SCOTTISH SKIN BIOLOGY CLUB

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Programme for the 87th SSBC, Thursday 17th May 2012, Ninewells hospital and Medical School, Dundee

10.15-10.45: Registration & Coffee

10.45-11.00 Business Meeting. Chair: Richard Weller

Chair: Richard Weller
11.00-12.20: Morning Session

11.00-11.20: H. WANG, A.T. MCHUGH, R. MATIN, C. FLEMING, I.M. LEIGH, C.HARWOOD, T. CROOK, G. INMAN & C.PROBY
Epigenetic regulation of potential novel candidate genes in malignant melanoma

11.40-12.00: R.Berends, M.Denyer, M.Youseffi
The influence of transforming growth factor β 1, 2 and 3 on LN332 deposition and wound closure in HaCaT keratinocytes

12.00 – 13.00 **Invited Speaker**: **Professor Mike Philpott**
Centre for Cutaneous Research
Queen Mary College London

Oxidative stress as a potential mechanism for androgenetic alopecia

13.00- 13.45 Lunch

Chair: David Greenhalgh
Afternoon Session:

13.50- 14.10 C. Pourreyron, I. Leigh and A. South
Role of actin associated proteins in cutaneous SCC keratinocyte invasion**.**

14.10 – 14.30 R.M. Valentine[1,2], K. Wood[2], C.T.A. Brown[2], S.H. Ibbotson[1] and H. Moseley[1]
Monte Carlo Simulations for Optimal Light Delivery in Photodynamic Therapy

14.30 Meeting closure and final comments.

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Agenda of the 87th SSBC Business Meeting, Thursday 17th May, Ninewells Hospital and Medical School, Dundee

1. **Apologies**
   Received to date from

Mary Norval
Professor KL Thoday
Malcolm Hodgins
David McEwan Jenkinson

2. **Approval of Minutes of 86th Meeting**

3. **Finances**

4. **New Members**

5. **Matters Arising: Items to discuss:**

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

7. **AOCB**

8. **Next meeting**

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

9. **Apologies** Mary Norval, Silvia Auxillia, James Ferguson, Ulrike Gartner, Andrew Cassidy, Jim Ferguson, Karin Krobooth, Keith Thoday, Sara Brown, Nicholas Wainwright, Sheila Graham, Vikas Hedge, Colin Munro, Andy South, Charlotte Proby.

10. **Approval of Minutes of 85th Meeting**
Minutes of the 85th meeting were approved by R Weller and D Greenhalgh

11. **Finances**

Income: MD Bioscience gave a generous contribution of £100 towards lunch
18 people attended £15 per head £270
TOTAL income £370

Expenditure: £42 requested for maintenance of web page for one more year
Lunch Edinburgh catering: £169
TOTAL expenditure: £211

12. **New Members**
Claire Lorraine (GCU) was proposed by Catherine Wright and 2nd by Patricia Martin
Siti Masre was proposed by Jean and 2nd by David Greenhaugh

13. **Matters Arising: Items discussed:**
    1. New web manager required as Andrew Cassidy is stepping down.
    ACTION
    PM has approached a GCU Bio technical unit and he has agreed to undertake the house keeping of the website. This would then link through to the Martin web page for direct contacts. Key point domain registration requires a yearly charge of £35
    Thank AC for work maintaining and promptly updating the site over last few years.

    2. **Bank details to be changed** – PM transferred to to become registered signatory in place of JW. The savings account with DG as only signatory will be closed and all transferred to one account.
    ACTION: JW, PM, DG
    PM and DG went to the bank and transferred details and closed the savings account with all funds now in the one account.
    Balance: -

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3. As of September 2011 account will be charged as a business account. TO avoid this we need to look into **charitable status** and turn over.
   ACTION: RW to look into getting charitable status
   Any comment Richard?

4. **Abstracts:** Requests for abstracts discussed as some viewed this was putting people off presenting. Others felt this a good exercise for students and evidence for the PDP and preparation for larger meetings. SSBC has always been informal setting. Therefore suggestion is that:
   Abstracts will continue to be requested for talks and provided as paper copies on the day and circulated prior to the meeting. Abstracts will not be posted on the webpage. Instead a short meeting summary will be provided with meeting highlights.
   ACTION
   Meeting announced on web page and the programme will be posted, no abstracts were posted this time.

