

Connective Issues

BSMB Newsletter

British Society for Matrix Biology

Committee: Prof. Tim Hardingham (Chairman), Dr. Rose Maciewicz (Secretary), Dr. Jay Dudhia (Treasurer),
Dr. Jo Lewthwaite, Dr. Louise McKenna, Dr. Garry Rucklidge, Dr. Ian Clark, Dr. Anthony Day, Dr. Alison Reith, Dr. Norman McKie

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Contents

- 2 Editorial *by Rose Maciewicz*
- 2 Current BSMB committee *contact information*
- 2 Call for nominations *BCTS Secretary and one new committee member!*
- 2 The BSMB Website: Facts and Figures *by Jay Dudhia*

Awards and

Competitions

- 3 Bursaries for Spring 2000 BSMB meeting in London *applications by February 14th 2000*
- 3 Bursaries for XVIIth FECTS meeting in Greece *applications by February 14th 2000*
- 3 BSMB Young Investigator Award *applications by December 31st 1999*
- 3 IJEP poster competition *win a prize for your poster at the London meeting*

Forthcoming

meetings

- 4 Autumn 2000 BSMB meeting in Newcastle-upon-Tyne *preliminary information*
- 4 FECTS XVIIth in Greece *preliminary programme*
- 5 Calcified Tissues meeting in Finland May 6-10th 2000 *call for abstracts*
- 6 50th Anniversary meeting of the Bone and Tooth Society in Cambridge July 10th-12th 2000.

Job

Advert

- 6 Lecturer in Biophysics University Exeter *applications by December 15th 1999*
- 6 Post-Doctoral Research Position at the University of Manchester

Reports of previous

meeting

- 6 Report of Autumn 1999 BSMB meeting in Aberdeen

Appended

Programme for Spring BSMB meeting London, April 3rd-4th 2000 *Register now*
Notes, Directions and Registration form for London 2000 BSMB meeting
Bursary application form for BSMB/FECTS meeting
Membership Application Form

Editorial by Rose Maciewicz

Welcome to the 55th edition of Connective Issues. You will find in this newsletter all the information (Programme, Registration form, Bursary application form and Travel directions) pertaining to the Spring BSMB meeting in London. This meeting will take place on Monday and Tuesday, 3rd and 4th April 2000. Please note that the registration, abstract and bursary deadline is Monday February 14th 2000. Please note that the deadline for applying for the **BSMB Young Investigator Award** has been extended to the end of December 1999. So if you are interested please find the details within this newsletter.

Many thanks to Dr Garry Rucklidge and Professor Stuart Ralston (from the Bone and Tooth Society) for organising a tremendous meeting in Aberdeen this past September. For those of you who could not attend, a report of this meeting can be found in this newsletter. The Secretary would like to thank Jim Huggett and Yee-Wah Lee for writing this and to Dr. Allison Reith for her editorial contribution. The BSMB Committee is pleased to announce that 4 Bursaries were awarded for this meeting. The recipients were: Sarah Howat and Yee-Wah Lee (The Royal Veterinary College London); Jim Huggett and Sam Webster (University of Wales, Cardiff).

Please make a note in you diaries of the Autumn 2000 BSMB meeting, which will take place in Newcastle-upon-Tyne on September 4th - 5th 2000. Read on for further information.

Please note the call for nominations for BSMB Secretary and one Committee member. If you are interested in working for the Society please apply.

Also please note the call for applications bursaries to attend the XVIIth FECTS meeting in Greece. The deadline is February 14th 2000.

Finally don't forget to check our website which can be accessed via <http://www.bsmb.ac.uk>. Between Newsletters all new information received by the Society can be found at the site. More information about the site can be found later in the newsletter.

Current BSMB Committee

Officers:

Chairman, Prof. Tim Hardingham (University of Manchester; tharding@fs1.scg.man.ac.uk)
Honorary Treasurer, Dr. Jay Dudhia (The Royal Veterinary College, London; jdudhia@rvc.ac.uk)
Honorary Secretary Dr. Rose Maciewicz (AstraZeneca Pharmaceuticals; rose.maciewicz@astrazeneca.com)

Elected Members:

Dr. Garry Rucklidge (Rowett Research Institute, Aberdeen; gjr@rri.sari.ac.uk)

Connective Issues No. 55 November 1999

Dr. Jo Lewthwaite (Eastman Dental Institute, UC J.Lewthwaite@eastman.ucl.ac.uk)

Dr. Ian Clark (University of East Anglia i.clark@uea.ac.uk)

Dr. Anthony Day (University of Oxford ajday@bioch.ox.ac.uk)

Dr. Alison Reith (University of Bergen, Norway alison.reith@pki.uib.no)

Dr. Norman McKie (Medical School, University of Newcastle-upon-Tyne; nmckie@hgmp.mrc.ac.uk)

Ex-officio Member:

Dr. Louise McKenna (University Erlangen, Germany louise.mckenna@patho.med.uni-erlangen.de)

Call for nominations for BSMB Secretary and Committee member

The Secretary (RAM) and one committee member (GR) are due to retire in Spring 2000. We are therefore looking for nominations for the positions. If you know of anyone who would like to be considered please write to the Secretary. Please note that this nomination must be seconded by another BSMB member. **Nominations must be received no later than January 31st 2000.** A postal ballot will be held prior to the AGM. If insufficient nominees are found from the general members the Committee will nominate as they deem appropriate. As regards the position of Secretary the Committee have nominated the current Secretary to stand for another 3 year term of office. She has agreed to this nomination.

