dependent fractionations, but as the underlying oxygen composition of each body is different, the data fall on different lines on the three-isotope plot. Oxygen isotopic composition has therefore become a crucial parameter in classifying meteorites.

How this oxygen-isotope variability arose, however, is not understood. Does it represent a heterogeneity inherited from the raw materials that made up the Solar System? Or is it the result of physical or chemical processes in the early Solar System[3–5]? The initial oxygen isotopic composition of the dust and gas from which our Solar System formed is not known. The Sun contains most of the matter in the Solar System, so its oxygen isotopic composition effectively defines the Solar System's oxygen composition. Models that generate the compositions of other bodies from an ^{16}O-rich composition are very different from those that start with an ^{16}O-poor composition. But measuring the chemical and isotopic composition of the Sun directly is difficult; the best data come from measurements of the stream of charged particles emitted by the Sun known as the solar wind.

One of the best places to measure the solar wind is in lunar soils. The Moon has no atmosphere and no magnetic field, so solar-wind particles are implanted directly into its surface. Measurements of matter from the solar wind have so far concentrated on elements such as the noble gases, nitrogen and carbon, which are not themselves significant components of minerals in lunar soil. Oxygen, by contrast, is found in many minerals. Therefore, solar-wind oxygen in lunar soils must be studied in minerals such as iron metal, which are by nature oxygen-free.

Hashizume and Chaussidon[2] were the first to separate iron-metal particles from lunar soils and measure their oxygen content using an ion microprobe. They found that oxygen in a few grains of their soil, which had been exposed to the solar wind between one billion and two billion years ago, was enriched in ^{16}O compared with the oxygen on Earth and that