5. **Nomination of invited speakers**. Nomination of invited speakers will be requested the week following the meeting and a speaker invited.

   Prof Mike Philpott invited as speaker

6. We were fortunate to receive some funding from MS Bioscience this time. Should anyone have any links with appropriate companies who would be interested in supporting the meeting please let PM know in advance.

14. Next meeting

The date for the next meeting will be mid November 2012 and dates will be provided well in advance. Venue TBA

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Role of actin associated proteins in cutaneous SCC keratinocyte invasion.

C. Pourreyron, , I. Leigh and A. South

Division of Cancer Research, Centre For Molecular Medicine, Ninewells Hospital and Medical School

Cutaneous squamous cell carcinoma (cSCC) affects over 20,000 people in the UK each year with a 5-year survival rate for metastatic disease estimated at 25-50%. Metastasis formation requires tumour cells to increase their potential of migration. Cell motility is critically dependant on the dynamic organisation of actin cytoskeleton to generate protrusive activity at the front of the cells and to induce contraction at the sides and rear. Such dynamism is regulated by actin-binding or actin-associated proteins.

We previously compared cSCC with normal skin using mRNA expression profiling and identified 4 genes involved in the regulation of the actin cytoskeleton dynamism, namely *FLRT3*, *FLNB*, *EPB41L3* and *PALLD*, were overexpressed in cSCC *in vivo* but were downregulated *in vitro* compared to normal. These data implicate that they are part of a small group of genes we have found to be entirely context dependent in their expression and specifically expressed in cSCC when compared to the similar condition psoriasis. Context dependent tumour specific expression suggests that they may be important in metastatic progression. Analysis of the expression of 2 of these genes in a prostate cancer dataset (GDS 2546) supports this hypothesis.

The aim of our study is to analyse the role of protein products of these genes, namely FLRT3, FLNB, EPB41L3 and Palladin in cSCC keratinocyte migration/invasion. First, we show by Western-blotting that the level of the 4 proteins was lower (FLNB, Palladin and FLRT3) or not detectable (EPB41L3) in 3 SCC keratinocyte populations in culture compared to 3 populations of normal human keratinocyte NHK, confirming the mRNA profiling data. We then used siRNA to knockdown each gene and observe migration and invasion in scratch-wound and organotypic culture assays and show that FLNB, Palladin and FLRT3 are involved in migration/invasion of cSCC keratinocytes. Our data show that the mRNA level of FLNB, Palladin and FLRT3 is increased in cSCC, that they play an important role in cSCC dissemination and could therefore provide new targets for cancer therapies.

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H. WANG, A.T. MCHUGH, R. MATIN, C. FLEMING, I.M. LEIGH, C.HARWOOD, T. CROOK, G. INMAN & C.PROBY
Skin tumor laboratory, Level 7 CRC building, Ninewells hospital, Medical school, University of Dundee, Dundee.

DD1 9SY

Background: Cutaneous melanoma (CM) accounts for 75% of skin cancer-related deaths in the UK. Targeted treatments for metastatic melanoma are effective but only extend overall survival by a few months. Improved molecular profiling and early detection of metastatic melanoma might have significant impact on overall survival. Current biomarkers of metastatic disease (LDH, S100) are insensitive and of limited clinical usefulness. This study aims to develop a portfolio of biomarkers of diagnostic and prognostic usefulness that will facilitate early treatment of metastatic disease. Cancer-associated gene promoter methylation is recognized as an important mechanism in tumour progression. Identification of cancer-specific methylation markers in melanoma patients' tissues and blood may help us to better understand the molecular mechanisms of melanoma, to develop prognostic biomarkers and to develop new targeted therapies.
Objectives: Identify candidate genes that are deregulated by DNA methylation in melanoma that may have clinical significance both as potential biomarkers and as potential therapeutic targets.
Methods: Seventeen melanoma cell lines, 2 normal melanocyte cultures, 122 melanoma tissue samples, 10 benign naevi, and 33 serum samples from patients with melanomas have been used. Methylation specific PCR and pyrosequencing were performed for methylation analysis. Quantitative PCR was used to evaluate mRNA expression of candidate genes.
Results: We have identified TFPI2 as promising candidates for serum epigenetics with apparent correlation between detectable methylated DNA in patient's blood and poor outcome in terms of metastatic melanoma. TFPI2 showed an intermediate frequency of methylation in melanoma cell lines (65%) and tissue samples (40%), and increased TFPI2 methylation level correlated with melanoma progression. TFPI2 methylation in serum samples correlated with metastasis, regardless of any other prognostic markers for patient outcome. In contrast, NT5E methylation correlated with melanoma with better prognosis, with NT5E more likely to be methylated in non-relapsing and non-visceral metastatic melanomas, but not in visceral metastatic melanoma. These data support a role for epigenetic silencing of TFPI2 and NT5E in melanoma. Detection of promoter hypermethylated TFPI2 in patient serum samples suggests "serum epigenetics" could provide novel biomarkers with clinical utility for early detection of metastasis.

