

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. Ian Clark, Dr. Anthony Day, Dr. Alison Reith, Dr. Norman McKie, Prof. Anthony Hollander

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XVIIth FECTS Brighton UK 2002 *1st Announcement*

Editorial by Rose Maciewicz

Welcome to the 59th edition of Connective Issues.

Items for your attention include:

- Programme and Registration form for the Autumn BSMB meeting at Norwich
- Minutes for the BSMB AGM held in Manchester on 2nd April 2001.
- Annual Financial Report for the BSMB for the year ending 2000.
- 1st Announcement for the XVIIth FECTS Brighton UK 2002

Many thanks to Professors Tim Hardingham and Kay Keilty for the organisation of the Spring 2001 BSMB meeting in Manchester. If you could not attend the meeting a report of it can be found in this newsletter. Thanks to Gillian McVey, Martin Cordell and Wa'el Kafienah for writing it. Four Bursaries were awarded at this meeting. The recipients were Katherine Lamb (RVC, London), Martin Cordell and Gillian McVey (MRC Immunochemistry Unit, Oxford) and Dr. Wa'el Lafienah (University of Bristol Academic Rheumatology). Congratulations to Katherine Lamb for winning the IJEP poster competition.

Note 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.

See you all at the Autumn meeting in Norwich.

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. Ian Clark (University of East Anglia; current e-mail ian.m.clark@astrazeneca.com)
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 Newcastle-upon-Tyne; nmckie@hgrp.mrc.ac.uk)

Prof. Anthony Hollander (University of Bristol Medical School; a.hollander@bristol.ac.uk)
Dr. Graham Riley (Soft Tissue Injury and Repair Group, Addenbrookes Hospital gpr1003@cus.cam.ac.uk)

Co-opted Member:

Two BSMB members have been co-opted onto the committee to help with the organisation of the XVIIth FECTS and are:

Dr. Jo Lewthwaite (The Royal Veterinary College, London; jlewthwaite@rvc.ac.uk)
Ms. Katherine Lamb (The Royal Veterinary College, London; klamb@rvc.ac.uk)

Autumn 2001 BSMB meeting University of East Anglia, Norwich

“The Impact of Proteinases on Matrix Biology”

The autumn 2001 meeting of the BSMB will be held at the University of East Anglia (UEA), Norwich on Monday 3rd and Tuesday 4th September 2001. This meeting is being organised by Ian M. Clark, UEA, Norwich; current contact details are: Tel. 01625-519834, e-mail: Ian.M.Clark@astrazeneca.com.

A programme and registration details for this meeting follow in this newsletter.

The University of East Anglia is a campus based university, situated on the outskirts of Norwich. Directions for travel to UEA by car, train or plane can be found at: http://www.uea.ac.uk/menu/campus_and_region/directions.shtml

Registration for the meeting will start at 11am in the Lower Common Room, Students Union Building. Posters, coffee and lunch (Tuesday) will also be in the LCR, with lectures in nearby Lecture Theatre 3. All accommodation will be in Norfolk Terrace. These will be signposted, but a campus map can be found at: http://www.uea.ac.uk/menu/campus_and_region/campus_map.shtml

There will be a wine reception and conference dinner on the Monday evening in the Sainsbury Centre for Visual Arts (on campus) and the chance to view the Robert and Lisa Sainsbury art collection. This is reputed to be one of the most stimulating collections formed in Europe during the 20th century, it combines modern Western art with fine and applied arts from

Africa, the Pacific, the Americas, Asia, Egypt, medieval Europe and the ancient Mediterranean. The Sainsbury Collection is particularly well known for its holdings of Francis Bacon, John Davies, Alberto Giacometti and Henry Moore.

Deadline for registration is Friday 3rd August, but please register as early as possible to allow us to organise poster boards, room numbers, meals etc. As usual, abstracts can be published in the International Journal of Experimental Pathology; please see details on the submission of abstracts form.

This meeting is currently supported by: Chemicon International and R&D Systems. Our thanks to them, and please visit their stands at the meeting.

BSMB Bursary for Norwich meeting

We are offering BSMB bursaries to attend the Autumn 2001 BSMB meeting in Norwich. Young members of the Society are encouraged to apply for bursaries (up to a maximum of £100 for the BSMB) to assist with attending this meeting. An application form can be found on Society's website <http://www.bsmb.ac.uk>.

