The second avenue is phylogenetic. The evolutionary scheme we have outlined implies that the transition from great appendage to labrum happened once in the common ancestor of all living arthropods apart from the pycnogonids, which must therefore be very basal in evolutionary terms. But if the pycnogonids truly are the sister group of the spiders and scorpions (which some molecular data suggest[9]), then the results of Maxmen *et al.* will be hard to square (Fig. 2). Testing the phylogenetic position of pycnogonids is therefore crucial.

The conclusions of Maxmen *et al.* overturn entrenched ideas about the body plan of the sea spiders and, furthermore, lend support to some controversial theories of arthropod evolution. Unlike their terrestrial analogues, sea spiders lack a poisonous bite, but this paper is bound to inject venom into what is already one of the most controversial of all zoological topics. ■

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QUANTUM PHYSICS

Atom waves in passing

Maarten DeKieviet and Joerg Schmiedmayer

Matter-wave interferometers are unique tools for exposing particles acting like waves — one of the stranger facets of quantum theory. They can even measure the quickening of an atom's 'pulse' as it flies past a surface.

Particles sometimes act like waves, and waves sometimes act like particles. This phenomenon, known as wave–particle duality, may seem to confuse what are (to everyday experience at least) two separate and unambiguous concepts. But 100 years after Albert Einstein first introduced the idea of waves behaving like particles to explain the photoelectric effect, and more than 80 years after the French physicist Louis de Broglie proposed the converse behaviour, wave–particle duality has become a staple food of the quantum diet. Writing in *Physical Review Letters*[1], John Perreault and Alexander Cronin expose a further experimental ramification of the effect, by measuring the shift in phase — a wave property — of an atom as it flies past, and interacts with, a surface.

In doing so, they take advantage of matter-wave interferometry, a technique that has in recent decades given fresh impetus to studies of the wave-like nature of particles. Pioneered for simple particles such as electrons[2] and neutrons (ref. 3 and references therein), the technique has since been extended to larger particles such as atoms and molecules (ref. 4 and references therein).

Interferometry as a generalized technique involves the superposition of two waves to gain information about their relative phase — where in their cycle they are in relation to each other. A simple analogy is a zip-fastener: for proper zipping, the teeth of one strand must fit perfectly with those of the other. If, however, they are shifted such that the teeth oppose each other, the zipper won't close. Analogously, if the peaks of one wave are next to the troughs of the other, the waves are perfectly out of phase, and their amplitudes cancel out — they interfere 'destructively'. Conversely, if the two waves are perfectly in phase, with the peaks and troughs matching, they interfere constructively to produce a net amplitude that is the sum of the two individual amplitudes.

In an interferometer, an incoming wave is split into two branches. One of these branches is subjected to an outside influence that slows down or speeds up the atom-wave's cycle, or pulse, thus shifting its phase relative to that of the other branch. These two branches are then brought back together and interfere, the amplitude of the resulting wave being proportional to the degree to which the two waves are in phase. Generally in wave mechanics only intensities — the squares of the amplitudes — can be measured, so phase information is lost. The power of interferometry is that it transforms a shift in phase to a change in amplitude, which can be measured as change in intensity.

And so it is in Perreault and Cronin's experiment[1]. They make use of a Mach–Zehnder interferometer, in which a nanoscale grating is used to diffract atomic waves, thus acting as a matter-beam splitter[5]. The authors inserted a further 250-nm-thick membrane with thousands of 50-nm-wide slits into one branch of this interferometer. As they pass through this additional membrane, the atoms experience a weak, attractive van der Waals force through electronic coupling with the membrane's walls. This interaction speeds up the atoms' pulse — the phase of the atom-wave becomes shifted with respect to the free-atom wave in the interferometer's other branch. From the measured interference, the phase shift caused by the atom–surface interaction can be exactly quantified.

This measurable change in the interference pattern arises from an atomic interaction that occurs over a distance up to 1,000 times that of an atomic diameter. Perreault and Cronin are, to their knowledge, the first to determine directly the phase shift caused by the van der Waals interaction between an atom and a surface. The acceleration towards the surface of the channels experienced by the sodium atom-waves is more than a million times that caused by Earth's gravitational field. The channels are, however, very short, so the actual time difference measured by the interferometer is only about 100 attoseconds (10^{-16} seconds). Contrasting this with the overall flight time through the device of around one millisecond gives an idea of the exquisite sensitivity possible with interference experiments. This experiment is a beautiful example of the many tools that are being developed in a true renaissance in the study of atom–surface interactions[6].

The potential impact of such work stems from its connection to the fields of nanotechnology and atom optics. Nanometre-scale structures could lead to smaller transistors and motors, or the ability to assemble molecules atom by atom. Exploiting the wave behaviour of atoms could lead the way to more precise gyroscopes for navigation, gravity gradiometers for subterranean mapping and other field sensors. The work of Perreault and Cronin[1] lies at the intersection of these two fields, putting a limit on how small nanotechnological and atom-optical devices can be made before the van der Waals interaction disrupts their operation. ■

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CELL BIOLOGY

A BID for the pathway

Michael B. Kastan

Cells have many ways of coping with damage to their DNA, but how are these all coordinated? It seems that BID — a regulator of programmed cell death — stands at the crossroads of several damage-response pathways.

