semiconductor interface is indeed the culprit, and they relate this trapping to electronegative hydroxyl (OH) groups in the insulator material. When they use materials that are free of hydroxyl groups, uninhibited electron transport is indeed observed. By using bisbenzocyclobutene as the insulator, for example, organic polymer FETs based on materials such as poly(fluorine-*alt*-bithiophene) and poly(fluorine-*alt*-benzothiadiazole) are shown to exhibit n-channel behaviour.

Chua *et al.* conclude that if the trapping of electrons by electronegative groups in the insulating layer could be avoided, then n-channel behaviour would be seen in a broad range of semiconductors. Their most convincing example is that of polythiophene, which is relatively prone to oxidization and therefore normally more difficult to use in n-channel FETs.

Of course, it remains to be seen whether, on prolonged exposure of the device to ambient conditions, the effects of atmospheric moisture and oxygen would negate those of a hydroxyl-free insulator material. But the finding is nevertheless a remarkable result and a major step forward in our understanding of the design principles of materials and devices for n-channel organic transistors.

Chua and colleagues' work also explains why some semiconductors transport both electrons and holes when used as an active layer in light-emitting diodes — where there are no insulating interfaces — but exhibit only n-channel behaviour in FETs[9]. The implication is that such materials, which readily exhibit n-channel behaviour but not p-channel behaviour, could also be made ambipolar by identifying what causes hole trapping at the semiconductor–insulator interface and eliminating it.

Another area that will benefit greatly from this study is the work on ambipolar organic FETs with a view to making efficient light-emitting transistors[10]. A wider choice of materials for this type of research will become available once electron trapping is eliminated or greatly reduced. ■

Ananth Dodabalapur is in the Microelectronic Research Center, University of Texas at Austin, 10100 Burnet Road, Building 160, Austin, Texas 78758, USA.
e-mail: ananth@mer.utexas.edu

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Developmental biology

Sperm–egg fusion unscrambled

Richard Schultz and Carmen Williams

The identity of the sperm molecules that are involved in fusion with an egg's membrane has eluded biologists. Will Izumo, a protein named after the Japanese shrine to marriage, bring harmony to the field?

In the life history of sexually reproducing organisms, fertilization is a defining event. In mammals, sperm and egg have a limited lifespan once present in the female reproductive tract. Fertilization 'rescues' these gametes in a multi-step process that ultimately results in the fusion of their membranes and formation of a zygote. Despite the importance of the interactions that lead to zygote formation — and despite decades of research — the molecular basis for sperm–egg fusion has remained poorly understood, and the field is littered with the carnage of erstwhile molecular candidates. The latest discovery is of a sperm-specific protein called Izumo, and the evidence that it is required for fusion, presented by Okabe and colleagues[1] on page 234 of this issue, is compelling.

The steps involved in sperm–egg fusion are illustrated in Figure 1. Briefly, the cumulus cells that surround an ovulated egg secrete a matrix containing hyaluronic acid. A sperm must first pass through this matrix, and then interact with the egg's coat (the zona pellucida); this stimulates secretion of the contents of the sperm's acrosome — an intracellular sack of molecules necessary for sperm to penetrate the zona pellucida. Once through this coat, the sperm gains access to the perivitelline space, and binds to the egg's plasma membrane. Sperm and egg membranes then fuse.

Historically, antibodies have been used to identify proteins from the surface of mouse sperm that are involved in fertilization. In this way, PH-20 was identified as an enzyme that helps sperm to pass through the hyaluronic-acid-containing matrix[2]. The same approach identified the fertilin αβ protein as a candidate for mediating sperm–egg fusion — an exciting finding because of the structural nature of the fertilins. These proteins were the founding members of the ADAM (for 'a disintegrin and metalloprotease') superfamily[3]. Fertilin α and β each contain a disintegrin domain, which might mediate cell–cell adhesion by interacting with an egg integrin protein; fertilin α also contains a domain related to that of viral fusion peptides, which might mediate sperm–egg membrane fusion.

Unfortunately, however, later work did not support a role for fertilin α in membrane fusion, and sperm derived from fertilin-β-deficient mice can still fertilize eggs. Furthermore, wild-type sperm can bind to and fuse with eggs deficient in each of the integrins that are likely to interact with ADAM disintegrin domains. These results deflated the previous excitement and left the field in a profound state of uncertainty.

