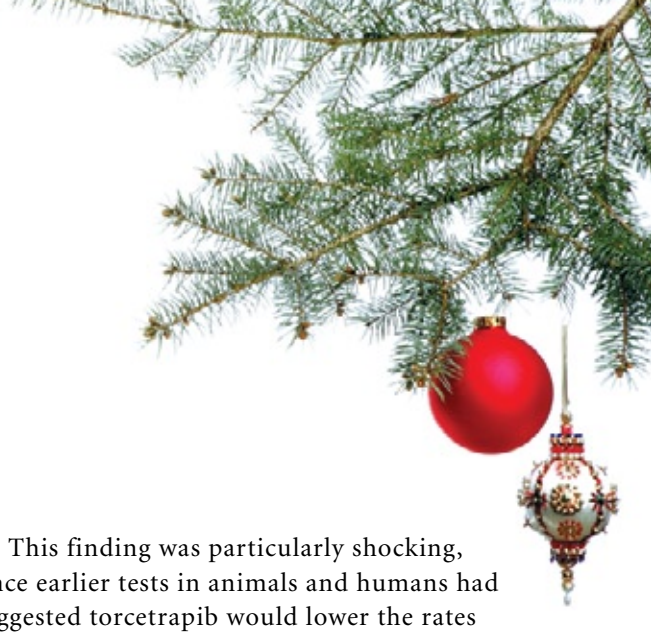

NEWS IN BRIEF

EMBRYOLOGY: THE MATTER OF THE HEART

Heart formation in the embryo requires three different cell types: endothelial, cardiac, and smooth muscle. Previously, these three cell types were thought to have different sources in the embryo. This belief has been challenged by Kenneth Chien and colleagues of the Harvard Stem Cell Research Institute in Boston. They used genetic fate-mapping studies to show that a single cell type can differentiate into cardiac, endothelial or smooth muscle cells. These cells may be the parent of a second cell type identified by Stuart Orkin of the Howard Hughes Medical Institute, also in Boston – this second cell type can differentiate into cardiac and smooth muscle (that is, two of the three types).

This finding has implications for stem cell therapies. While embryonic stem (ES) cells have been suggested as a renewable source of cardiac muscle cells, there have been problems generating sufficient numbers of homogeneous cardiac myocytes. Furthermore, there is a potential risk of teratomas with some ES cell therapies. The current study suggests that specific cardiac cell precursors could be used as an alternative.

(Source: Cell (2006) early online publication 10.1016/j.cell.2006.10.028 and 029 and highlighted in Nature (2006) 444:522-523)

CARDIAC COMPLICATIONS AND THE TROUBLES OF TORCETRAPIB

Drug company Pfizer announced on 2 December 2006 that it was cancelling all clinical trials of torcetrapib. The drug was designed to raise high-density lipoproteins (HDL) which have a protective role against ischaemic heart disease. Unfortunately, in a trial of 15,000 patients, a safety board found that more people died or suffered cardiovascular complications when taking the drug together with a cholesterol-lowering statin, compared to the control group which took the statin alone.

This finding was particularly shocking, since earlier tests in animals and humans had suggested torcetrapib would lower the rates of cardiovascular disease. The drug works by blocking a protein called cholestrol ester transferase protein (CETP), which normally transfers cholesterol from HDL to lower density lipoproteins, the latter of which are implicated in atherosclerotic plaque formation.

The reasons for the drug's adverse effects are not yet clear. Earlier trials showed a slight increase in blood pressure when patients were treated with torcetrapib, but it is unclear if all the blame can be attributed to this side effect.

Although the drug torcetrapib may have failed its trials, many scientists still support raising HDL as a pharmacological strategy. One approved drug, niacin, achieves this but can cause unpleasant side effects of heat sensation and tingling. Other drugs operating on the HDL pathway are in development.

(Source: Nature news online publication doi:10.1038/news061204-8)

MYOCARDIAL INFARCTION: REDUCING THE DOOR-TO-BALLOON TIME

In a survey of 365 acute care hospitals in the United States, Bradley et al studied the internal processes for identifying and treating patients with acute myocardial infarction with ST segment elevation (STEMI) who underwent percutaneous coronary intervention (PCI). In particular, they looked at factors influencing the door-to-balloon time, as shorter times are correlated with improved patient survival.