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 the meeting is Monday, July 30th 2001.

The applications will be reviewed rapidly by the Committee and applicants will be informed by email by Thursday August 2nd.

Criteria for Bursaries

1. Applicants should have been members of the Society for at least 1 full calendar year before the 1st day of the meeting for which they are seeking a Bursary.
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.

XVIIIth FECTS

The XVIIIth FECTS will be hosted by the BSMB in the UK and take place on July 27th - 31st 2002 at the Brighton Centre. If anyone would like to help with the organisation please contact the FECTS Secretary, Dr. Jo Lewthwaite (The Royal Veterinary College, London; jlewthwaite@rvc.ac.uk). A copy of the 1st announcement is included in this Newsletter.

12th UK Adhesion Meeting

The 12th UK Adhesion Meeting will be held on Thursday 13th September at The University of Sheffield, Medical Education Centre, Northern General Hospital, Sheffield S5 7AU.

Preliminary Programme

Rod McEver, University of Oklahoma
Selectin-PSGL-1 interactions in shear flow

Rick Cummings, University of Oklahoma
Selectin Recognition of the Glycosulfopeptide Domain of PSGL-1

Beat Ernst, University of Basel
Rational Design of E-Selectin Antagonists

Keith Norman, University of Sheffield
Selectin inhibition in vivo: expectation and reality

Abstracts are invited for oral and poster presentations. Deadline for submission of abstracts and Registration is 10th August 2001
Registration fee: £20

For further information contact:
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BSMB Meeting Report
Spring 2001 BSMB meeting in
Manchester
**'Cellular and Molecular Mechanisms in
Tissue Engineering'**
by Gillian McVey, Martin Cordell and
Wa'el Kafienah

The spring meeting of the BSMB, "Cellular and Molecular Mechanisms in Tissue Engineering", was held at Hulme Hall, University of Manchester on 2nd-3rd April. The meeting was organised by Profs. Cay Kielty and Tim Hardingham and attracted 140 delegates. Financial support was provided by The Wellcome Trust and Arthritis Research Campaign.

Tony Ratcliffe (La Jolla, USA) presented work on vascular graft development and gave an overview of tissue engineering as a new field which brings together polymer science, cell biology, bioengineering, biochemistry and transplantation. A cell-scaffold approach to tissue engineering was described in which human cells were seeded onto a bio-absorbable scaffold; they multiplied and secreted growth factors and matrix proteins. Two clinical examples were described: Transcyte, a human fibroblast-derived temporary skin substitute used to treat 2nd and 3rd degree burns and leading to a faster recovery and Dermagraft, a living, bioengineered human dermal replacement with a biodegradable scaffold used in the treatment of diabetic ulcers, venous ulcers and pressure sores. Viable cells are important in this treatment as they secrete factors including angiogenic factor. The role of Dermagraft in angiogenesis was investigated. It was hypothesised that an epicardial patch would cause an angiogenic response. SCID mice with ischemic/infarcted injury, treated with a Dermagraft patch, showed an increase in small blood vessel number and density compared to patches with non-viable cells and untreated controls after 14 and 30 days. Similar

experiments are being performed on pigs. Future studies are to grow tissue that is functional on implant e.g. blood vessels. Clinical demand for this technology is great due to the high number of coronary bypass procedures. The objective is to produce a small diameter, tissue engineered vascular graft. Cells can be cultured on an elastic scaffold and fluid flow can be used to orient the cells in the direction of flow.

Richard Black (Liverpool, UK) presented studies on *in vitro* haemodynamic modelling which related clinically to vein grafts, vascular prostheses, vascular stents and angioplasty procedures. Intimal plaques occur between graft and host artery (anastomotic intimal hyperplasia). Various haemodynamic factors are believed to be involved in platelet deposition, vessel compliance and compliance mismatch, and wall shear stress, in particular, regions of stagnation and low wall shear stress. Physical modelling has the advantage of better control of physical and biological variables. Tissue-engineered blood vessel constructs composed of cells embedded in a collagen-gel scaffold were subjected to mechanical conditioning in the form of cyclic strain. The embedded cells responded as early as 4 days by reorganising their surrounding matrix, resulting in increased contraction and mechanical strength compared to statically cultured controls. The effects of dynamic mechanical conditioning on vascular endothelial cells and smooth muscle cells and the effect of cell growth and ECM production on the mechanical properties of constructs requires further study.