The BSMB Website: Facts and Figures by Jay Dudhia

The BSMB website seems to be well received judging by the level of activity monitored over the past 8 months. The average number of 'hits' was about 20 per day, which in internet language translates to an average of about 6 'users' per day. The meetings and jobs pages were the most popular. The highest number of users recorded over this period was 68 in one day. The site also received visits from abroad, including the US. Curiously, another day of intense activity was recorded on Halloween weekend in October, when 51 users were recorded! Can anyone out there enlighten us on what the connection between Halloween and the BSMB might be? (Editors note - suggestions via a postcard to the Treasurer!) Anyone who may have concerns about the data collection please be assured that the monitoring did not record the identity of individual users. Only the connecting server, country location and pages visited were recorded.

As I have not received any comments from the membership to the contrary, I guess everyone fin

the contents useful and of interest. If you have suggestions which would improve the website or would like to see other information included please do let me know.

BSMB Bursaries for London BSMB meeting and FECTS.

We are offering BSMB bursaries to attend the Spring 2000 BSMB meeting in London as well as to the XVIIth FECTS meeting to be held in Greece in the Summer. Young members of the Society are encouraged to apply for bursaries (up to a maximum of £100 for the BSMB and £500 for the FECTS) to assist with attending these meetings. An application form is included with this newsletter. Bursaries will only be considered if they are submitted on a current BSMB Bursary application form. Applications should be sent to the Secretary and not to the meeting organiser. **The application should be accompanied by a copy of the abstract to be presented at the meeting and a one page curriculum vitae.**

The deadline for receipt of bursaries to attend either meeting is Monday February 14th 2000. The applications will be reviewed rapidly by the Committee and applicants will be informed of the outcome on or around 15th March 1999.

Criteria for Bursaries

1. Applicants should have been members of the Society for at least 1 full calendar year.
2. Applicants should be submitting an abstract and presenting a poster for the meeting to be attended.
3. Applicants should be at an early stage of their career (i.e. < 5 years from award of PhD) and unlikely to have access to travel funds. Most often where support for an overseas meeting is given this is the first such meeting they attend. For this reason emphasis is always given to young researchers who are generally in short term contract positions, i.e. mainly graduate students and occasionally early Post-docs. In addition the Committee will also take into account whether the applicant has received support from the BSMB within the last two years.
4. The work described in the abstract must be novel and likely to be of a quality that would reflect well as a BSMB supported contribution.

BSMB Young Investigator Award

This award aims to recognise the contribution made by younger researchers to the field of matrix biology. The recipient will be invited to give a special seminar at the spring meeting of the Society and will be awarded a one hundred pound honorarium and presented with a certificate. The cost of attending the meeting will be met by the Society including registration, reasonable travel

Connective Issues No. 55 November 1999 costs, accommodation and meals. The new closing date for receipt of applications is the end of t Millennium, 31st December 1999 and should be sent to BSMB secretary.

Guidelines for applicants for BSMB Young Investigator Award

1. The applicant should be 35 years or under on the date of the presentation of the award.
2. The applicant should have been a member of the Society for at least 12 calendar months.
3. The applicant should apply in writing to the secretary of the Society providing a letter (1 side of A4) stating why they should be considered for the award; a 1 page CV; and a supporting letter from their head of department. The applicant should send one copy of the publication that they think definitively describes the research they have carried out in the field of matrix biology.
4. A committee of four (BSMB Chairman, BSMB Secretary and 2 co-opted BSMB members) will review the application and decide on a winner.

Support of IJEP Poster Competition

Win a prize for your poster

Will you be presenting a poster at the Spring BSMB meeting? It took hours to put together, you're presenting some good work and you are pleased with how your poster looks. THEN WHY NOT ENTER OUR NEXT POSTER COMPETITION AND WIN ONE HUNDRED POUNDS? The poster competition which is sponsored by the International Journal of Experimental Pathology, is designed to reward Post-graduate students and Post-docs, who put a lot of time and effort into making an excellent collection of posters at the BCTS meetings each year. If you are a Post-graduate student or Post-doc please enter the competition. You have nothing to lose and you may just win one hundred pounds. The next competition will be held at the Spring BCTS meeting in London in April 2000. If you are a supervisor, encourage your Post-graduate students and Post-docs to enter the competition. Not only will they receive some money, but more importantly it will draw attention to their work and the receipt of the reward might be a useful addition to their CV!

IJEP Poster Competition Rules:

1. It will be held once per year and at a BSMB meeting selected by the Committee.
2. The competition will be publicised well in advance.
3. The competition is open to PhD students and recent qualified post-docs (up to 2 years), who must indicate prior to the meeting their intention to enter the competition.
4. Up to 3 scholarships of £100 each will be awarded dependent on the quality of the presentations. If the quality is low, no awards will be made.
5. The posters will be judged by at least 3 Committee members who will view the posters as well as discuss the work with the poster presenter. Criteria for judging the posters will be: clarity of the presented poster; scientific content; and scientific understanding of the work.
6. The award to be used by the recipient as they choose.

7. The recipients of the award to be notified at the meeting and also to be listed in the next newsletter issue.

Autumn 2000 BSMB meeting in Newcastle-upon-Tyne

The Autumn 2000 meeting of the BSMB will provisionally take place on the 4th and 5th September 2000. The venue for this meeting will be the University of Newcastle-upon-Tyne and will be organised by Dr N.McKie and Dr M.A. Birch [Telephone 0191-222-5902; Fax 0191-2225455 Medical School, Framlington Place, Newcastle NE2 4HH; e-mail nmckie@hgmp.mrc.ac.uk]. Talks are scheduled to take place in the Medical School Lecture theatres at the University and are an approximately 10 minute walk from the Leazes Halls of residence where the main accommodation will be located.

The topic for this meeting is '**Cell-Cell and Cell Matrix Interactions in Connective Tissue Development**'. It is envisaged that there will be three main sections to the meeting dealing with the three main connective tissues: cartilage; bone; and muscle; and will focus on proteins that modulate cellular behaviour and matrix turnover.

