of APCs, a particular subset of dendritic cells. Although other subsets of dendritic cells still need to be examined, these observations suggest that the ICOS–B7RP-1 pair is not involved in the initial activation of the T cell, but rather is important later on, when the B cells and macrophages are activated (Fig. 1).

The effects of inactivating ICOS in mice, described by Dong et al., McAdam et al., and Tafuri et al., are consistent with this idea. The ‘knockout’ mice have few germinal centres — the lymphoid factories where B cells manufacture antibody molecules. And certain types of antibodies, such as immunoglobulin E, are not generated at all in these mice. This can be partly explained by the decrease in production of specific cytokines (such as interleukins 4 and 13) by T cells. But the fact that there is decreased production of almost all antibody types suggests a more general defect.

One potential explanation is a slight decrease in the production of interleukin-2, described by Dong et al. in vitro analyses. But it might be more fruitful in the future to study the expression of chemokine receptors and their soluble ligands, chemokines. The chemokine-receptor family of cell-surface molecules, involved in the migration of immune cells during an immune response, is essential for the formation of germinal centres. ICOS is expressed mainly on activated T cells that come into germinal centres, and its stimulation might amplify chemokine production to recruit more activated B and T cells to this site. In support of this idea, a recent study showed that ICOS would be expected to alleviate allergic reactions to antigens such as pollen or dust mites. So the diminished production of this antibody in mice lacking ICOS suggests that the ICOS–B7RP-1 pair is well worth further investigation in connection with several human immune-mediated diseases.

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Molecular electronics

Nanowires begin to shine

David H. Cobden

It is not easy finding a worthy successor to highly refined microchip technologies. But electronic devices built from molecular-scale components are fast becoming a good bet.

Unless you’ve been on a long vacation recently, you have probably heard a lot of hype about nanotechnology. Although many alternatives to existing microsystems are being considered, few would deny that there are formidable obstacles along this path. For example, the success of ‘molecular electronics’ — a potential successor to microelectronics — depends on the development of so-called bottom-up manufacturing techniques, in which molecular-scale components are chemically synthesized in large numbers and assembled into useful circuits. The difficulties are daunting but, as Duan et al. show on page 66 of this issue, real molecular-electronics devices are getting tantalizingly close. These authors have built nanometre-scale transistors and the smallest ever light-emitting diodes by exploiting two recent developments in the bottom-up approach to nanotechnology.

The first development was the perfection of techniques for growing nanometre-scale semiconductor wires. Until recently, such nanowires could be made only by depositing material on linear templates, such as natural fibres, the edges of thin films and the inside of membrane pores. The resulting wire structures are often polycrystalline and non-uniform. In contrast, the new methods require no template and produce nearly perfect single-crystal nanowires. The original idea goes back to the 1960s, when vapour-growth techniques were developed to produce crystalline semiconductors from hot gaseous reactants. It was discovered that whiskers of the semiconductor would spontaneously grow out of gold particles placed in the reaction chamber. This is because atoms in the gases, such as gallium and arsenide, dissolve in the molten metal much more easily than they attach to the surface of existing crystals. Once the metal is saturated, the atoms readily pass out of solution onto the end of a monocrystalline whisker growing out of the particle (Fig. 1a).

The latest techniques are clever variations on this theme, which use much smaller (nanometre scale) metal particles that may be sitting on a substrate, suspended in a colloidal solution, or floating in the hot gas. Duan and others in Charles Lieber’s group at Harvard have perfected the latter method to produce a wide variety of semiconductor wires, with well-controlled diameter, length and composition. Lieber’s group have even shown that chemical dopants (impurities that add or remove electrons) can be incorporated during the growth of the nanowires, thereby controlling whether the nanowires are n-doped (having extra conduction electrons) or p-doped (with some electrons removed to leave positively charged ‘holes’).

The second development concerns an old method for positioning objects such as nanowires where they are wanted. Because a nanowire is elongated, and so easily electrically polarized, it is attracted towards a high electric field, with which it lines up. So when a voltage is applied between two electrodes, a nearby nanowire suspended in liquid is drawn in to bridge the gap between them...
Duan et al. have now created a junction by placing a p-doped and an n-doped nanowire across each other (Fig. 1c). Strong competitors for the same jobs as nanowires are single-walled carbon nanotubes, which are seamless hollow cylinders rather than solid rods. Both nanowires and nanotubes can be many micrometres long, making them far easier to work with than other popular molecular tools, such as conjugated molecules and nanocrystals, which are a thousand times shorter. This is why molecular field-effect transistors have previously been made only from nanotubes, and now by Lieber’s group from nanowires. Unlike nanowires, nanotubes have completely smooth surfaces free from dangling bonds. They can be either semiconducting or highly metallic, and also have tiny diameters (down to less than 1 nm), giving them fascinating one-dimensional electronic properties. But control of the diameter, crystal-lattice orientation and doping seems to be much easier in nanowires, and their extra rigidity can make it easier to assemble them into position. Another big advantage is that semiconductors are known to emit light, something that has never been seen in carbon nanotubes.

Junctions between crossed metallic and p-doped semiconducting nanotubes have previously been shown to behave as electronic diodes — that is, current flows quickly, and to decide on the most appropriate treatment — stitches, a drug or maybe an operation? A similar problem occurs during DNA replication in living cells, when the replication machinery — consisting of enzymes called DNA polymerases — encounters a damaged DNA site. Standard DNA polymerases cannot continue to copy DNA once they reach a lesion. But every species has several polymerases that can do so, in a process called translesion synthesis. Why are there so many of these ‘translesional’ polymerases? And how does a cell decide which polymerase to use? Writing in *EMBO Journal and EMBO Reports*, Fuchs and colleagues reveal some of the answers for the bacterium *Escherichia coli*.

There are five DNA polymerases in *E. coli*. Three of these — DNA polymerases II, IV and V — are induced as part of the cellular SOS response to DNA damage, and are involved in translesion synthesis. It was already known that DNA polymerase V (pol V) allows DNA replication to continue over bulky damage such as abasic lesions (when a base is lost from one strand of DNA) or errors produced by ultraviolet light. Pol V is error-prone, and often leaves mutations in its wake within the newly synthesized strand opposite the damaged region. However, at certain types of lesion its activity is free from errors. It can also copy undamaged DNA; again, this is error-prone, although the mutations are ‘untargeted’ — they do not occur at a specific point in the DNA.

Pol IV, by contrast, is involved in getting replication started again after it stalls, and in inducing untargeted mutations when copying phage λ (ref. 7) — a small, circular DNA molecule (or plasmid) in *E. coli* that is replicated independently of the main chromo