Tony Freemount (Manchester, UK) discussed new approaches to the management of back pain by highlighting the central role that the intervertebral disc plays. Discal degeneration is characterised by chondrocyte clustering and 'slit' formation. A key feature is the close proximity of the cells and the slits. Degradation of OA cartilage is caused by the local production of cytokines (e.g. IL-1b) leading to the production of degrading enzymes. It was hypothesised that, as in OA, disc degeneration was driven by IL-1 leading to matrix degrading enzyme production. A novel technique, *in situ* zymography with a specific IL-1 receptor antagonist, was used to investigate this. How does disc degeneration lead to back pain? Examination of the pathology of intervertebral root canals showed a variety of features including: nerve damage; fibrosis; discal protrusion; distortion of facet joints; venous thrombosis; blood vessel ingrowth; nociceptive nerve ingrowth. Production of cytokines (e.g.,

vascular endothelial growth factor and nerve growth factor, NGF) leads to nerves and vessels growing into usually aneural and avascular structures. Ingrowing vessels make NGF and local ingrowing nerves express its high affinity receptor. Discal degeneration may be controlled using anti-cytokine therapy. IL-1 is a candidate target but delivery of anti-IL-1 is a problem as the tissue is not particularly vascular and difficult to reach by injection. One possible approach is to use gene therapy to introduce a 'chemical factory' *in situ*. Some AF tissue could be removed by biopsy under local anaesthetic and the discal chondrocytes cultured *in vitro* and turned into NP cells. These chondrocytes, infected with adenovirus carrying IL-1 antagonist under the CMV promoter, can be infected back into discs under local anaesthetic. An *in vitro* model is currently being developed. It may be possible to reconstruct the intervertebral disc in the future. TGF β may stimulate chondrocytes to make their own matrix but chondrocytes are load sensitive. Possibilities exist to normalise the load using an external fixator developed in Nottingham. An internal balloon designed in Liverpool may help this load bearing and gene therapy altered chondrocytes from Manchester can then form new matrix.

Wael Kafienah (Bristol, UK) presented the use of nasal chondrocytes in the tissue engineering of articular cartilage. Cartilage was taken from nasal and articular cartilage of adult cows or humans and expanded in monolayer culture for 1 week in the presence of bFGF-2. Cells were seeded on scaffolds for 40 days. Bovine and human articular cartilage contain many cells but little matrix and levels of type II collagen and GAG are very low. Engineered cartilage from bovine and human nasal chondrocytes had a more extensive matrix with higher type II collagen and GAG content. Quantitative PCR of some human specimens gave a ratio of type II to type I collagen mRNA of 1.0 for the articular constructs and 15.0 for nasal constructs, suggesting that the nasal chondrocytes were more differentiated than articular chondrocytes. This suggests that nasal cartilage may be a more efficient source of chondrocytes for tissue engineering.

Andrew Parker (AstraZeneca, UK) used microarray technology to examine time dependent expression of ECM genes in chondrocytes cultured in alginate beads. Bovine articular chondrocytes, extracted from cartilage by collagenase digestion, were encapsulated in alginate beads. The beads were cultured in DMEM with daily media changes. RNA was

extracted from intact cartilage and from chondrocytes immediately after collagenase digestion and time points up to 120 hours. RNA was reverse transcribed, labelled with ^{33}P -dATP and hybridised to a microarray containing cDNA from over 13,000 genes. The results showed that chondrocytes have a dramatic transcriptional response to removal from their matrix. Types I and II collagen were substantially upregulated in the first 24 hours in alginate culture and fell after 5 days in culture but were still more than 10-fold higher than in cartilage. Fibronectin was upregulated more than 30-fold for the entire period investigated while type VI collagen expression increased continually over the timecourse. These results indicate that chondrocyte behaviour in the alginate bead system is not identical to that of chondrocytes in cartilage and hence the composition of the matrix may be different to that found normally in cartilage.

