# SCOTTISH SKIN BIOLOGY CLUB

*CHAIR: Dr Richard Weller, MD FRCP (Edin)*
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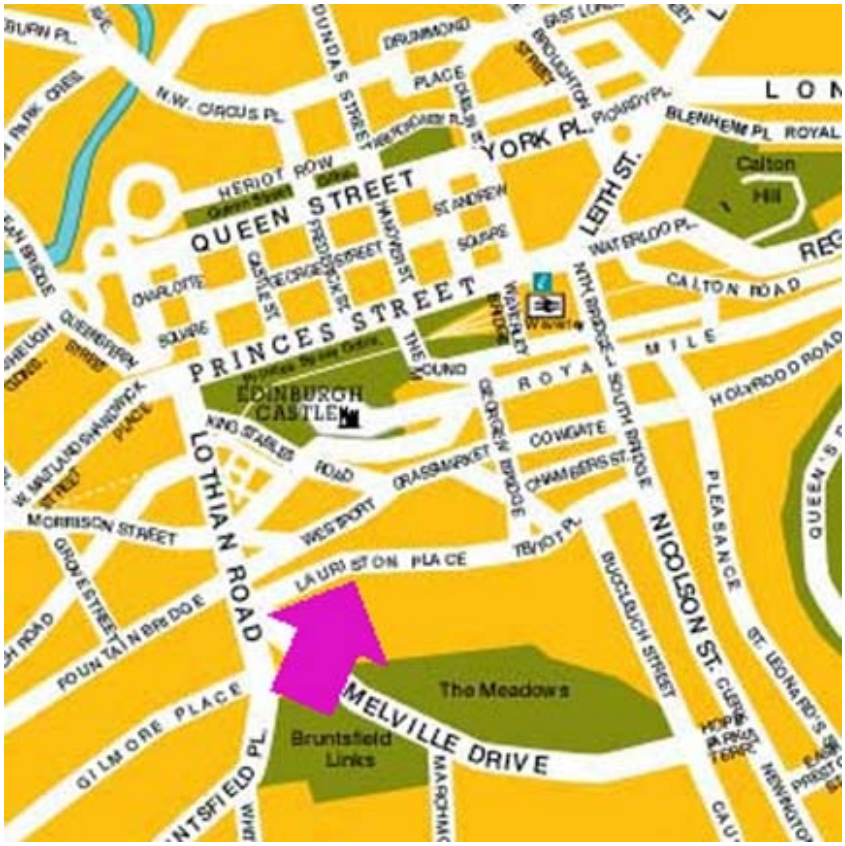
## 86th Meeting Scottish Skin Biology Club
## Thursday 17th November 2011
## Venue: Dermatology, First Floor, Lauriston Building. Lauriston Place. Edinburgh EH3 9YW
## Room Number: Seminar Room First floor (see below)

**Directions:**




Or see
http://maps.google.co.uk/maps?hl=en&tab=wl
When you enter the concourse there are 2 sets of doors, you want to take the doors on your left and come up to the first floor. You will see a cafe on the right hand side as you exit the staircase/lifts, the seminar room is just along from it on the right hand side (you will see it signposted).

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## Agenda of the 86th SSBC Business Meeting, Thursday 17th November 2011, University of Edinburgh

1. **Apologies**
   **Received to date from**

Mary Norval
Silvia Auxilia
Professor James Ferguson
Ulrike Gartner
Andrew Cassidy
Jim Ferguson
Karin Krobooth
Professor KL Thoday
Sara Brown
Silvia T Auxilia
Ulrike Gartner
Nicholas Wainwright

2. **Approval of Minutes of 85th Meeting**

3. **Finances**

   £35 requested for maintenance of web page for one more year

4. **New Members**

5. **Matters Arising: Items to discuss:** A new Web page manager required

   Improve attendance, is there a need for abstracts, nomination of invited speakers

6. **AOCB**

7. **Next meeting**

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## 8. Minutes of the 85th SSBC Business Meeting. Thursday 23rd June, Glasgow Caledonian University

9. *Apologies:*
Received from Sally Ibbotson, Irene Leigh, Keith Thoday, Silvia Auxilia, Charlotte Proby, David McEwan Jenkinson

10. *Approval of Minutes of 85th meeting*:
These were adopted. Approved by David Greenhalgh and seconded by Richard Weller.

