

## NEWS

# French agency head resigns in cancer row

The resignation on 8 October of Christian Bréchet, director-general of the French medical research agency, INSERM, is the latest and highest-profile fallout of a bitter conflict about new technologies for screening cancer cells. The dispute pits Bréchet's wife, Patrizia Paterlini-Bréchet, an INSERM oncologist, against the current management of Metagenex, a company the couple founded in 2001. The clash has triggered lawsuits and investigations by France's top ethical and health authorities.

The pair created the firm to commercialize a filtration technique they developed called ISET (isolation by size of epithelial tumour cells). ISET can detect circulating tumour cells (CTCs) in the blood, picking out individual tumour cells from billions of blood cells (G. Vona *et al. Am. J. Pathol.* 156, 57–63; 2000). Detection of CTCs is a hot area of cancer research. Combined with research on genetic markers, it promises insight into disease progression and metastasis; it could lead to better tailored treatments or, more speculatively, earlier diagnosis.

## Promising technique

Klaus Pantel, chairman of the Institute of Tumor Biology at the University of Hamburg in Germany and an expert in CTCs, says he is a "very strong protagonist" of CTC technology: "I want it to go into the clinic." But he warns against excessive hype for any one system, saying, "it's a complex field". All of the existing systems for analysing CTCs, including contenders from Immunicon of Huntingdon Valley, Pennsylvania, and Veridex, a subsidiary of Johnson & Johnson based in New Jersey, as well as ISET, have their "pros and cons", he adds. "We mustn't push too early, and create too high expectations."

Whether high or not, Metagenex says that its legitimate expectations have been thwarted by the company's founders. On 13 July it filed a lawsuit claiming €43.2 million (US\$61.3 million) in damages against Bréchet, Paterlini-Bréchet and INSERM's technology transfer arm, INSERM Transfer. The suit claims that Bréchet and Paterlini-Bréchet "voluntarily paralysed" the company by blocking its access to exclusive licences held by INSERM, the Assistance Publique-Hôpitaux de Paris, and

the University of Paris V, promised under a rider to an agreement between the parties.

David Znaty, the company's director-general, claims that this was part of a wider campaign by Paterlini-Bréchet, in particular, to damage the company and eventually force him out. The terms of his contract require him to sell his shares to her in such circumstances. The suit claims Paterlini-Bréchet's motivation was to regain control of the company, a result that the sale of Znaty's shares would provide. On 28 September, Paterlini-Bréchet filed a countersuit against Znaty for the same sum.

Bréchet, who like his wife denies any wrong doing, says that his resignation was in part so that he can have his hands free to fight the case; he also talks of pursuing new career challenges. He vehemently denies the company's accusation that, as the chief official at INSERM, he faced a conflict of interest in decisions about licensing after disagreements arose between his wife and Metagenex's management. He is not a shareholder himself, having divested his shares when he took up his INSERM position. The shares are now held by the couple's children.

The conflict between the company's founders and managers began shortly after Znaty, an engineer and entrepreneur trained at the Massachusetts Institute of Technology, was invited by Paterlini-Bréchet to join the company in April 2006 when it was at risk of bankruptcy. But it got worse after a €2.5-million investment by AXA, a financial services company, and Banexi, a venture-capital firm, three months later. This reduced the Bréchet family's shareholding from 83% to 44%.

Paterlini-Bréchet alleges that Metagenex went on to commercialize the ISET technology without fully disclosing its experimental nature, that it broke an agreement to pursue multicentre trials to clinically validate applications for the follow-up of cancer patients, and that it illegally used the test for the commercial diagnosis of cancer. Znaty flatly rejects the allegations as a "smokescreen". His suit in turn



Patrizia Paterlini-Bréchet (above) is suing the company she and her husband (left) founded.

T. BOUÏT, E. FEFFERBERG/AFP/GETTY

accuses Paterlini-Bréchet of various breaches.

The legal battle is only one side of the dispute, which is also being fought in the arena of medical ethics and public opinion. Paterlini-Bréchet has personally solicited investigations into the Metagenex affair by the National Consultative Ethics Committee for Health and Life Sciences (CCNE) and INSERM's own ethical committee, billing the Metagenex case as being central to the ethics of developing diagnostics for severe diseases, such as cancer. Reports from both bodies backed the principle that such tests need rigorous multicentre trials to validate their sensitivity and specificity, and to assess any correlation with disease progression. As a result, the government has decided to clarify relevant legislation and to close up some loopholes.