We will look forward to welcoming everyone to Newcastle and will not be placing any restrictions on those who wish to visit the city's famous Quayside where there is entertainment of a quality rarely seen outside London. Newcastle is readily accessible from all major UK train stations directly and by air from several UK airports.

XVIIth FECTS

The XVIIth Meeting of the Federation of the European Connective Tissue Societies (FECTS) will be held in Patras Greece on July 1-5, 2000. Further information can be found on their website: <http://www.chemistry.upatras.gr/fects/Index.html>. The preliminary programme follows.

The Chairman of this meeting is C.Tsiganos, +30-61-997154; constiganos@chemistry.upatras.gr. The Scientific Secretary is N. Karamanos (+30-61-997153; N.K.Karamanos@upatras.gr). Correspondence concerning the meeting should be addressed the Organising Secretariat: Erasmus Horison Ltd, FECTS erasmhor@athena.compulink.gr

Preliminary Scientific Programme

July 1 Saturday

17.00 Opening of registration
20.30 Honorary lecture: **H. Arweiler** (France)
"Ethics and Science"

21.30 Welcome reception

July 2 Sunday

8.30-12.20 Five 40 min lectures with 30min coffee break

Proteoglycans, collagens and matrix protein
T. E. Hardingham (UK) Supramolecular structure of proteoglycan aggregates

J. Engel (CH) Collagen and coiled-coil domains matrix proteins mediate oligomerisation of functional domains

M. Paulsson (Germany) The matrilins: a novel family of extracellular adaptor proteins

J. T. Gallagher (UK) Glycosaminoglycan sequences - functional domains

L.-A. Fransson (Sweden) Biosynthesis of decorin and glypican

12.20-14.00 **Lunch**

14.00-16.00 **Posters**

16.00-18.30 **Workshops**

July 3 Monday

8.30-13.00 Six 40 min lectures with coffee break

Cell-matrix interactions, Development aspects

N. Perrimon (USA) Genetic analyses cytoarchitecture in Drosophila

G. David (Belgium) Cell surface heparan sulphate proteoglycans

K. von der Mark (Germany) Mechanism of alpha-beta1-integrin mediated signalling in cell migration and adhesion in laminin

H. Rauvala (Finland) Heparin-binding proteins H-GAM and amphoterin/HMG1 in motile responses cells

R. Perris (Italy) title to be announced

M. Maragoudakis (Greece) Activation angiogenesis by thrombin

13.00-14.00 **Lunch**

Free Afternoon, organised excursions

July 4 Tuesday

8.30 - 11.55 Five 35 min lectures with coffee break

Matrix genes, Connective tissue disorders

D. Heinegard (Sweden) Connective tissue genes encoding proteins with roles in tissue building and remodeling

R. Hata (Japan) Connective tissue gene regulatory splice variants, tissue - specific expression

L. Peltonen (Finland) Genetics of osteoarthritis

T. Krieg (Germany) Fibroblast - collagen interactions in wound healing and fibrosis

R. Fessler (Sweden) to be confirmed

11.55-13.00 **Business meeting**

13.00-14.00 **Lunch**

14.00-16.00 **Posters**

16.00-18.30 **Workshops**

21.00 - **FECTS Dinner**

July 5 Wednesday

8.30-12.30 Five 40 min lectures with coffee break

Connective tissue remodeling, Biomechanics and biomaterials

B. Caterson (UK) Mechanisms involved in cartilage proteoglycan catabolism

H. Nagase (UK) to be confirmed

J. C. Monboisse (France) Control of tumor invasion by domains of extracellular matrix

E. B. Hunziker (CH) Biomechanics of intercellular substance and cartilage tissues

A. Ratcliffe (USA) Cell - scaffold based tissue engineering for wound repair and replacement of mechanically functional tissues

13.00-14.00 **Lunch**

14.00-16.00 **Posters**

16.00-18.30 **Workshops**

We anticipate to organise 15-20 workshops to cover specific topics (see below). The final number will be dependent upon the abstracts received.

Workshop areas

1. Structure-function relationship
2. Novel analyses of matrix macromolecules
3. Biosynthesis, post-translational modifications and catabolism
4. Gene expression, regulation, post transcriptional modifications
5. Genetic manipulations
6. Cell-cell and cell-matrix interactions
7. Receptor, signal transduction
8. Cytokines, growth factors and ECM
9. Development
10. ECM and cancers
11. Tissue regeneration and repair
12. Ageing, apoptosis
13. Angiogenesis and neovascularisation
14. Biomineralisation
15. Genetic, autoimmune and degenerative diseases
16. Basement membranes: structure, function and pathobiology
17. Modified biopolymers and artificial tissues
18. Tissue properties and response to mechanical load

27th European Symposium on Calcified Tissues

The 27th European symposium on Calcified Tissues will be held in Tampere Finland on 6th -10th of May 2000. The Congress is being organised by the European Calcified Tissue Society and hosted by the Finnish Bone Society. The 2000 meeting will feature a special emphasis on basic and clinical advances relevant to skeletal health. Themes of Osteoblasts, Osteoclasts, Bone Matrix, Signal Transduction, Mechanotransduction, Growth Factors and Cytokines, Calcitropic Hormones, Estrogens and SERMS, Diagnostics, Osteoporosis (Epidemiology, Pathophysiology, Treatment), Metabolic Bone Disease, Cancer and Bone, and

Connective Issues No. 55 November 1999

Genetics of Skeletal Disorders will be discussed. Further information about the meeting can be found on www.congcreator.com/ects-2000

fax: +358 9 4542 1930

e-mail: ects2000@congcreator.com

Please note that the abstract deadline is 1. December 1999 for a paper version and 3. December via the internet.