David Gilham (University of Manchester, UK) gave a talk entitled 'Tissue engineering and gene therapy: lessons from T cells'. Problems associated with gene therapy include accessing target tissues and the method of delivery of the therapy. Viral vectors are favoured as a method of gene transfer due to their high efficiency. Those currently in use are derived from adenoviruses and retroviruses. Retroviral vectors have a low immunogenicity and allow for long term gene expression by their integration into the host genome whereas adenoviruses do not integrate and are only capable of short term gene expression. The use of gene therapy to target T cells to tumours is currently being investigated. Access is not a problem as primary lymphocytes can be harvested from the peripheral blood of patients. Following transduction, cells can be re-introduced into the patient. A highly efficient system known as 'kat' has been developed for the retroviral transduction of primary human T lymphocytes. A system has also been developed which confers long-term expression to retroviral vectors which involves the insertion of a human beta interferon scaffold attachment region (IFN-SAR) into the vector. However, there are barriers to the immunotherapy of cancer. Tumour cells lack an antigen to illicit an MHC response. Cytokines, such as IL-10, are produced which are immunosuppressive and tumour cells express the Fas ligand which can cause apoptosis of T cells on contact. Appropriate T cells to the tumour may not exist as it is 'self'. An approach which will by-passes the MHC is being explored to accommodate

these problems. Interferon γ produced from specific modified T cells leads to T cell activation in the absence of MHC restriction. The gene effect may be sufficient to deliver success in *in vitro* assays but the modified cells may be less effective in a whole organism. The target cells or tissue will ultimately determine the choice of gene therapy vector. Advances in technology are ongoing, e.g. improvements in duration and level of gene expression. Single gene therapy may be insufficient and vectors capable of expressing multiple genes to high levels may be required, e.g. genes for survival, gene to counteract immune surveillance (IL-10 and anti-CTLA4).

Sharon O'Kane (Renovo, UK) presented the role of stem cells in dermal wound healing. Normal wound healing of chronic wounds leads to hypertrophic scarring and keloid formation. There can also be failure of wounds to heal such as in venous and diabetic ulcers and pressure sores which are all common in an ageing population. Tissue engineering may have a role in treating these conditions. Stem cell therapy could be used in the replacement of damaged tissue, the acceleration of the closure of chronic wounds and the improved integration of tissue engineered skin grafts. A stem cell is a multipotential self-renewing cell which does not senesce and can differentiate, under the right conditions, into any type of cell. Using CD34 (a cell surface glycoprotein) as a marker for stem cells, their role in dermal wound healing has been investigated *in vivo*. Having received a 1cm wound onto the dorsal skin, adult mice had stem cells introduced at the wound site. The wounds were examined at 1, 6, 12 hours and 1-7 days post-therapy. Immunolocalisation of CD34 +ve cells was found at the wound site and new blood vessels were formed by these cells ~3 days post-wounding. After 7 days, the basement membrane had reformed. The CD34 +ve cells were successfully incorporated into the healing wound in the very early stages, and cells were present in the blood 1 day post-healing. *In situ* vasculogenesis was suggested in the model as was angiogenesis. The role of mesenchymal stem cells in wound healing is underway. This targets the improvement of initial graft take at wound sites and a subsequent reduction in scarring.

Chris Murphy (Imperial College, London, UK) discussed chondrogenic differentiation of mesenchymal and embryonic stem cells. Problems associated with cartilage tissue engineering, such as the limited capacity of cartilage as an avascular tissue for repair and

regeneration were highlighted. The process requires a large scale-up of cell numbers and the differentiated chondrocyte phenotype is lost during the amplification of cell cultures. One solution to this problem is to identify alternative sources of cells. Stem cells are an obvious candidate and the objective of this work is to gain enhanced chondrogenic differentiation from these cells. Pluripotent embryonic stem cells (ES) are derived from the inner cell mass of pre-implantation embryos. These cells expand in an undifferentiated state and have the potential to differentiate into all cell lineages. Mesenchymal stem cells (MSC) are multipotent cells, easily collected and isolated from bone marrow, capable of limited self-renewal. Human MSC (hMSC) were isolated from bone marrow and monolayers of the cells were expanded and seeded into droplet cultures. These were treated with either TGF- β 3 or DHCB. Analysis of the TGF- β 3 treated cultures showed hMSC condensation. This was seen as a positive result as in normal cartilage development, MSC are thought to condense together. TGF- β 3 induced chondrogenesis and treatment with DHCB resulted in decreased collagen production and increased aggrecan core protein gene expression. The proliferation of ES cells was performed on LIF containing media and the formation of intact and dispersed embryoid bodies (EB) was observed after 5 days and significant chondrocyte gene expression detected as early as 2 days after EB formation. It was concluded that both ES cells and hMSC could potentially offer an alternative cell source for the production of chondrocytes for use in cartilage tissue engineering.