Exposure to DNA-damaging agents can cause mutations, developmental abnormalities or cancer, and cells have developed numerous ways to minimize these effects. Such mechanisms include cell-cycle checkpoints to prohibit damaged cells from dividing while the cell deals with the damage; processes to repair the DNA; and programmed cell death (apoptosis). Although it makes sense that there should be coordinated regulation of these different processes, they have mostly been studied as independent pathways. A new link between these mechanisms comes from work reported in *Cell* by Zinkel *et al.*[1] and Kamer *et al.*[2] demonstrating an unexpected role for the protein BID, a known regulator of apoptosis, in the control of cell-cycle progression following DNA damage.

Apoptosis can be initiated by external signals from other cells — TNF-α, for instance, which is released by certain immune cells to kill infected cells — or by internal warnings resulting from DNA damage or other cellular stresses. Regardless of the stimulus, the death process is controlled by one of several signalling pathways, all of which include one or more members of the BCL-2 family of proteins. The binding of external factors to their cognate 'death receptors' on the cell surface leads to the cleavage and activation of BID[3] — a BCL-2 family member. BID, in turn, activates BAX and BAK, both of which are BCL-2 proteins that then trigger apoptosis (Fig. 1)[4]. By contrast, DNA damage causes activation of the ATM or ATR protein kinases (enzymes that phosphorylate certain target proteins), and this activation leads to a rise in p53 protein levels[5]. This protein can switch on a number of target genes, including those encoding the BCL-2 family members BAX, PUMA and NOXA, each of which contributes to apoptosis in specific cell types[6]. In certain cell types or physiological settings, however, the induction of p53 protein, instead of initiating apoptosis, causes arrest of the cell cycle at the G1 phase. Moreover, other targets of ATM and ATR also contribute to cell-cycle arrest in the S and G2/M phases[5].

Previously, the p53-dependent activation of the genes encoding BAX, PUMA and NOXA was thought to be the main link between DNA damage and the control of apoptosis. Now, Zinkel *et al.*[1] and Kamer *et al.*[2] show that another pathway links the control of apoptosis to that of the cell-cycle arrest following DNA damage. Both groups found that BID is phosphorylated in an ATM-dependent manner after DNA damage and that some of the BID protein then moves into the nucleus. Unexpectedly, both groups also found that arrest of the cell cycle in S phase in response to DNA damage requires BID phosphorylation. Moreover, the domains of the BID protein responsible for control of the cell cycle are distinct from that involved in its apoptotic function. These observations add BID to a surprisingly long list of proteins that are phosphorylated by ATM or ATR to control the progression through the cell cycle after DNA damage (Fig. 1). Furthermore, Zinkel *et al.*[1] demonstrate that cells lacking BID suffer more chromosomal aberrations after DNA damage than those that have BID, raising the possibility that this protein participates in repair of the DNA as well as in cell-cycle control and apoptosis.

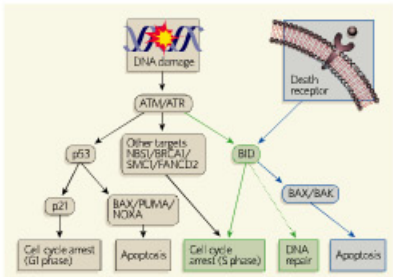

Figure 1 | BID linking two pathways. Zinkel *et al.*[1] and Kamer *et al.*[2] find an unexpected role for BID in the ATM pathway that responds to DNA damage (new steps in green). Following DNA damage, ATM and ATR are activated and, through p53, can cause either cell-cycle arrest at the G1 stage or apoptosis. ATM and ATR also activate several other protein targets, causing the cell cycle to stall in the S phase. Now BID can be added to this list of ATM/ATR targets. Although BID clearly induces apoptosis following activation of death receptors, its role in controlling apoptosis following DNA damage needs to be clarified. The dotted arrow shows a link that is suggested from Zinkel and colleagues' results, but has yet to be demonstrated.

Although the two papers agree in several aspects, there are some apparent discrepancies and some findings that require further clarification. The importance of BID and its phosphorylation by ATM in influencing cell survival following DNA damage varied in different experiments in the two papers. These discrepancies may have resulted from differences in cell types, agents or doses used, but they need to be explained if we are to understand the physiological roles of this branch of the ATM pathway. Furthermore, there were inconsistencies between the two studies regarding which DNA damaging agents activate the ATM–BID pathway. For example, Zinkel *et al.*[1] found that ATM was required for BID phosphorylation following exposure to many different types of agents, including hydroxyurea and ultraviolet light, whereas Kamer *et al.*[2] observed BID phosphorylation and ATM-dependence only after treatment with agents that introduce breaks in DNA strands, such as ionizing irradiation and the drug etoposide. The specificity of ATM-dependence for responses to ionizing irradiation would be consistent with a large amount of data in the literature[7].

Although there are some confusing results, the two papers convincingly establish that the apoptotic protein BID is a target of ATM and that it has an unanticipated role in controlling cell-cycle progression following DNA damage. The data demonstrate that BID and ATM come together in one arm of one pathway, but also underscore the notion that the two proteins have other distinctive biochemical and functional roles. Thus, it is not surprising that the effects of their loss are quite different: mice lacking BID develop a blood disorder resembling chronic myelomonocytic leukaemia[8], whereas mice and humans lacking ATM develop acute lymphoid leukaemias and lymphomas[8]. It makes sense that cells would have a multi-pronged, coordinated response to stresses such as DNA damage, because it would be advantageous to simultaneously control DNA repair, cell-cycle progression and programmed cell death. BID is unlikely to be the last example of a protein that stands at a crossroads to influence multiple parts of the stress response. ■

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