50th Anniversary meeting of the Bone and Tooth Society

The 50th anniversary meeting of the Bone and Tooth Society will be held at Churchill College Cambridge Monday 10th to Wednesday 12th July 2000. Guest speakers include: Professor Jack Mar (Melbourne); Professor Barbara Maw (Manchester); Professor Gregory Mundy (Texas) and Professor Michael Parfitt (Arkansas). The deadline for abstracts is 1st March 2000. Further information can be obtained from:

Ms Janet Crompton, Conference Organiser, The C White Hart, North Nibley, Dursley, Gloucestershire GL11 6DA

tel:01453 549929

fax:01453 548919

email janetcrompton@compuserve.com

LECTURER IN BIOPHYSICS University of Exeter

This position is in support of the recent appointment of Professor P Winlove and the establishment of Biophysics / Biomedical research group. The group is concerned with the physical properties and physiological functions of the extracellular matrix and its constituent macromolecules, the biophysical properties, the cytoskeleton and of cell-matrix interactions and microvascular physiology through the application of physical techniques such as microelectrodes, MRI, NIR and surface plasmon resonance and fluorescence microscopy. **Salary within the Lecturer A grade: £17,238 pa £22,579 pa.** Further information from the Personnel Division, University of Exeter, Exeter EX4 4QJ; Fax: (01392) 263122
e.mail: V.P.Fieldhouse@exeter.ac.uk
quoting ref. 1118
Closing date: 15th December 1999.

Post-Doctoral Research Position University of Manchester

Post-Doctoral Research position within the group of Professor Tim Hardingham (*Wellcome Trust Centre for Cell-Matrix Research; School of Biological Sciences, University of Manchester*) to work on matrix signals regulating transcription factor control of phenotype in chondrocytes and early events in cartilage matrix assembly. Experience in mat

biochemistry, cell transfection and molecular biology would be an advantage. The Wellcome Trust Centre is part of a highly rated grade 5 Biochemistry Division and has an excellent research environment and technical facilities. The appointment funded by The Wellcome Trust is available immediately for 1 year with the possibility of a long extension. For further details contact Tim Hardingham - 0161-275-5511 Tim.E.Hardingham@man.ac.uk

Report on the BSMB Meeting University of Aberdeen 6th - 7th September 1999 by Jim Huggett and Yee-Wah Lee (edited by Dr. Alison Reith)

Prof. J. Risteli (University of Oulu, Finland) opened the meeting with an insight into the use of collagen type I as an indicator of bone metabolism. Type I collagen is synthesised as a pro-collagen which has large additional domains at both ends: the carboxy PICP and amino terminal PINP. During collagen biosynthesis these domains are cleaved and released into the serum. In growing individuals the serum concentration of these proteins, which are degraded at differing rates, reflect the bone growth rate. The ratio of the two peptides alters during certain pathologies, which may relate to the presence of an α_1 -homotrimer. The use of immunoassays for different cross-linked telopeptides to measure collagen degradation was discussed. There are a number of potential mixtures of cross-linked N and C telopeptides and different assays have been developed to distinguish between Cathepsin K and metalloproteinase mediated degradation.

Prof. Paul Bornstein (University of Washington, Seattle) described the use of mouse transgenics to investigate two areas of matrix biology. He discussed the role of the transcription binding regions that occur in the first intron of the *Col1a1* gene. The targeted disruption of the thrombospondin 2 gene (TSP2) an ECM protein, has a function which is poorly understood. Loss of the TSP2 gene leads to a complex phenotype with multiple matrix pathology. TSP2 was hypothesised to influence the growth of nascent collagen fibrils through interactions with fibroblast cell receptors.

Dr Nick Bishop (University of Sheffield) gave a detailed account of the types of osteogenesis imperfecta that have been reported to date. Treatment of these diseases was limited to surgical correction of skeletal abnormalities: The recently discovered bisphosphonates has advanced treatment of these conditions tremendously. Pamidronate has both reduced pain and increased mobility, with remodelling actually repairing previously damaged bone. Work is currently focused on optimising the correct doses of these drugs for clinical use.

M.L. Stewart (University of East Anglia) described the ability of MMP 2 (Gelatinase A) to degrade triple helical type I collagen. A number of recombinant MMP2 molecules, some of which had domains removed, were expressed to further characterise this molecule. MMP2, like MMP1, uses a haemopexin-like domain to interact with collagen and can catalyse the degradation of denatured collagen by interacting with the fibronectin type II-like domain.

Richard Aspden (University of Aberdeen) spoke about work that compared the microscopic appearance and mineral content of femoral heads from patients with osteoporosis (OP) and osteoarthritis (OA). Both diseases result in less bone stiffness, density and mineral content. OP, however, does not result in the same loss of cartilage observed in OA. OP differs from normal only by the

Connective Issues No. 55 November 1999
thickness of the calcified cartilage layers. OAs pathology more complicated, a change in matrix composition suggested.

H.A. Eriksen (Robert Jones & Agnes Hunt Orthopaedic hospital NHS trust, Oswestry), described work on type I collagen matrix cross-linking in Achilles tendon a healthy human bone. The new assay enables quantitative analysis of cross-linked C-terminal telopeptides and distinguishes between new and mature collagen.

Prof. Robin Poole (McGill University, Canada) talked on the extracellular matrix of growth plate cartilage. He discussed the matrix production of prehypertrophic chondrocytes and how, as they differentiate, the extracellular matrix is resorbed. Type IX NC4 domain is removed and the matrix calcifies type II is partially degraded by MMP-13. Inhibition of MMP-13 reduced COL II loss but has a major inhibitory effect on matrix mineralisation and differentiation. He went on to describe the ability of MMP-13 degraded COL II fragments to increase the expression of MMP-13. Such a positive feedback loop may well be an important physiological control and an ideal target for therapy.