## An ethical dilemma?

Bréchet says that the results of these investigations vindicate the July 2006 decision by the patent holders to block Metagenex's licences until it was clear that the test had been validated clinically. Given that the ethical and legislative situation has now been made clearer, he says, there should no longer be any obstacle to Metagenex having access to the patents. That is perhaps putting a brave face on the matter; Bréchet's resignation was prompted by a letter to INSERM from the research and health ministries on 21 September. The letter said that in

**"This whole story is bizarre."**

— Claude Kordon



view of their own ongoing investigations into the Metagenex affair they thought it “in the best public interest” to allow the company to exploit the patents.

Yvon Cayre, an INSERM haematologist at the Hôpital Robert Debré in Paris who replaced Paterlini-Bréchet as Metagenex’s scientific consultant in January 2007, says the ethical debate has nothing to do with the company. He says he has shifted the company away from Paterlini-Bréchet’s focus on cancer diagnostics to refinement of the machine designed to let researchers and doctors “use CTCs as a non-invasive way to survey treatments and specially targeted therapies in patients with cancer”.

Claude Kordon, a retired INSERM researcher who coordinated the CCNE panel on the Metagenex affair, says he was surprised that Paterlini-Bréchet brought the ethical issues before the committee. It is “not an ethical problem. It is about a conflict between parties who signed contracts, and did not agree on the interpretation of the contract,” says Kordon. “This whole story is bizarre.”

The court cases are not the only ongoing investigation. The IGAS, the powerful ‘police’ of the French health system, is due to release the results of yet another investigation shortly. It has sent a preliminary version to the parties to allow their comments. The draft version concludes that the reports by the two ethics committees “cannot be used to justify the refusal to sign the rider”, and that Paterlini-Bréchet began to pose ethical questions only as a result of conflict in the company. She denies this absolutely. ■

Declan Butler



#### CONFERENCE BLOG

Catch up with the meeting of the American Society for Reproductive Medicine.

<http://blogs.nature.com/news/blog>

## Particle collider is on schedule...just

Rumours of construction delays at the world’s largest particle accelerator have exaggerated the size of the problem, according to the project’s head. “There have been no show stoppers,” wrote Robert Aymar, director-general of CERN, the particle physics lab near Geneva, Switzerland, in the 8 October issue of the lab’s *CERN Bulletin*. “We can all look forward to the LHC producing its first physics in 2008.”

His reassuring announcement came after gossip on physics blogs of new problems that could set the lab’s Large Hadron Collider (LHC) even further behind its already delayed start date. But for all the reassurance, the LHC schedule remains tight, says project leader Lyn Evans. Relatively small mishaps could push the opening back beyond July 2008, when the LHC is supposed to start doing physics.

The machine is a CHF10-billion (US\$8.4-billion) accelerator designed to slam protons into each other at energies of up to 14 teraelectronvolts — 7 times the current record. Detectors will comb through the debris from the collisions for evidence of the Higgs mechanism, which is believed to endow all other particles with mass, and for signs of physics beyond the ‘standard model’, the current theoretical framework of particle physics.

LHC construction has already faced a number of setbacks and delays. For example, in March, a support holding a superconducting magnet in one section of the machine failed, leaving engineers scrambling for a fix (see *Nature* doi:10.1038/news070402-3; 2007).

The latest round of speculation was

sparked in September when engineers found that several pieces of tubing between magnets had crumpled as the machine was being prepared for servicing. Just six out of 424 sections collapsed, according to Raymond Veness, who leads the LHC’s vacuum engineering team. But the failures blocked the beam line, along which particles will eventually travel. “This is a potentially nasty problem,” Veness says.

For the time being, engineers have improvised a solution. Using compressed air, they are firing a small plastic ball equipped with a radio-transmitter through the line. By detecting where the ball comes to a halt, they have been able to spot collapsed sections in a matter of minutes. But changing the defective sections, a half-day task, adds to an already full maintenance schedule. “Everyone is stretched in all directions,” adds Veness.

“I don’t think anyone sees it as an insurmountable problem,” says Peter Limon, a high-energy physicist at Fermilab in Batavia, Illinois, the only other lab currently working with very high-energy protons. But whether the July date can be met will depend on how the magnet systems behave in additional tests this winter, says Evans. A magnet or other component failure in a section of the ring cooled to liquid helium temperatures for testing could set things back by months because of the time needed to warm the section up for repairs and cool it back down.

“The next three months are going to be pretty critical,” says Evans. “If something unforeseen comes up between now and then, it will slip. There’s no doubt.” ■

Geoff Brumfiel



The Large Hadron Collider, a 27-kilometre accelerator, is due to start operation in July 2008.

D. PARKER/SPL