

only 0.033 photons at a time to entice the atom to continuously, without interruption, produce squeezed light. They had to ensure that the atom was always set in place, just where they expected to find it, ready to receive photons, so they trapped and cooled it to prevent it from moving around too much. The atom was not trapped in empty space but between two mirrors, separated by about 1 millimetre (or, to use the technical jargon, it was trapped inside an optical cavity to which its coherent dipole, or polarization, would strongly couple).

This arrangement induced the necessary cooperation. Thus arranged, the atom and

cavity formed a composite quantum entity, a 'molecule' or polariton, one-half atom and the other half photon (the light inside the cavity). This atom–light molecule is highly nonlinear and can readily produce squeezing — although being restricted to a mere fraction of a photon of excitation, only by a very little. It is remarkable that, after 30 years of waiting⁶, the little has been seen. ■

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REGENERATIVE MEDICINE

Muscle for a damaged heart

When cardiac muscle cells die during a heart attack, this can lead to heart failure and even death. It now emerges that stem cells of the 'sheet' enveloping the heart can be coaxed to form new muscle after such an event. [SEE LETTER P.640](#)

VINCENT CHRISTOFFELS

The heart fails if it cannot supply sufficient blood flow to meet the body's needs. This functional deficit can be caused by the death of cardiac muscle cells due to an insufficient blood supply to the heart itself, or to defects in the inner workings of the muscle cells or in the heart as a whole. When a fish or a newt loses a piece of its heart, it can generate new muscle cells and fully restore function¹.

Mammals, however, are not so fortunate, with damage to the heart muscle resulting in tissue scarring and limited regeneration of muscle^{2,3}. On page 640 of this issue, Smart *et al.*⁴ report a promising finding: they identify resident stem cells in the epicardial layer of the mouse heart that can be persuaded to form muscle cells within the damaged heart itself.

Investigators have long pursued strategies for replacing lost heart muscle. One approach has been to isolate stem cells from bone

marrow, blood, skeletal muscle or fat tissue and to inject them into the damaged heart. But although this trick improves heart function in some cases, it cannot generate new cardiac muscle.

Another strategy, established mainly through animal studies, has been to force muscle cells to divide. Furthermore, embryonic stem cells, induced pluripotent stem cells derived from a patient's own differentiated cells, and even stem cells present in the heart itself, can all be obtained, cultured, made to multiply and steered towards specialization into cardiac muscle. Although this is a promising approach, much more knowledge is required, and many hurdles must be overcome, before it can be used to heal the human heart.

In Smart and colleagues' paper⁴, all the action happens in the heart itself, or more specifically, in the epicardium, a protective layer of connective tissue that covers the heart muscle. The epicardium forms during embryonic development from pro-epicardial cells that migrate over the heart muscle. This layer delivers signals that control the growth of both

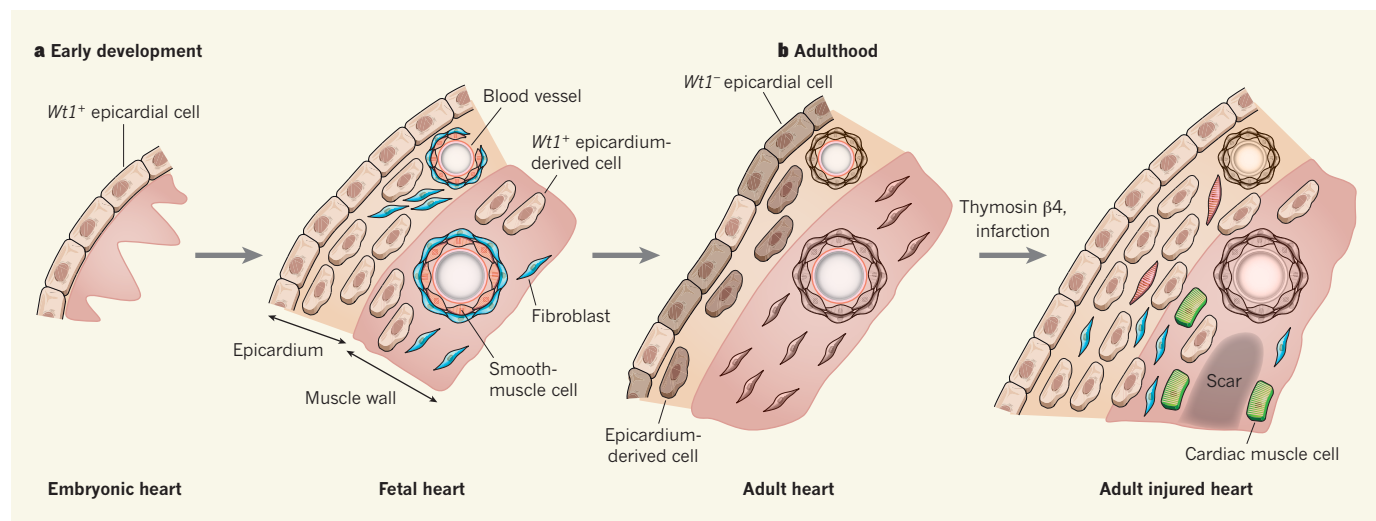


Figure 1 | Recapitulating heart development. The epicardium envelops the heart. **a**, During embryonic development, epicardial cells expressing *Wt1* (*Wt1*⁺) give rise to cells that migrate into the muscle wall to form fibroblasts and the smooth-muscle cells of the coronary vessels. Their contribution to cardiac muscle cells, or to endothelial cells of the coronary vessels, is

controversial. **b**, In the adult, few *Wt1*⁺ cells are seen in the epicardium. Smart *et al.*⁴ show that previous stimulation with thymosin β4 results in *Wt1* expression in the mouse epicardium when a heart attack is induced. Subsequently, epicardium-derived cells migrate into the muscle wall to differentiate into fibroblasts, smooth-muscle cells and cardiac muscle cells.

the fetal heart muscle and the coronary vessels that will service the heart, and generates cells that can migrate into the muscle wall (Fig. 1a). The latter are closely akin to stem cells, and give rise to the smooth-muscle cells and fibroblasts that surround the coronary vessels; they are also present in the muscle walls.