Prof. Bruce Caterson (Cardiff University) gave a detailed account of the work on aggrecanase performed in his laboratory. Aggrecanase, a term used to describe the matrix proteinase(s) responsible for degradation of the cartilage proteoglycan aggrecan, is implicated in the pathogenesis of arthritis. He described two soluble aggrecanases, which may be related to the ADAM-TS, derived from explant cultures which have different mRNA expression levels to observed protein activity when stimulated with IL-1 or retinoic acid. A third membrane associated aggrecanase activity has also been identified, by the group, which has a different inhibitor profile to the soluble forms described above. The group has also investigated the "protective" effect of N-3 fatty acids on IL-1 induced aggrecanase activity. These data suggest that there are a number of candidate molecules with aggrecanase activity that may have differing roles both in normal and diseased tissue.

C.E.M Berger (University of Newcastle-upon-Tyne) described work investigating ADAMs metalloproteinases that degrade proteoglycans. This study focussed on bone using the human osteoblast cell line MG63 and rat primary osteoblast cultures. Both cell types express three of the proteoglycan degrading ADAMs: ADAMs1, ADMP1 and ADMP2. They have discovered a splice variant of the ADAMs1 enzyme expressed in MG63 but not in rat primary osteoblasts. Further study will investigate whether the enzymes have any substrates in the bone ECM.

M.W. Hui (University of Newcastle) talked on the ability of TGF β -1 to block the release of collagen from bovine nasal cartilage subsequent to stimulation by IL-1 in combination with oncostatin. This study demonstrated that TGF β -1 can down regulate expression of collagenases (MMP-1 & MMP-13) at the mRNA level.

Clare Curtis (Cardiff University) summarised her work on n-3 fatty acids and their influence on chondrocyte expression. IL-1 induces expression of both aggrecanase and 2 in chondrocytes. However when the n-3 fatty acid linolenic acid is present this induction is abolished. The effect, which is specific to n-3 fatty acids, could explain the observed reduction in inflammation observed in degenerative joint disease, when n-3 fatty acids are supplemented in the diet.

A.D. Rowan (University of Newcastle Medical School) closed the session with work that looked at the effect of oncostatin M on collagen fragment release from explant cultures catalysed by MMP-1. Results demonstrated that this was mediated by binding to the OSM/gp130 domain and IL-1R1 surface receptor; no increase in these receptor expression was observed.

The first day of the meeting concluded with the conference dinner and Ceilidh on the University campus.

Prof. Timothy Chambers (St. George's Hospital, London) opened the Osteoclast-Matrix Interaction theme on the second day with an overview of the recent advances in osteoclast biology. TRANCE, the ligand involved in the induction of osteoclasts from bone marrow progenitor cells and the activation of their resorption as a member of the TNFR family, was identified using expression cloning of the inhibitor of osteoclastogenesis, OPG, by two independent groups. Deletion of the gene for TRANCE caused osteopetrosis with the absence of osteoclasts. Together with TRANCE and M-CSF (necessary for progenitor proliferation), TGF β was found to have a dose-dependent effect on osteoclast formation; producing a ten-fold increase compared to TRANCE alone. This suggested a possible role for cytokines acting through TRAFs (TNFR-associated factors) to sensitise precursors to the effects of TRANCE.

Dr Miop Helfrich (Aberdeen) reviewed the multiple adhesion mechanisms in bone, focusing on data obtained in osteoclasts relating to the expression and function of integrins. Although several classes of adhesion molecules have been implicated in bone cells, many of their functions are still unknown. They may be involved with matrix adhesion, osteoclastogenesis, cell differentiation and osteoblast apoptosis amongst others. Integrins are heterodimeric proteins composed of α - and β -subunits with a RGD recognition site. Expression is very widespread in osteoclasts apart from the actin ring. Compounds containing the RGD motif inhibit osteoclast resorption and inhibit osteoclast adhesion to Type I collagen, as do α -antibodies. Knockout mice lacking the subunits result in osteosclerosis and prenatal death of embryos. It is thought that ligand binding to the integrin leads to cytoskeletal reorganisation and signal transduction.

Dr Mike Rogers (Aberdeen) discussed the new insights into the molecular mechanisms of the action of bisphosphonates. Bisphosphonates have become the treatment of choice for diseases involving osteoclast-mediated bone resorption. It has recently been proposed that there are two classes of these compounds with distinct molecular mechanisms of action. The nitrogen containing series (N-BPs) affect the biosynthetic mevalonate pathway - inhibition of protein prenylation prevents the formation of geranylgeranylated proteins which leads to loss of the actin ring and membrane ruffling in osteoclasts, and disruption of the cytoskeleton which are fundamental to osteoclast activity and survival. The other class, the non-N-BPs are metabolised intracellularly in osteoclasts and cause apoptosis by accumulating in high concentrations and thereby inhibiting bone resorption.

Neil McGowan (Aberdeen) discussed the role of the endothelium in targeting the migration of osteoclast precursors (OCL-P) and the development of an in vitro model for study. Working on the hypothesis that adhesion of circulating osteoclast precursors was a primary event in the targeting of bone resorption, peripheral blood mononuclear cells (PBMC) were isolated from healthy volunteers and patients with metabolic bone diseases. The ability of the PBMCs to adhere to human umbilical vein endothelial cells (HUVEC) under basal and stimulated conditions was quantified. Parallel studies investigated the ability of adherent PBMCs to develop into osteoclasts. Initial results show that OCL-P do adhere to the endothelium and suggest a possible role for OCL-P - endothelium interactions in targeting bone resorption.

K.E. De Rooij (Leiden, The Netherlands) described a protocol used in identifying differential gene expression in osteocytes. Using the subtractive hybridisation procedure; expression of genes in osteocytes were compared to that in osteoblasts and periosteal fibroblasts which were isolated from foetal chicken calvariae. A large number of cDNA fragments have been obtained and identified as being preferentially expressed in osteocytes. Characterisation of their role in bone cells should greatly enhance knowledge of

Connective Issues No. 55 November 1999
the differentiation of osteocytes and their function mechanosensor cells.