They found six strategies to be significantly associated with a faster door-to-balloon time:

- Having emergency medicine physicians activate the cardiac catheterisation laboratory (mean reduction of 8.2 minutes in door-to-balloon time).
- Having a single phone call to a central page operator activate the laboratory (13.8 minutes).

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- Having the emergency department (ED) activate the catheterisation laboratory while the patient is *en route* to hospital (15.4 minutes).
- Designating staff to arrive in the laboratory within 20 minutes from being paged, versus more than 30 minutes (19.3 minutes).
- Always having an attending-level cardiologist on-site (14.6 minutes).
- Providing ED and catheterisation laboratory staff with real-time data feedback on door-to-balloon time (8.6 minutes).

False alarms were quite rare in this study, with a median of two false alarms over a six month period.

These findings highlight the role of systems improvement in achieving better clinical outcomes.

(Source: NEJM (2006) 355:2308-2320)

SMARTER CHOICES IN HIV TREATMENT

The benefits of combination antiretroviral therapy for HIV have been recognised since the late 1990s. Antiretroviral therapy is not without its side effects, however. Concerns regarding these side effects have spurred studies regarding limiting exposure to antiretroviral therapy.

The SMART trial (Strategies for Management of Antiretroviral Therapy) tested intermittent retroviral therapy in patients with chronic HIV. Interruption of therapy in the drug conservation group was decided on the basis of the CD_4+T cell count.

Although a trial duration of six years was originally expected, SMART was terminated early due to a significant increase in the hazard ratios for the drug conservation group. The ratio was 2.6 for opportunistic disease or death from any cause, and 1.7 for major cardiovascular, hepatic or renal disease.

The study outcome raises many important questions. For example, how might uncontrolled HIV replication contribute to cardiovascular risk? It also emphasises the role of continuous antiretroviral therapy and the suppression of viral replication, even if the CD_4+ count has not dropped below 250 cells/mm^3.

(Source: NEJM (2006) 355:2283-2296)

QUANTUM LEAP IN SMELLY RESEARCH

Work by researchers at University College London (UCL) has supported a controversial theory about our sense of smell. Current models of smell use a "lock and key" paradigm, where receptors in the nose detect the shape of incoming molecules, triggering signals to the brain. The "lock and key" model is thought to lie behind many of the body's detection systems, including elements of the immune system and taste sensation.

In the mid-1990s, biophysicist Luca Turin proposed that smell could not be explained by this model alone. Similar-shaped molecules can smell very different: for example, the oxygen-hydrogen groups of alcohols smell like spirits, while the sulphur-hydrogen groups of thiols smell like rotten eggs. More strikingly, some molecules smell different simply because they contain different isotopes (atoms which are chemically identical but with different masses).

Turin invoked the science of quantum mechanics, theorising that the vibrations of an odour molecule can be sensed by receptors in the nose, in addition to the shape of the molecule.

The work at UCL has shown that odour identification using quantum vibrations is theoretically possible. While this is a long way from proving the theory, it opens the way to designing experiments to test the hypothesis.

(Source: Nature online news doi:10.1038/news061204-10)

SKIN TANNING WITHOUT SUNLIGHT

Many "fair-skinned" individuals have difficulty tanning their skin in response to ultraviolet (UV) light. This has been correlated with defects in the melanocortin-1 receptor (MC1R), which mediates the response to melanocyte stimulating hormone (MSH).

D'Orazio and colleagues, reporting in *Nature*, have now shown that UV light induces MSH expression in skin keratinocytes, but fails to stimulate pigmentation in the absence of the functional receptor. However, pigmentation could be rescued by topical application of the drug forskolin. Induction of pigmentation by forskolin does not require ultraviolet light. Furthermore, this pigmentation could protect against UV-induced DNA damage and cancer tumorigenesis.

These findings have implications for the synthetic skin tanning industry. They may also lead to topical sunblock lotions that induce a physiological tan with enhanced UV protection.

(Source: Nature (2006) 443:340-344) ■