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R.Berends, M.Denyer, M.Youseffi, Department of Life Sciences, University of Bradford

The influence of transforming growth factor β 1, 2 and 3 on LN332 deposition and wound closure in HaCaT keratinocytes

Transforming growth factor β (TGFβ) isoforms have been implicated in the scarless healing seen in the fetus. Addition of exogenous TGFβ 3 and the neutralisation of TGFβ 1 and 2 has been shown to reduce scar formation in adult wounds. Although known to be important the mechanisms by which these growth factors mediate their effects have yet to be fully elucidated. There has also been little focus on comparing the effects of TGFβ 1, 2 and 3 and more specifically determining how these different isoforms affect keratinocyte cell behaviour during reepithelialisation. We have shown that TGFβ isoforms are different in their effects on keratinocyte cell behaviour in culture. Our results found that TGFβ 2 and 3 increase the rate of wound closure in an *in vitro* model wound and enhanced laminin 332 deposition in HaCaT cell monolayers. The addition of TGFβ 1 to HaCaT cells in culture also increased laminin deposition however it had little effect on the rate of wound repair when compared to controls. We also show the differential effects of TGFβ isoforms on integrin subunit expression, highlighting the possibility that integrins together with laminin 332 are rate limiting factors in the closure of monolayer wounds.

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Monte Carlo Simulations for Optimal Light Delivery in Photodynamic Therapy

R.M. Valentine[1,2], K. Wood[2], C.T.A. Brown[2], S.H. Ibbotson[1] and H. Moseley[1]

[1] Photobiology Unit, University of Dundee, Ninewells Hospital & Medical School, Dundee, DD1 9SY, Scotland

[2] School of Physics & Astronomy, University of St Andrews, North Haugh, St Andrews, KY16 9SS, Scotland

Background:
The choice of light source is important for the efficacy of photodynamic therapy (PDT) of nonmelanoma skin cancer (NMSC). As light is an important component of PDT, the characteristics of any light source will have an impact on PDT dosimetry.

Objective:
We simulated the photodynamic dose (PDD) deposited to a tumour during PDT using theoretical radiation transfer simulations performed via our 3D Monte Carlo Radiation Transfer (MCRT) model for a range of light sources with light doses up to 75 J/cm^2.

Method:
The PDD delivered following superficial irradiation from a) non-laser light sources, b) monochromatic light, c) alternate beam diameters and d) re-positioning of the tumour within the tissue was computed.

Results:

a) The administered PDD to the tumour by the Aktilite was 2.6 times greater than the Waldmann 1200 at a tumour depth of 2 mm. b) Tumour necrosis occurred at a depth of 2.2 mm and increased to 3.8 mm for wavelengths 405 nm and 630 nm, respectively. c) Increasing the beam diameter from 10 to 50 mm had very little effect on depth of necrosis. d) As expected, necrosis depths were reduced when the tumour was re-positioned deeper into the tissue.

Conclusion:
These MCRT simulations show clearly the importance of choosing the correct light source to ensure optimal light delivery to achieve tumour necrosis. Our model is a useful tool for evaluating the significance of the source characteristics.

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