Katherine Lamb (Royal Veterinary College, London, UK) spoke about the selective expression of ERK-1/2 (extracellular-signal-related kinase 1/2) at the presumptive joint line. The aim of this work is to identify the upstream mechano-sensitive cellular signalling pathways responsible for regulating the events which occur in joint cavitation with the focus on the MAPK (mitogen-activated protein kinase) cascade and its possible role in controlling local differentiation during the cavitation process. An *in ovo* model was used where white leghorn embryos were treated with either decamethonium bromide (to cause paralysis); 4-aminopyridine (AP neuromuscular-active agent inducing hyperactivity) or a control (tyrode solution), the treatments were administered at 24 hour intervals onto the chorioallantoic membrane. The joints were later sectioned and primary antibodies applied, these being detected

using the appropriate FITC-conjugated secondary antibody. Polymerised actin filaments were localised using FITC-conjugated phalloidin. Confocal microscopy showed that active phosphorylated ERK-1/2 was predominantly expressed at the joint line in fully cavitated joints. Co-localisation of polymerised actin and phosphorylated ERK-1/2 was observed. These observations were not seen at the joint lines in immobilised limbs. Results suggest that ERK is involved in an articular surface-selective event and may have a role in the upstream signalling events associated with joint line related differentiation.

Martin Cordell (Oxford, UK) presented work on the sequencing of bovine TSG-6 and confocal microscopy studies on the localisation of HA and TSG-6 in cultured bovine chondrocytes. TSG-6 (the protein product of the tumour necrosis factor (TNF)-stimulated gene-6) is present in cartilage from patients with OA and RA, but is not detected in tissues from healthy individuals. The role of this protein is being investigated in a bovine chondrocyte system and the sequence of the bovine protein was required to confirm its similarity to that of human. The sequence was amplified by PCR using primers based on a cross-species alignment of human, rabbit and mouse. The 3' end was amplified using RACE-PCR, and the 5' end was amplified using a primer based on sequence found in an EST database. TSG-6 is highly conserved throughout vertebrate evolution with the bovine amino acid sequence being 96% identical to the human. Confocal microscopy showed hyaluronan (HA) staining as a halo around each cell or cell cluster but with some unstained areas probably corresponding to HA chains already saturated with aggrecan and link protein. A TSG-6 antiserum raised against the final 16 amino acids of the human sequence (which are identical in the bovine sequence) showed that TSG-6 was located intracellularly, possibly within vesicles. Incubation of the chondrocytes with IL-1 β for 24 hours results in a clear increase in TSG-6 staining within the cell.

Daniel Aeschlimann (Cardiff University, UK) spoke of a new strategy for functionalisation of hyaluronic acid and its use in the formation of novel biodegradable hydrogels for tissue repair. A method has been developed for the chemical modification of high molecular weight HA which yields derivatives which can then be cross-linked under physiological conditions resulting in the formation of biocompatible and biodegradable hydrogels and peptide-functionalised forms of HA with particular

release characteristics of the bio-active agent. Derivatives of HA were formed with amino, sulfhydryl or aldehyde functionality and used to generate hydrogels composed of HA derivatives and bifunctional crosslinkers or mixtures of the HA derivatives carrying different functionalities. Using HA derivatised to a varying degree crosslinked to crosslinkers of differing size, hydrogels were created with varied crosslinking densities and pore size. The HA hydrogels were evaluated in a rat model for biodegradability and biocompatibility. Several formulations exhibited excellent cell infiltration and BMP-2/IGF-1 induced chondrogenesis. These gels were shown to be non-toxic. It was concluded that the appropriate ECM scaffolds and signalling molecules can be used to induce and control tissue differentiation and consequently facilitate tissue repair.

