Annual Report
on
Chemokine Roles in Melanoma Metastasis

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The incidence of Malignant Melanoma is rising faster than any other cancer in the UK at present, now with over 8000 new cases and 1800 deaths per year. The cancer is caused by damage to the skin during intense sun exposure (sun burnt skin). The initial tumour is small around 1cm in diameter, but is able to spread around the body easily after it has grown only 1-2mm thick. Most commonly the first site of spread is to the regional lymph nodes. Death results from the effects caused by the spread of the disease. Unfortunately as yet no one knows how melanomas spread around the body.

One of the biggest problems with melanoma is that after surgery there is no successful chemotherapy agent or radiotherapy regime to treat the disease. Surgery is used to remove the initial tumour and is curative if the cancer has not already spread. Surgical cure rates once melanomas have spread are poor, only 20% after spread to the lymph nodes. Another problem with surgery is the disfiguring scars that patients are left with, as it is not only the tumour that needs to be removed but also large areas of bordering normal tissue.

My research has been looking into a recent theory of how malignant melanoma is hijacking the body's normal methods of transporting white cells (the bodies infection fighting cells) to and from areas of inflammation.

I have been able to show that a specific system (CCR7-CCL21) increases the movement of melanoma cells towards Lymph cells. Another system (CXCR4-CXCL12) was found abnormally in melanomas that have spread around the body prior to surgical excision. These findings are important breakthroughs within the field.

Using this knowledge I have shown experimentally that treating melanoma cells that can spread to lymph cells with a new protein capable of preventing the two systems above from working prevents the predicted migration to lymph cells.

This is a very exciting new discovery that will hopefully lead to treatments preventing cancers (not just melanoma) from spreading (and unsightly surgical scars). This could lead to patients living normal lives with cancer not dying from it.

PUBLICATIONS

Full papers

1. *__Dunn DBA__, *Pritchard-Jones R, Qiu Y, Orlando A, Rigby H, Harper S, Bates D.
Expression of $VEGF_{xxx}b$, the inhibitory isoforms of VEGF, predicts metastasis of malignant melanoma.
Accepted for publication Journal of Pathology.
*Denotes equal first authors

2. *Shields JD, *Emmett MS, *__Dunn DBA__, Joory KD, Rigby H, Mortimer PS, Orlando A, Levick JR, Bates DO,
Chemokine mediated migration of melanoma cells towards lymphatics – a mechanism contributing to metastasis.
Oncogene, early on-line publication 27/11/06, PMID 17130836.
*Denotes joint first authors

Abstracts

3. __Dunn DBA__, Pritchard-Jones R, Qui Y, Rigby H, Orlando A, Harper S, Bates D. VEGF-A isoform ratios are altered in metastasis in primary malignant melanoma. Melanoma Research. 2006 Sept: 16 Supplement 1;S50-S51.

4. Emmett M, __Dunn DBA__, Bates D. Lymphatic secreted chemokines mediate migration of melanoma cell lines.
Melanoma Research. 2006 Sept: 16 Supplement 1;S12.

5. __Dunn DBA__, Emmett MS, Orlando A, Bates DO. Directed growth of malignant melanoma towards endothelial cells in vivo.
Microcirculation, 2006 Sept: 13(6); p522.

6. __Dunn DBA__, Pritchard-Jones RO, Qui Y, Rigby H, Orlando A, Harper SJ, Bates DO. $VEGF_{xxx}b$ levels predict metastasis in melanoma.
Microcirculation, 2006 Sept: 13(6); p519.

7. Pritchard Jones RO, __Dunn DBA__, Qui Y, Rigby H, Orlando A, Harper SJ, Bates DO. Immunohistochemical expression of $VEGF_{xxx}b$ predicts metastasis in primary melanoma.
Journal of Pathology 2006 Mar: 208 S1; p32