11. *Finances:*

Income: 24 people attended £15 per head = £360
Two people still to pay
**Total: £360**

Expenditure: Lunch: £327 to GCU catering
Guest speaker Simon Wilkinson £38.70
**Total: £ £365.70**

**Meeting just broke even**

12. *New members*:

Robert Dawe proposed by Julie Woods, Seconded by June Gardner.

13. *Matters arising*
. Dr Patricia Martin (Glasgow) will take over the position for a year in the first instance.
David Greenhalgh asked for the minutes to be longer and more detailed.

14. *AOCB*:

15. *Next meeting*:
The next meeting will take place on November 17th, University of Edinburgh. Host: Dr Richard Weller.

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**Preliminary Programme for the 86th SSBC, Thursday 17th November 2011, University of Edinburgh**

10.15-10.45: Registration & Coffee

10.45-11.00 Business Meeting. Chair: Richard Weller

**11.00-12.20: Morning Session**

11.00-11.20: **MR Simons,** CM Proby, IM Leigh, AP South, C Pourreyron**,** Centre of Oncology and Molecular Medicine, Dundee
*MMPs are essential for cutaneous SCC keratinocyte invasion in organotypic culture*

11.40-12.00: **Catherine Wright** and Patricia Martin, Department of Life Sciences, Glasgow Caledonian University

In vitro skin models and the GCU Skin Tissue Bank

12.00 – 13.00 **Invited Speaker**: **Professor Jonathan Rees**, University of Edinburgh
'Attaching semantics to images'

13.00- 13.45 Lunch

**Afternoon Session:**

13.50- 14.10 **Ewan McNeil**, Martin Wear, Malcolm Walkinshaw, David Melton
MRC Institute of Genetics and Molecular Medicine, University of Edinburgh,

Screening for drugs to overcome chemoresistance in metastatic melanoma

14.10 – 14.30 **Polly Dunne**, Richard Weller, Department of Dermatology, University of Edinburgh
UVA irradiation increases forearm blood flow independently of nitric oxide synthase

14.30 Meeting closure and final comments.

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**MMPs are essential for cutaneous SCC keratinocyte invasion in organotypic culture.**
**MR Simons,** CM Proby, IM Leigh, AP South, C Pourreyron,
Centre of Oncology and Molecular Medicine, Dundee

Cutaneous squamous cell carcinoma (cSCC) affects over 20,000 people in the UK each year with a 5-year survival rate for metastatic cSCC estimated at 25-50%. Matrix metalloproteinases (MMPs) are known to be involved in the invasion of many types of cancer cells. More than 20 members of the MMP family have been identified and numerous MMP inhibitors have been used unsuccessfully in clinical trials. This may be in part because these trials recruit patients with advanced metastatic cancers whereas MMPs tend to act earlier in the tumour progression. Therefore, MMP inhibitors might prove beneficial in skin cancer therapy because skin cancers will usually be detected relatively early.

The aim of this project is to identify the MMPs specifically involved in SCC keratinocyte (SCCK) invasion. Our approach was to test inhibitors to six MMPs previously described as involved in skin cancer cell invasion (MMP1, 2, 3, 7, 9, 13). We have tested the effect of these MMP inhibitors on proliferation, migration (2-D scratch assay) and invasion (3-D organotypic culture) in 2 different human cSCC keratinocyte populations.
First we have confirmed the presence of the six MMPs in human cSCC using immunofluorescent staining.
Secondly, we have shown a decrease in migration and invasion of both SCCK populations without any effect on cell proliferation using 4 broad-spectrum MMP inhibitors.

Currently, we are using MMP-specific siRNA in scratch assay and organotypic culture to identify which of these six MMPs are essential in SCCK migration/invasion. In this work we show that members of the MMP family play an important role in cSCC invasion. We hope that the exact identification of these MMPs will lead to more targeted cSCC therapy.