Vivek Mudera (University College London, UK) described the production of fibronectin (FN) scaffolds used in tissue engineering and the influence of shear force during the production of such materials. Mechanisms were uncovered by which FN can be aligned and aggregated *in vitro* to produce fibres, and a number of FN materials (aligned and fibrous) have been produced. The common factor in the production of these FN materials is that the FN molecules in solution are all exposed to shear force during the production process and this appears to induce the unfolding and aggregation of the FN molecules into aligned fibres. Solutions of FN where exposed to shear by extrusion through a narrow orifice or by physical pulling of the material. Non-shear materials were freeze-dried as a solution. Microscopy showed that sheared materials contained long, oriented FN fibres, whereas non-sheared FN lacked this structure. The stability of the sheared and non-sheared material was examined at 37°C in both PBS and DMEM + 10% FCS. This assessed the influence of fibrous aggregation on longevity of the materials. The non-sheared FN dissolved rapidly, the shear-aggregated material (which contained a large proportion of oriented fibres) was stable, some material staying intact for weeks in the 10% FCS. This demonstrates that some form of mechanical shear is required to produce aligned fibres of FN. These durable materials have great potential in tissue engineering.

Ali Mobasher (University of Liverpool, UK) presented work on sodium potassium pumps, epithelial sodium channels (ENaC) and voltage gated calcium channels (VGCC) and their co-localisation with β 1-integrins in mouse limb-bud chondrocytes in organoid culture. Interactions between the ECM of articular cartilage and

chondrocytes are known to be partly mediated by integrin receptors. Recent studies suggest that integrins and growth factor receptors co-localise and collaborate in common biochemical signalling pathways. As growth factors influence the activity and expression of certain ion channels, the possible co-localisation of integrins with selected ion channels, ion pumps and transporters, previously identified in chondrocytes, was investigated. Having established mouse limb-bud cultures, the expression and cellular localisation of ENaC, VGCC and Na, K-ATPase in cartilage derived from the limb-buds of 12 day old mice were examined using monoclonal and polyclonal antibodies. The integrins and all of the selected transport systems were expressed in mouse limb-bud chondrocytes. Immunostaining showed correlation between the expression of $\beta 1$ -integrins, VGCC and Na, K-ATPase. $\beta 1$ -integrins co-localised with ENaC on the cell surface. Immunoprecipitation experiments gave good evidence for the co-localisation and association of integrins with ENaC, VGCC and Na, K-ATPase. This is the first report

Brian Ashton (Oswestry, UK) reviewed autologous chondrocyte implantation (ACI) focussing on work done in Oswestry. Various statistics on cartilage injuries in the UK and their traditional treatment were reported. ACI was proposed as a long-term method for the treatment of some cartilage injuries. The procedure involves taking a biopsy from a non-weight bearing area, expanding chondrocytes *in vitro*, and finally seeding these chondrocytes back in the injury site under a periosteal flap. Patient follow up at one year included repeated MRI, a 2mm biopsy for histology and arthroscopy to identify the stiffness of neocartilage compared to the surrounding cartilage. Neocartilage formed was fibrocartilage, hyaline cartilage, or a mixture of both. It was as stiff as the normal surrounding cartilage with good lateral integration. Seventy-four patients have been treated in Oswestry with 21-68% satisfaction level determined by the Lysholm score.

Brian Johnstone (Cleveland, USA) talked about meniscal cartilage repair. He explained the anatomy of the meniscus and how injury of that tissue affects load bearing and femur movement. He proposed tissue engineering of the meniscus as a possible repair method using bone marrow mesenchymal stem cells as a cell source. These cells can be harvested from bone marrow and expanded *in vitro* before seeding onto biomaterial scaffolds. These cells could

differentiate into fibro/cartilage during *in vitro* culture in a micromass pellet system. Medium supplementation with TGF- β and dexamethasone was essential for encouraging stem cell differentiation in the system. *In vivo* studies using hyaluronon/gelatin scaffold implants was carried out using a rabbit model. These scaffolds were implanted with or without seeding of expanded stem cells. The results show that scaffold/cell constructs outperformed scaffolds implanted alone as evident by staining for type II and type I collagen and their better integration with the surrounding tissue. The current protocol targets the middle third of the lunar-like meniscus for ease of suturing but future studies will consider the tips of the meniscus and the use of larger, more weight-bearing animal models such as the goat.