Colin Farquharson (Roslin, Edinburgh) discuss the expression of parathyroid hormone-related pepti (PTHrP) and its receptor in the growth plate a maturationally distinct chondrocyte populations. Recent situ hybridisations have indicated that PTHrP, Indian Hedgehog (ihh) and their receptors are expressed at discrete locations. PTHrP is thought to be a negative regulator of chondrocyte terminal differentiation and mediates the effect of ihh on bone growth. Studies examining the pattern of PTHrP-ihh axis component expression in the chick growth plate have indicated that PTHrP, ihh and their receptors are all present in the growth plate itself. It is suggested that diffusion of ihh to the perichondrium and PTHrP from the periarticular region, may not be necessary for control of chondrocyte terminal differentiation by the PTHrP-ihh autoregulatory loop.

E. Hobson (Aberdeen) described how deletion of the first intron of the Collagen I α 1 (COL1A1) gene altered geometric and predicted biomechanical properties of bone mice. Studies in transgenic mice, where the first intron of the COL1A1 gene had been deleted, were subjected to peripheral quantitative computed tomography. Although there was no significant difference in body weight or bone density when compared to wild type controls, bone area, cortical thickness, periosteal and endosteal circumferences were significantly reduced as were indices of bone strength cross-sectional moment of inertia and the strength strain index. These data suggest that the first intron of the COL1A1 gene play an important role in determining bone geometry.

A. White (Manchester) outlined the work carried out to isolate the genes involved in endochondral ossification where cartilage is subsequently replaced by bone. Chondrocytes within the growth plate proliferate, mature and undergo hypertrophy, controlling longitudinal bone growth and progression of ossification. An inappropriate reactivation of the differentiation pathway is thought to occur in the cartilage of osteoarthritic joints, giving rise to bony outgrowths called osteophytes. Using subtractive hybridisation to isolate genes extracted from epiphyseal growth plate chondrocytes from bovine foetuses, a number of positive clones have been identified. Three of the clones show increased expression in growth plate compared to epiphyseal chondrocytes and the specific functions of these proteins are currently under investigation.

S. Roberts (Shropshire) discussed the use of COL2-3/4m monoclonal antibody to investigate collagen remodelling in Autologous Chondrocyte Implantation (ACI). ACI is a technique used in several orthopaedic centres worldwide as a treatment to repair articular cartilage defects. COL2-3/4m which is immunoreactive against an epitope denatured, but not, native type II collagen and also the α 1 chain of type XI collagen, has been used to examine collagen turnover in biopsies obtained 5 - 30 months post implantation. Although all samples were positive for collagen II, except for the fibrocartilage-like biopsy, immunostaining for COL2-3/4m was very variable. The study indicated that type II collagen is degraded with the variability of immunopositivity to COL2-3/4m perhaps indicating a transient exposure of this epitope. The degradation may be due to either a pathological catabolism or a remodelling of the matrix allowing collagen to be laid down in a more organised form as seen in some hyaline-like repair tissue.

The focus of the final session was on cell therapy and cartilage. **Dr. Anders Lindahl** (Gothenburg, Sweden) discussed the technique of autologous cultured chondrocyte transplantation (ACT) for patients with cartilage injury. Chondrocytes are isolated from the patients cartilage and cultured in the presence of serum from the patient. The patient undergoes surgery to remove damaged cartilage and cover the joint with a sutured periosteal covering. Cultured chondrocytes are then reimplanted under the periosteal covering and allowed to grow over the damaged cartilage.

The injured tissue was replaced with healthy tissue and regeneration of cartilage was demonstrated in follow up studies on these patients.

Dr. Frank Berry (Baltimore, USA) looked at mesenchymal stem cells (MSC) derived from bone marrow. These cells have been shown to differentiate down a number of cell lineages such as cartilage, bone, adipose tissue, tendon and muscle. During chondrogenesis MSC cells synthesise an ECM which is rich in the proteoglycans, collagens and glycoproteins which are detected in cartilage. The use of these cells as a model for studying matrix biosynthesis and assembly were discussed as was the potential of these cells to be used therapeutically for cartilage regeneration.

The meeting concluded with **Prof. James Richardson** (Owestry) showing us the clinical results of the ACT method discussed by Dr. Lindah. We were shown video footage of the operation procedure and follow up successes of this clinical procedure. The disadvantages and limitations of the technique as well as the technical difficulties in performing these operations were discussed. The outcome however suggest that this will be a valuable treatment for repairing degenerating cartilage.



The British Society for Matrix Biology
Year 2000 Millennium Meeting
Molecular Cell Biology of the Synovial Joint

The Royal Veterinary College
London 3-4 April, 2000
Professor Mike Bayliss and Dr Jay Dudhia

Monday 3rd April

10.30 - 1.05 Registration, Lunch and Poster set-up
1.05 - 1.15 Welcome and Introduction

Session I: Bone and Cartilage

Chair: Professor M. Bayliss

1.15 - 1.55 Professor Lance Lanyon, (RVC, London)
 'The responses of bone cells to biochemical and biomechanical stimuli'
1.55 - 2.35 Professor Klaus von der Mark, (Erlangen-Nürnberg, Germany)
 'Cartilage: a tissue designed to be transient in development, but permanent in the articulating joint'
2.35 - 3.20 *Three 15 presentations to be selected from abstracts submitted*
3.20-3.50 Tea/Coffee

Session II

Chair Professor S. May

3.50 - 4.30 Professor Peter Roughley, (Shriners Hospital, Canada)
 'Ageing changes in the biochemistry of articular cartilage'
4.30 - 5.00 Veterinary Award Lecture (*to be announced*)
5.00 - 5.30 AGM
5.30 - 6.00 Poster Session and Trade Exhibition
7.00 - 8.30 Reception at the 'Web of life Exhibition', London Zoo
8.30 - 11.00 Conference Dinner Venue at The London Zoo