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**In vitro skin models and the GCU Skin Tissue Bank**

**C.S. Wright and P.E.M. Martin, Dept Life Sciences, Glasgow Caledonian University, Glasgow, G4 0BA**

We have developed several 2D and 3D models of mouse and human skin within the Martin laboratory. These models have been used for studies into the cell-cell communication via gap junctions and connexin hemichannels of epidermal keratinocytes and dermal fibroblasts, and in particular the role of connexins in wound healing. They have also allowed us to examine many areas in skin and wound-healing biology, including proliferation and differentiation markers in the skin, genes involved in wound healing, the role of diabetes and the IGF system in wound healing, and the interaction of keratinocytes and fibroblasts with the extra-cellular matrix. The 3D skin models have been developed to be amenable to live cell staining and confocal microscopy. These models are now being expanded to use cells from diabetic human sources which will give further insight into the differences between normal and diabetic wound healing and aid the development of new wound healing therapies. Central to obtaining skin cells from diabetic tissue has been the formation of the GCU Skin Tissue Bank, which allows clinical samples to be brought in to our laboratory.

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**Polly Dunne and Richard Weller, Department of Dermatology, University of Edinburgh**

**UVA irradiation increases Forearm Blood Flow independently of endothelial Nitric Oxide Synthase:**
*Further evidence to support the existence of cutaneous stores of photo-liable nitric oxide derivatives*

**Introduction:** The beneficial effects of sun exposure on cardiovascular health may be mediated by UVA photo-decomposition of cutaneous stores of nitric oxide (NO) derivatives to vasoactive NO. We investigated whether UVA irradiation increases forearm blood flow (FBF) independently of nitric oxide synthase (NOS).

**Methods:** 12 healthy human volunteers were recruited. Tests arms were infused with intra-arterial NOS inhibitor (L-NMMA) and exposed to 20J/cm2 UVA. FBF in the infused and contralateral control arm were monitored using venous occlusion plethysmography. Venous blood samples were taken to quantify changes in plasma nitroso-species. Forearm temperature during irradiation was maintained as close as possible to pre-irradiation using a fan.

**Results:** Reported here are the first 3 volunteers' FBF data. No statistically significant changes were seen. FBF increased in the infused arm after active irradiation (average increase: 17.66±10.04%), maximal at 30 minutes post-irradiation (42.56±13.91%), with a smaller increase in the control arm (average increase: 9.07±7.86%). These changes were not seen during sham irradiation.

**Conclusions:** Our data is beginning to show that the UVA acts independently of eNOS to increase FBF locally and perhaps exerts systemic effects; however no definitive conclusions can be drawn as no results were statistically significant.

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**Screening for drugs to overcome chemoresistance in metastatic melanoma**

Ewan McNeil, Martin Wear, Malcolm Walkinshaw, David Melton
MRC Institute of Genetics and Molecular Medicine, University of Edinburgh, Western General Hospital, Edinburgh, EH4 2XU

Cutaneous melanoma is the sixth most commonly diagnosed cancer in the UK and the second most common in young people aged 15-34 (excluding non-melanoma skin cancer). Furthermore, while less common than NMSC, malignant melanoma accounts for 4% of skin cancer cases and 74% of skin cancer related deaths. Although early surgical removal of primary tumours is an effective treatment, patients that develop metastatic melanoma have a very poor prognosis (5 year survival rate is only 5%).

Elevated expression of a number of DNA repair genes has been reported in primary melanomas that subsequently metastasised when compared to non-recurrent primary tumours. In addition, patients who do not respond to chemotherapy have elevated expression of DNA repair genes. One chemotherapeutic that is effective against a range of other cancers, but not melanoma is cisplatin. Elevated levels of the DNA repair enzyme ERCC1, which is needed to remove cisplatin-induced DNA damage, has been found to be an indicator of poor prognosis in ovarian and lung cancer.

To test our hypothesis that elevated ERCC1 levels account for an increased resistance to cisplatin in melanoma, a xenograft experiment was performed. Our results show that melanoma xenografts initially responded to cisplatin treatment however resistance soon followed. Tumours deficient in ERCC1 however could be cured after only two treatments of cisplatin indicating a novel method to overcome chemoresistance in metastatic melanoma. We therefore performed a drug screen to identify small molecule inhibitors that would bind to the recombinant protein, inhibiting an in-vitro endonuclease assay. Our findings demonstrate a novel approach and class of compounds to overcome chemoresistance in malignant melanoma.