The results described in this issue by Okabe and colleagues[1] should rekindle a sense of vitality in this area of research. Okabe and colleagues[4] reported 18 years ago that a particular antibody, OBF13, recognizes a molecule on the sperm head that is exposed following the acrosome reaction. A later study[5] indicated that although this antibody did not inhibit sperm–egg binding, it did prevent fertilization *in vitro*, hinting that the protein it binds is involved in fusion. Now, Okabe and colleagues[1] have used liquid chromatography tandem mass spectrometry to identify this protein, and have named it Izumo. The protein sequence indicates that Izumo (and its human counterpart) is a member of the immunoglobulin superfamily, and other experiments show it to be sperm-specific.

The authors used a knockout approach to assess a role for Izumo in fertilization. Females lacking the protein were phenotypically normal and fertile. In contrast, although Izumo-deficient males were phenotypically normal — and their sperm were also normal in morphology and motility — they were completely infertile. The Izumo-deficient sperm could reach eggs *in vivo*. They showed no reduction in their ability to bind to and penetrate the zona pellucida *in vitro*. And, once in the perivitelline space, they could bind to the egg plasma membrane. But not a single Izumo-deficient sperm was observed to fuse with the egg membrane. The authors ascribe this inability directly to the lack of Izumo, because expressing this protein in Izumo-deficient males restored fertility. Finally, they found that bypassing membrane fusion by injecting Izumo-deficient sperm into eggs resulted in activation of the eggs and development to term. These results, and more, strongly suggest that the sole function of Izumo is in sperm–egg fusion.

So, how does Izumo promote membrane fusion? Because its extracellular region lacks sequences like those found in viral fusion peptides, it is unlikely that Izumo is inherently fusogenic. A more likely possibility is that it serves as an adhesion molecule, given that it has an immunoglobulin-like domain — a well-defined domain for mediating cell–cell adhesion (see, for example, ref. 6). In contrast to most members of the