From studies in mice, it has been postulated^{5,6} that epicardium-derived cells also have the capacity to form cardiac muscle cells during development. However, this ability has not been confirmed, because the techniques used to track the fate of epicardial cells during development were not robust enough to provide unambiguous results⁷. Intriguingly, there has also been evidence^{8,9} that, after injury, the adult epicardium displays properties reminiscent of the embryonic epicardium, including growth, differentiation of smooth-muscle and fibroblast cells, and secretion of factors that stimulate blood-vessel formation, thereby improving heart function.

Smart *et al.*⁴ describe a clever approach to identifying and studying the role of epicardial cells in mice. The authors find that when a heart attack (myocardial infarction) is induced, the epicardium of the adult heart reactivates the expression of certain embryonic genes, including *Wt1*. They use genetically engineered mice in which cells that express *Wt1* are fluorescent, allowing the cells to be identified and isolated.

Previous work⁸ has shown that a peptide called thymosin β 4 stimulates the epicardium and induces the formation of coronary vessels. Smart *et al.* report that *Wt1* activation is indeed much stronger in mice that receive thymosin β 4 before the infarction. In fact, they find that stimulation with thymosin β 4 is instrumental in the differentiation of *Wt1*-expressing cells into cardiac muscle cells in the injured heart. The new muscle cells are fully functional and become readily integrated into resident muscle tissue. Moreover, pretreatment with thymosin β 4 results in better recovery of heart function after infarction, although the extent to which this can be attributed to the newly formed muscle is unclear.

Previous misinterpretation of data and failure to establish cell-lineage relationships unequivocally have made researchers in the field of cardiovascular biology somewhat sceptical of claims that stem cells or progenitor cells form heart muscle cells. Bearing this in mind, Smart *et al.* show through a series of experiments that *Wt1* fluorescence is selectively activated in the epicardium and in cells derived from it, but not, for instance, in existing muscle cells. Furthermore, they establish a lineage relationship between these precursor cells and the newly formed muscle cells. Although the authors have not identified the precise origin of the *Wt1*-fluorescent cells in the adult heart, they show evidence that the cells represent epicardium-derived progenitor cells (Fig. 1b).

Future efforts will undoubtedly focus on

translating the present work⁴ to humans and identifying compounds that optimize the relatively inefficient thymosin β 4-induced progenitor differentiation and replacement of dead heart muscle. Who knows, combined with other strategies for improving heart function and reducing scar-tissue formation, resident-cell-based therapy of the injured heart may become a genuine treatment option. ■

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MOLECULAR PHYSICS

Matter-wave interference made clear

Interference patterns are generated when light from a point source passes through two parallel slits. Electrons emitted from diatomic molecules produce analogous patterns, but these couldn't be observed directly — until now.

UWE BECKER

Writing in the *Proceedings of the National Academy of Sciences*, Canton *et al.*¹ report the direct observation of interference patterns in the spectra of electrons produced when diatomic molecules are irradiated with ultraviolet light. The patterns provide the first unambiguous proof that such molecules can behave as two-centre emitters of electron waves.

The question of whether light consists of particles or waves has been debated for centuries. Although Christiaan Huygens proposed in 1678 that light consists of waves, the photon was generally considered to be a particle until Thomas Young reported his classic double-slit experiment in 1803. Young illuminated a panel containing two parallel slits with a point source of light, and observed that the light passing through the slits formed an interference pattern — a series of light and dark bands — on a screen behind the panel. This unambiguously proved the wave character of light. Imagine the confusion, then, when Arthur Compton also unambiguously proved the particulate nature of light in 1923, in studies of the scattering of high-energy photons.

Young's and Compton's contradictory results were explained by light's particle-wave duality. This duality is at the heart of quantum mechanics, and is one of the prominent conceptual deviations of the field from classical physics. In fact, particle-wave duality is not limited to photons — it is a basic property of all quantum objects, including matter, as shown in 1961 by double-slit experiments involving electrons² rather than photons.

In these experiments, an interference pattern analogous to that produced by light was observed, proving that electrons have wave properties. Since then, double-slit experiments have shown the wave character of increasingly larger quantum objects, including fullerenes³ (buckyballs) and huge organic molecules⁴. Experiments to extend double-slit diffraction to truly macroscopic structures, including living organisms, are under way.

The basis of all double-slit experiments is the Heisenberg uncertainty principle, which constrains the precision with which the position and momentum of quantum objects can be measured. To obtain interference patterns, the momentum must be so precisely defined that the position of the quantum object is delocalized by more than the slit width; under these circumstances, the quantum objects are said to be coherent. If this delocalization is lost, decoherence occurs and the interference pattern disappears. Whether it is possible to determine through which slit an object passes without losing interference patterns is a long-standing question that continues to be the subject of research and controversy⁵.

In addition to uncertainty-based coherence, another mechanism can give rise to the same kind of phenomenon: coherent superposition of quantum objects emitted from spatially separated positions, often referred to as 'the molecular double-slit' (Fig. 1). An example of this occurs when homonuclear diatomic molecules, such as nitrogen (N_2), emit electrons in response to irradiation with light⁶ (a process known as photoelectron emission). Electrons can be emitted coherently from both of the atoms in these molecules in such a way that