Tuesday 4th April

Session III: Synovium

Chair: Dr. J. Dudhia

9.10 - 9.50 Professor Roger Mason, (Imperial College, London)
 'The synovium - provider and gatekeeper of the synovial joint'
9.50 - 10.30 Professor Jo Edwards, (UCL, London)
 'Where do synovial stromal cells come from?'
10.30 - 11.00 Tea/Coffee
11.00 - 12.05 *Four 15 minute presentations to be selected from abstracts submitted*
12.05 - 1.20 Lunch

Session IV: Tendon and Vasculature

Chair: Professor R. Mason

1.20 - 2.00 Professor Kate Vogel, (University of New Mexico, USA)
 'Differentiation of tendon tissue'
2.00 - 2.30 Young Investigator Award (to be announced)
2.30 - 2.50 Tea/Coffee
2.50 - 3.30 Professor David Blake, (Bath)
 'Rheumatoid synovium, the microvasculature and oxidative stress'
3.30 - 4.10 Professor Peter Winlove, (University of Exeter)
 'Microvasculature exchange in nutrition of cartilage'
4.10 **End of Meeting**

MEETING SPONSORS

The British Society for Matrix Biology wishes to acknowledge the following organisations who have provided generous support for the meeting

The Wellcome Trust	Vétoquinol	Merck
Home of Rest for Horses	Smith & Nephew	Life Technologies
Janssen Animal Health	Intervet Int. BV	R & D Systems Europe Ltd

TRAVEL INFORMATION

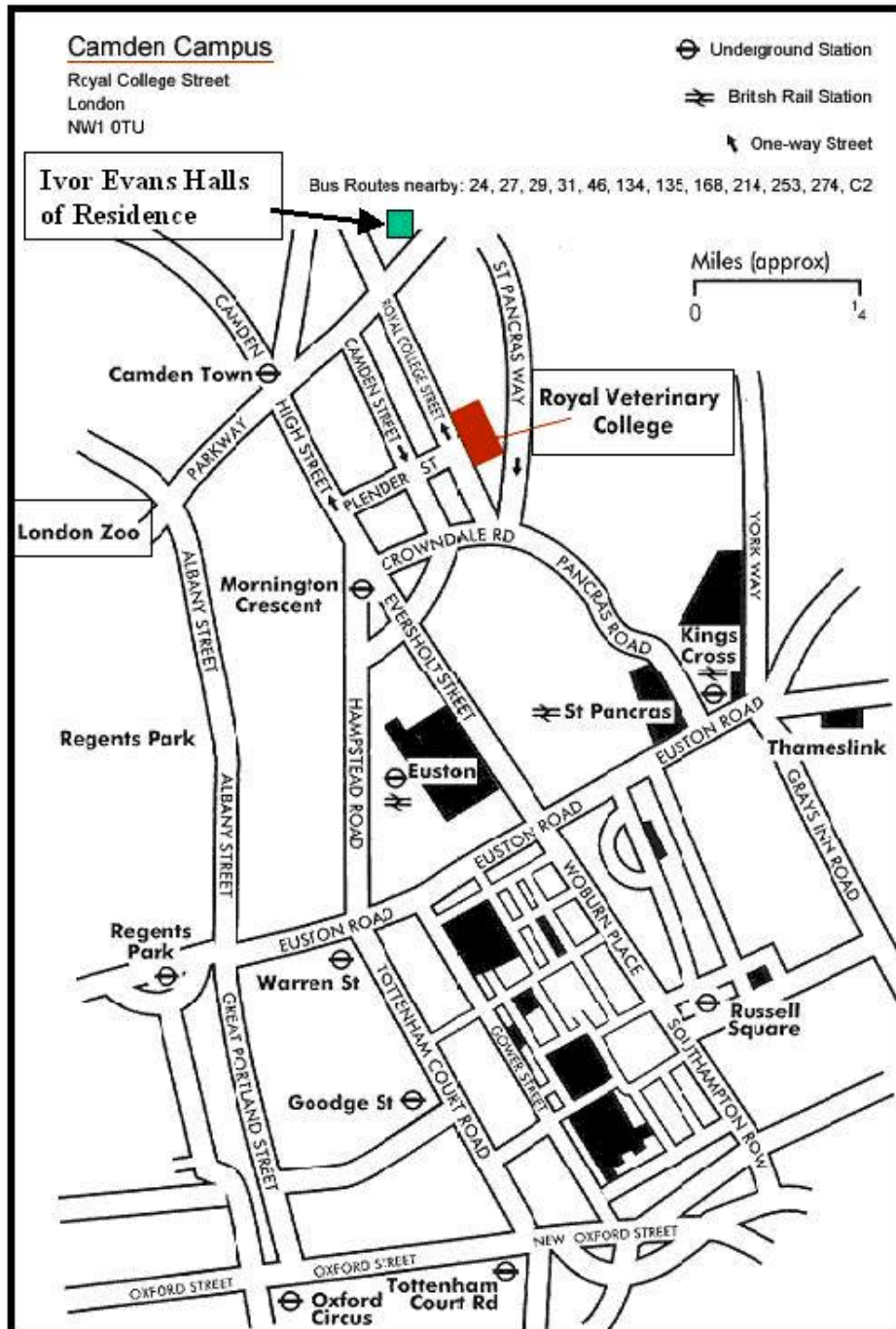
Trains

The Meeting and Registration venue is at the Camden Campus of The Royal Veterinary College which is easily accessible by London Underground, Main Line Stations and by Road. Three tube stations serve this Campus within a short walking distance - Camden Town (Northern Line), Mornington Crescent (Northern Line) and Kings Cross/St. Pancras (Circle, Hammersmith & City, Metropolitan, Northern and Picadilly Lines). **A detailed road map from these stations to the College can be found on**

<http://www.rvc.ac.uk/contact.htm#Maps and Travel Information>. A copy is also attached. The London Underground also connects to all the major Main Line Stations, including Euston, Paddington, Waterloo, and Kings Cross/St Pancras stations as well as Heathrow Airport. Please check the Underground Map for the tube line connections for the above stations.