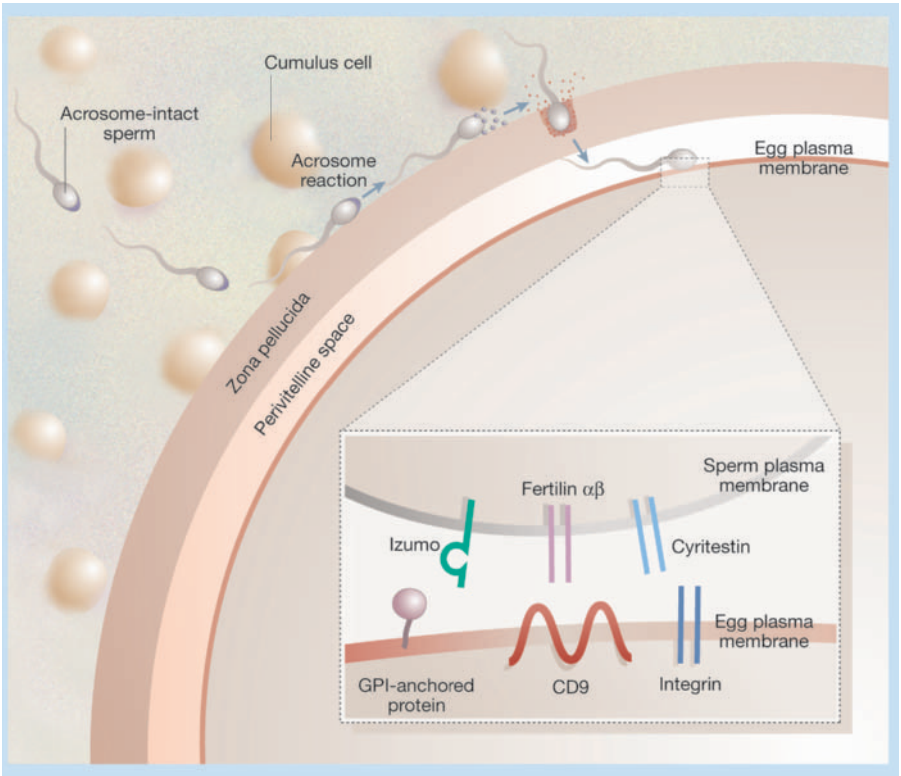

Figure 1 **Events leading to fertilization. A sperm (whose acrosome compartment is intact at this point) passes through the hyaluronic-acid-containing matrix secreted by cumulus cells. Interaction with the egg's coat (the zona pellucida) leads to the secretion of acrosomal contents and exposure of molecules needed for sperm–egg binding and fusion. Although the zona pellucida is well characterized biochemically (it is composed of several glycoproteins), the molecular basis for how sperm bind to it and undergo the acrosome reaction is not resolved[12]. The sperm then penetrates the zona pellucida, gains access to the perivitelline space and binds to the egg's plasma membrane. Inset, molecules on the sperm surface, such as fertilin and cyritestin[3], may be involved in sperm–egg binding; Okabe and colleagues[1] find that Izumo is essential for membrane fusion. On the egg, CD9 is required for fusion and might collaborate with other proteins such as integrins or glycosylphosphatidylinositol (GPI)-anchored proteins.**

immunoglobulin superfamily, the relatively small extracellular region of Izumo contains only a single immunoglobulin-like domain. But, by interacting with an egg surface protein, this small domain could permit the close membrane apposition requisite for membrane fusion.

Assuming that Izumo binds to egg proteins, what might they be? So far, the tetraspanin-superfamily protein CD9 is the only egg protein documented to function in sperm–egg fusion[7,8]. Tetraspanins mediate protein interactions to create unique cell-surface regions that contain specific proteins, including integrins, immunoglobulin-superfamily members and other tetraspanins. Female mice without CD9 are phenotypically normal but infertile. Sperm bind normally to CD9-deficient eggs but fail to fuse; this defect is eliminated by injecting CD9-encoding messenger RNA[9]. Because CD9 can interact with other immunoglobulin-superfamily members — such as pregnancy-specific glycoprotein 17 (ref. 10) — it is possible that it also interacts directly with Izumo. Alternatively, a CD9-associated protein, perhaps a glycosylphosphatidylinositol-anchored protein, might participate; sperm do not fuse with eggs lacking such proteins[11]. Crosslinking experiments, using Izumo as a probe, would be an obvious way to try to identify potential partners in the egg, as well as sperm proteins that interact with Izumo.

Finally, although most of Okabe and colleagues' work[1] was conducted using mice, they also note that humans express a counterpart of Izumo on the sperm head, and that an antibody raised against this protein blocks the fusion of human sperm with hamster eggs — a test for male fertility. These findings raise the exciting possibility that, because Izumo is sperm-specific and extracellular, this protein and its interacting partners could be new targets for non-hormonal contraception. ■

Richard Schultz is in the Department of Biology and Carmen Williams is at the Center for Research on Reproduction and Women's Health, University of Pennsylvania, Philadelphia, Pennsylvania 19104, USA.
e-mail: rschultz@mail.sas.upenn.edu

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Planetary sciences

A smashing pair

Jay Melosh

The likely origin of Pluto and its satellite Charon, like the Earth and Moon, is an impact between two planet-sized bodies. Refined simulations show that there may be two distinct modes for the birth of such twins.

Since Galileo's unexpected discovery of Jupiter's four large moons in 1610, astronomers have continued to discover satellites in strange places, with the latest found among the distant, icy objects in the Kuiper belt. However, our understanding of how these satellites came into existence has not kept pace with discovery. Indeed, the origins of the satellites of Mars and the irregular satellites of Jupiter are still fraught with uncertainty.

The origin of our own Moon was similarly shrouded in confusion until the mid-1980s, when a new and dramatic idea, the giant-impact hypothesis, swept all others before it[1]. During the heated debates about the origin of Earth's moon, it was suggested that the Solar System's other planetary twins, Pluto and Charon, might also be the offspring of a gigantic collision[2]. Now Robin Canup, the leading researcher into simulations of the terrestrial giant impact, has applied her computer models to the Pluto system and added detail and precision to the violent birth of Pluto's moon[3].

Unlike the rather loosely bound systems