IN THE NEWS

UK approves screening embryos for cancer

The 'designer baby' debate has been further fuelled with the news that the UK's fertility watchdog, the Human Fertilisation and Embryology Authority (HFEA), has granted University College Hospital (UCH), London, a license to screen embryos for the gene that causes familial adenomatous polyposis (FAP). FAP is an autosomal dominant condition that predisposes to colorectal cancer.

This is not the first pre-implantation genetic diagnosis license issued in the UK, but marks a move away from screening only for childhood or untreatable disorders. Furthermore, as Paul Serhal, of UCH, remarked, "It's a shift in thinking, from trying to treat cancer to preventing cancer" (NewScientist.com, 05 November 2004).

Serhal also challenges criticisms of the license. He emphasizes that it is not a matter of 'design', but of giving nature a helping hand: "Selection does happen in nature, there's lots of embryo wastage normally". He adds, "We are not screening for physical characteristics. This is a sensible approach to preventing cancer" (NewScientist.com, 05 November 2004).

Others, such as Mohammed Tarannisi, Director of the Assisted Reproduction and Gynaecology Centre, London, have used the ruling as an opportunity to encourage public debate. He comments, "These are conditions that may or may not develop 20, 30, 40 years down the line. Is this the right thing to do?" (http://news.bbc.co.uk/, 08 November 2004).

Licenses to screen for other cancer-predisposition genes could follow. For example, the HFEA are considering an application from Tarannisi to test for *BRCA1* and *BRCA2*, genes that increase the risk of breast cancer by up to 80%.

Oliver Childs

METASTASIS

Causing cancer spread

Solid tumours look for ways to escape their confines so that they can metastasize to different parts of the body. They do this by promoting the formation of blood and lymphatic vessels through the processes of angiogenesis and lymphangiogenesis. Although the mechanisms that underlie angiogenesis are relatively well known, insight into those that govern lymphangiogenesis is limited. Now, Yihai Cao and colleagues report in *Cancer Cell* that platelet-derived growth factor (PDGF)-BB and its receptor tyrosine kinase PDGFR promote lymphangiogenesis and lymphatic metastasis.

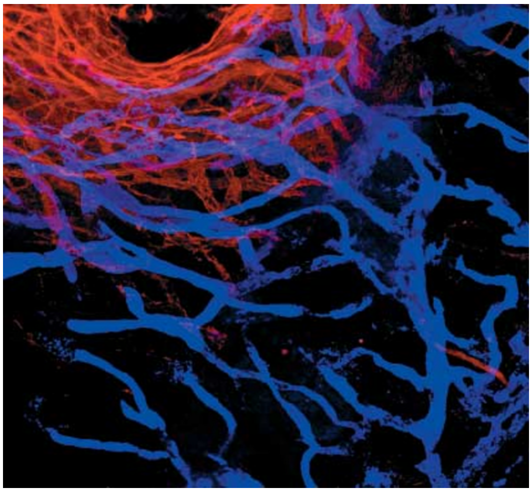

Image courtesy of Yihai Cao

The authors investigated the role of PDGF-BB in lymphangiogenesis because it was expressed to high levels in cancer tissues with high lymphatic metastatic ability. They used a mouse corneal model and lymphatic-vessel-specific markers to show that extensive lymphangiogenesis occurred after the implantation of PDGF-BB (see image, blood vessels are stained red, lymphatic vessels are stained blue). They found that PDGF-AA and PDGF-AB could also initiate lymphangiogenesis in this model, although PDGF-AA induced fewer lymphatic vessels than PDGF-AB and PDGF-BB. Unlike PDGF-AA, both PDGF-AB and PDGF-BB interact with the receptor tyrosine kinase PDGFRβ, indicating that this receptor could have an important role in transducing the signal to induce lymphangiogenesis. Studies on isolated lymphatic endothelial cells (LECs) show that intracellular pathways are also activated, as levels of phosphorylated SRC, ERK1/2 and AKT also increase following stimulation by PDGF-BB.

But is the signal direct, or does it activate the vascular endothelial growth factor (VEGF C/D)–VEGFR3 system, which is known to be involved in lymphangiogenesis? Inhibition of VEGFC/D or VEGFR3 did not prevent PDGF-BB-induced lymphangiogenesis, which indicates that the signal is not conveyed through the VEGFC/D–VEGFR3 system.

So, it seems likely that PDGF-BB acts directly on LECs, and to test this the authors isolated LECs from humans, mice and rats. They found that PDGF-BB stimulates the migration of LECs, and that this can be inhibited by the PDGFR inhibitor imatinib (Glivec), but not by VEGFC/D and VEGFR3 inhibitors.

The authors next investigated the effect of PDGF-BB expression on tumour growth. They implanted PDGF-BB-expressing tumour cells into mice and found that there was accelerated tumour growth, compared with control tumours. These tumours also had a high density of lymphatic vessels.

To further clarify the role of PDGF-BB in tumour lymphangiogenesis, the authors developed a mouse corneal tumour model. Tumour tissue was implanted into the corneal micropockets, and this resulted in tumour growth and neovascularization. PDGF-BB-expressing tumours had more extensive and disorganized blood vessels than wild-type tumours, and sprouting lymphatic vessels, which were disorganized and leaky.

So, PDGF-BB can induce tumour lymphangiogenesis, but does it also induce lymphatic metastasis? Subcutaneous T241 tumours were grown in mice, the primary tumours were then removed and the authors investigated whether metastatic lesions developed in the axillary lymph nodes. Most PDGF-BB-expressing tumour-bearing animals did develop metastatic lesions and invasive tumour cells were found in the lymph nodes: these were ~20 times larger than the lymph nodes of mice with wild-type tumours. Tumour-bearing mice were then treated with imatinib to see whether tumour burden could be decreased. They found that the weight and volume of PDGF-BB-expressing tumours was decreased following treatment with imatinib, as was the number of lymphatic vessels and blood vessels.

PDGF-BB expressed by tumour cells therefore seems to act directly on PDGFR expressed by LECs, to induce lymphangiogenesis and metastasis through the lymphatic system. The fact that the selective PDGFR inhibitor imatinib seems to be effective at reducing tumour burden and lymphatic metastasis is a promising sign for the treatment of solid tumours, and should be tested further.

Emma Greenwood
NPG Executive Editor, Oncogene

References and links

ORIGINAL RESEARCH PAPER Cao, R. *et al.* PDGF-BB induces intratumoral lymphangiogenesis and promotes lymphatic metastasis. *Cancer Cell* **6**, 333–345 (2004)