Road

If travelling by road, please allow plenty of time for Central London traffic. Parking places are at a premium near the College (Metered bays only). There is limited parking space on the Campus, and parking must be arranged prior to arrival. Contact Professor Bayliss or Dr Dudhia if you wish to park on site. For a London road map, visit <http://uk.multimap.com/map/> for road routes to the College.



The British Society for Matrix Biology ***Instructions for Submission of Abstracts*** **London, 3-4 April, 2000**

Abstracts should be submitted on an A4 sheet of paper and structured according to the format below using a 12-point font.

Title in bold

Authors

Affiliations

Introduction

Materials and Methods

Results

Discussion

References

Authors (Date) Title *Journal Name* **vol.** xx-xx

The deadline for submission of abstracts is Monday, February 14th 2000. Abstracts (4 hard copies PLUS electronic copy, either on floppy disc or by email as an attached file) should be submitted to:

Professor M. Bayliss
Royal Veterinary College
Royal College Street
London NW1 0TU
Email: mbayliss@rvc.ac.uk

When you submit your abstract, please indicate the name of Corresponding Author, with Fax, phone and email details

Also indicate whether you wish your abstract NOT TO BE

- **considered for an ORAL presentation**
- **published in the International Journal of Experimental Pathology (IJEP)**
- **entered into the IJEP poster competition.**

Those selected for oral presentations (10 min + 5 min discussion) will be notified in the first week in March. **Poster boards (1.5m x 1m) and fixings will be supplied.**

Year 2000 Millennium Meeting

REGISTRATION FORM

THE BRITISH SOCIETY FOR MATRIX BIOLOGY

ROYAL VETERINARY COLLEGE, LONDON, 3RD – 4TH APRIL 2000

Deadline for Registration is 14th February 2000

NAME TITLE.....

ADDRESS

.....

.....

TEL: FAX: EMAIL:.....

REGISTRATION: - £24.00 (includes hot lunch and tea/coffee for both days) £.....

NON-MEMBERS - £10.00 (in addition to the above) £.....

ACCOMMODATION: Male Female

Single room plus breakfast at Ivor Evans Hall – please tick dates required

Sunday 2nd April £26.00 £.....

Monday 3rd April £26.00 £.....

Tuesday 4th April £26.00 £.....

CONFERENCE DINNER: - £27.00

Monday 3rd at the London Zoo, including pre-Dinner Reception at the 'Web Of Life Exhibition'. Please note that seating capacity is limited to the first 110 people. £.....

TOTAL £.....

DIETARY REQUIREMENTS - Vegetarian YES/NO (circle as appropriate)

Other (please give details)

Please make cheques payable to "BRITISH SOCIETY FOR MATRIX BIOLOGY" and return with this form to:

Dr. J. Dudhia
Royal Veterinary College
Royal College Street
London NW1 0TU

Tel: 0171-468 5269

Fax: 0171-388 1027

BRITISH SOCIETY FOR MATRIX BIOLOGY
BURSARY APPLICATION FORM

Application form to be completed and returned with a copy of the completed Conference application form, a copy of the abstract to be presented at the meeting and a one page *curriculum vitae*, to:

BSMB Secretary
Dr Rose Maciewicz
Cardiovascular, Metabolism & Musculoskeletal Research Department
Zeneca Pharmaceuticals
Alderley Park, Macclesfield
Cheshire, SK10 4TG UK

The applicant should have been a member of the British Society for Matrix Biology for 12 months prior to this application. Applicants will be informed as soon as possible and should not await such notification before submitting their Conference application.

Name.....Date.....

Address.....
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e-mail:.....tel:.....fax:.....

Conference Name.....

Venus and Date.....

Costs (accommodation, registration, travel).....
.....

Additional sources of support (Indicate other sources to which you will apply for financial assistance to attend the Conference and the amount you might expect to receive.)

Support statement (A brief supporting recommendation by the applicant's Head of Department or Supervisor.)

Date.....Name (HOD).....Signature.....

Date.....Signature of Applicant.....

BRITISH SOCIETY FOR MATRIX BIOLOGY

APPLICATION FOR MEMBERSHIP

To be completed in **BLOCK CAPITALS** and returned to the Secretary. Please include appropriate membership fee.

Secretary: Dr Rose Maciewicz, Respiratory & Inflammation Research Department, AstraZeneca Pharmaceuticals, Alderley Park, Macclesfield, Cheshire, SK10 4TG UK. email: rose.maciewicz@astrazeneca.com

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Should you not know any member of the Society personally, please write to the Secretary.

SIGNATURE OF APPLICANT.....

MEMBERSHIP FEES: *Please indicate ✓*
Full membership £10 p.a......**Student membership £2 p.a.**.....

STUDENT MEMBERSHIP (To be signed by the student's supervisor)

I certify that..... is a non-salaried research student.

NAME.....

SIGNATURE.....

The application should be accompanied by a cheque, made payable to the **BRITISH SOCIETY FOR MATRIX BIOLOGY**, for the subscription for the current year January to December.

Please complete the banker's order for future subscriptions.

Should your application be unsuccessful your cheque and banker's order will be returned.

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the **BRITISH SOCIETY MATRIX BIOLOGY**, Account No. 09670343 quoting reference no.
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and make similar payments annually on the 1st January until this order is cancelled in writing, charging such payments to:

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