High PSA levels may show body is fighting cancer

Debbie Josefson *San Francisco*

New research shows that prostate specific antigen (PSA), a commonly used serum marker of prostate cancer, inhibits the formation of new blood vessels and consequently slows the progression of the disease (*Journal of the National Cancer Institute* 1999;91:1635-40).

The finding may explain the characteristic indolent nature of most prostate cancers and calls into question experimental vaccine strategies that involve vaccinating people against the antigen.

Angiogenesis, or the formation of new blood vessels, is essential for tumour growth and metastasis, and many cancers are thought to produce angiogenic substances to promote their own growth. Accordingly, several research groups and biotechnology firms are hunting for angiogenesis inhibitors to use as antineoplastic agents.

Although used as both a screening test for prostate cancer and as a marker of disease recurrence, PSA has not been found to promote the growth of prostate cancer cells themselves.

What, then, is the antigen doing in such cancers and why is it raised? Researchers at EntreMed, a biotechnology firm in Rockville, Maryland, evaluat-

ed the effect of PSA on endothelial cell proliferation, migration, and invasion, key steps in angiogenesis. Dr Anne Fortier and colleagues conducted in vitro cell proliferation and inhibition studies on both human and bovine endothelial cell cultures, as well as human dermal cell cultures. The cell cultures were incubated with endothelial growth factors (fibroblast growth factor 2 (FGF-2) and vascular endothelial growth factor (VEGF)) in both the presence and absence of PSA.

The antigen was found to inhibit growth factor-stimulated vascular endothelial proliferation in a dose dependent manner.

The team next conducted a "wound" assay to determine whether PSA inhibited endothelial cell migration. Cells were grown in a Petri dish until they covered it, and then an area was scraped off. The cell cultures were treated with FGF-2 and VEGF in the presence and absence of PSA, and wound recovery was assayed by counting how many cells migrated into the denuded area of the Petri dish.

The cells treated with PSA reduced endothelial cell migration.

A clear relation exists between the numbers of guns in a society and the numbers of deaths from use of firearms, according to David Meddings, an epidemiologist with the Red Cross in Geneva. Using data collected by Professor Wendy Cukier of Ryerson Polytechnic University, Toronto, Mr Meddings produced the graph above. Speaking at a recent BMA conference on wounds, weapons, and doctors, he said that the widespread availability of light weapons after wars and other conflicts leads to increased injuries from violence. Development aid might need to be spent on enforcing disarmament to improve security, he added.

Finally, the researchers tested the antigen's ability to reduce metastases. Mice were intravenously inoculated with a melanoma cell line at day 0. On day 3, experimental mice received 9 $\mu\text{mol/l}$ of PSA and continued to receive these injections once a day for the next 11 days. Control mice were injected with phosphate buffered saline solution. On day 14, the mice were killed and the number of melanoma nodules in their lungs counted. The mean number of lung metastases in the control mice was 115, compared with 70 in the PSA treated mice.

This corresponded to a reduction of metastases of 40% ($P=0.3$). The investigators concluded that the antigen had antiangiogenic and antimetastatic properties and suggested that raised levels of PSA in prostate cancer may show that the body is fighting the disease rather than acting as a bad prognostic sign.

They state that the "administration of prostate specific antigen as a drug to augment endogenous concentrations could provide a rational approach to the treatment of cancer." □

Prodi proposes food agency for the EU

Rory Watson *Brussels*

The new European Commission has placed food safety at the top of its political agenda. Within weeks of being voted into office, the commission's president, Romano Prodi, has begun canvassing the idea of establishing an independent food agency for the European Union.

He announced to MEPs in early October that the commission would present a white paper on food safety before the end of the year. This would contain an action plan setting out a

clear timetable for action over the next three years.

"Our aim is a fundamental review of food law, with all commission proposals to be put forward before the end of 2000. On this basis, we intend to establish a coherent and up to date body of food legislation by 2002," he said in a European parliament public debate on food safety.

The white paper would be accompanied by a separate document on the precautionary principle. This concept allows for provisional safety measures to be taken where scientific information is incomplete and there are still safety concerns. Although the principle is closely followed in the European Union, the United States adopts a less rigid approach,

and the differences have led to high profile transatlantic trade disputes.

The political importance being given to food safety comes against a background of intense public debate over the properties of genetically modified food and a series of scandals involving animal feed. These have ranged from the contamination of Belgian food by dioxins to the use of treated sewage sludge in feed in France, Germany, the Netherlands, and Belgium.

Mr Prodi stressed that to win back public confidence, the scientists who advise the European Commission should be seen to be totally independent from policymakers. This, he suggested, could be achieved by creating a European Food Agency—several

national governments have already taken similar steps in their own countries.

But he displayed an open mind on whether this should be based on the lines of the US Food and Drug Administration. This has substantial powers and can intervene without prior political approval. Another model could be the London based European Medicines Evaluation Agency.

The white paper will aim to establish a single, coherent body of legislation "from farm to fork," emphasising the need to tighten up the food inspection system and modernising legislation so that this is in line with advancing scientific knowledge, new production techniques, and the discovery of new health hazards. □