



Waging war on cancer cells

A researcher at UCD may have found a useful drug for use on kidney cancers that are notoriously difficult to deal with, writes Dick Ahlstrom

Kidney cancer can be notoriously difficult to treat, given that the organ tries to filter out the chemo drugs sent in to destroy the cancer cells. A researcher at University College Dublin is working on a new type of anti-cancer drug that looks very promising for treating the disease.

Dr Matthias Tacke is an organometallic chemist, a specialist in metals that bond with carbon atoms. He now finds himself in the front line fighting against the most common form of kidney cancer, renal cell cancer, a major killer worldwide. In Ireland alone 266 new cases and 140 deaths are reported per year, says Tacke. Finding a chemotherapy drug against this form of the disease is difficult, given the organ's role as a filter.

Some drugs aren't toxic enough to kill the cancer cells, but may still trigger unwanted inflammation of the organ or even organ death, he explains. "A chemotherapy agent against renal cell cancer is not known at the moment. He believes however an organometallic agent known as titanocene dichloride has potential as an anti-cancer agent.

"It is known from the literature there is biological activity from these agents," he says, but Phase II trials in Germany in the 1990s produced poor results. "The agent wasn't optimised," he said.

He started studying the titanium-based organometallic agents about five years ago, realising that with a bit of tweaking, their biological activity could be improved. "Nobody really looked deeply into changing the chemical agent," he suggests.

"Titanocene dichloride is a cytotoxic anti-cancer drug, which means that it can selectively kill cancer cells," says Tacke, a senior lecturer in UCD's

school of chemistry and chemical biology and a researcher with the Centre for Synthesis and Chemical Biology.

Given the failure of earlier trials, he decided to test derivatives of the compound, synthesising 25 novel substances in the lab that were structurally identified and then biologically evaluated.

The two key problems in trying to optimise the agent related to solubility, how easily it distributed itself in a water-based system and permeability, its ability to pass through the cancer cell membrane and kill the cell, he explains.

He began changing the compound's "cyclopentadienyl complexes", rings formed by groups of five carbons and five hydrogens. "We had to introduce substitutes to the rings to change the solubility and uptake into the cancer cells," he says.

"Results from the *in vitro* testing of these compounds were really encouraging," he says. Tacke estimates that he still needs a 10-fold improvement in cancer cell toxicity to justify pre-clinical trials.

Even so the new agent looks very promising, he suggests. It is not very toxic for the liver and kidneys, does not interfere with blood formation and activates the immune system instead of weakening it like most other anti-cancer drugs.

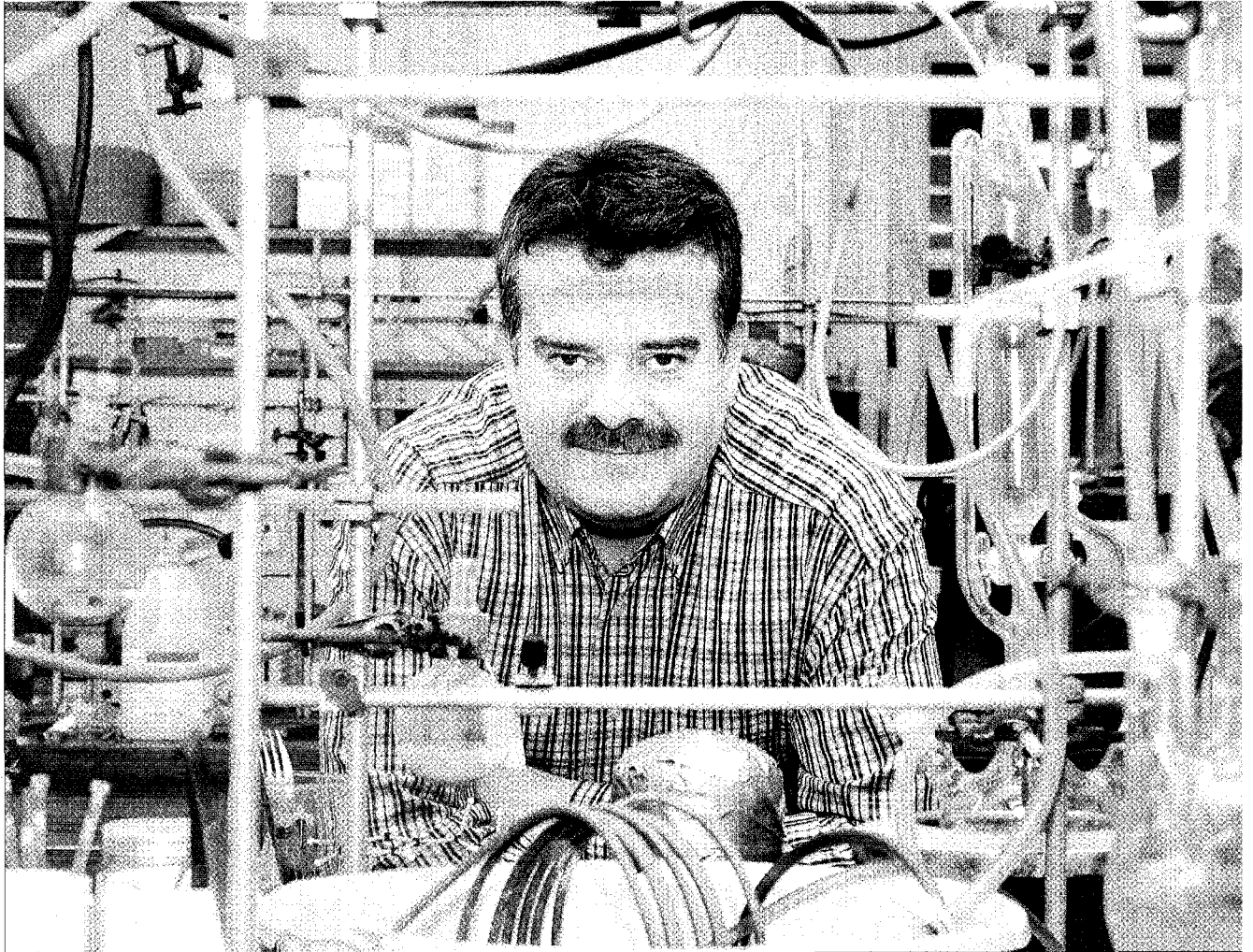
He believes this compound may be useful in the treatment of other cancers occurring in the prostate, breast, cervix and ovaries. "It is very unlikely that these compounds only target one cancer type, but renal cancer is one of the black spots," says Tacke. "There is very little you can do but take out the kidney."

His new compound could provide an answer however and he hopes it

may soon undergo a Phase I trial. "This could mean that we are on our way here in Ireland to finding an improved chemotherapy product for treating renal cell cancer."

Funding for his work has come from a number of sources including the Higher Education Authority, Science Foundation Ireland, Enterprise Ireland, the EU's Cost programme and from UCD.





The right tack: Dr Matthias Tacke in his lab at UCD Belfield.
Photograph: David Sleator