Robert Brown (London, UK) discussed cytomechanics and matrix architecture in soft tissue engineering. He proposed that matrix architecture and spatial organisation were critical to the success of tissue engineering. Disorganisation of matrix due to scarring or mechanical forces affects cell behaviour. Matrix organisation is governed by both substrate cues and mechanical cues. Substrate cues guide matrix structure regeneration. For example, fibronectin around nerve gaps in experimental models, provide structure and guidance for cells to grow and recruit in the fibre direction. Mechanical cueing affects the growth and metabolism of cells. This was exemplified using fibroblasts in a contracted gel test system. Tension applied in the cell bundle orientation increased their propagation and matrix synthesis while cyclic loading increased MMP-9 production and matrix degradation. In practise, these adaptive cytomechanical responses should be considered when designing bioreactors for tissue engineering which can load in an organised fashion.

**BRITISH SOCIETY FOR MATRIX BIOLOGY
ANNUAL GENERAL MEETING
2nd April 2001
Hulme Hall, Manchester University**

The Annual General Meeting of the British Society for Matrix Biology (BSMB) was called to order at 17:20 by the Chairman, Professor Tim Hardingham. Thirty four eight members were in attendance, including the BSMB Committee members - Ian Clark, Jo Lewthwaite, Anthony Hollander, Jay Dudhia, Rose Maciewicz and Tim Hardingham. Apologies for absence were received from two other Committee members Anthony Day and Allison Reith.

1. Minutes

The minutes of the last AGM held on the 3rd April, 2000 at the Great Hall, Royal Veterinary College, London were taken as a true and accurate record of that meeting and were accepted.

2. Matters Arising:

All matters arising have been discussed at the Committee Meetings held in 2000.

- The Committee decided not to hold a 20th Anniversary meeting.
- They agreed to sending Newsletters by e-mail but this is on hold awaiting updating of the membership's email addresses.
- The Young Investigators Awards has been put on hold until further funding can be found, at that point the Committee would have further discussion about how to attract more multiple applicants.

3. Secretary's report

Membership: The Society currently has 507 members on it's mailing list. 35 new membership were received in the last year and 10 members had left the Society, mainly due to their departure from science. At present the Society has 123 student members.

Newsletters: The Secretary reported that since the last AGM three BSMB Newsletters were sent out: Connective Issue 56 (March 2000); Connective Issue 57 (July 2000); and Connective Issue 58 (January 2001). She reported that in the interim, additional information was available from the BSMB website (<http://www.bsmb.ac.uk>).

Meetings: The Society had organised two meetings in 2000 - 2001 year. Both meetings were successful and demonstrated the continuing support and interest in the UK and internationally for the BSMB.

The Spring BSMB meeting was held at Royal Veterinary College, University of London. The topic was '**Molecular Cell Biology of the Synovial Joint**' and was organised by Professor Mike Bayliss and Dr. Jay Dudhia. The Secretary reported that abstracts were published in the *Int. J. Exp. Path.* (2000) **81:A1-A38**). The BSMB awarded four bursaries. The recipients were David Mahoney (MRC Immunochemistry Unit, Oxford); Marie-Claire Hall (School of Biological Sciences, UEA, Norwich); J.Anderson-Mackenzie (Collagen Research Group, Langford, Bristol); and Jan Olaf Stracke (School of Biological Sciences, UEA, Norwich). The IJEP poster competition was won by Emma Blain (Connective Tissue Biology Laboratories, Cardiff) and Mireille Vankemmelbeke (Dept. of Human Metabolism and Clinical Biochemistry, Sheffield). In addition the Veterinary Investigator Award, sponsored by the Charity - Home of Rest of Horses, was awarded to Dr. Roger Smith, Royal Veterinary College, London

The Autumn BSMB meeting was held in Newcastle-upon-Tyne. The topic was '**Cell-Cell and Cell Matrix Interactions in Development and Pathology**' and was organised by Drs N. McKie and M. A. Birch. Three bursaries were awarded: Dr. John Tarlton (Collagen Research, Bristol University); Mr. Daniel Bax, (Wellcome Trust Centre for Cell-Matrix Research, University of Manchester); Miss Philippa Callender, (Connective Tissue Biology Group, Cardiff University). Abstracts were to be published in the March 2001 issue of IJEP.

Future Meetings: The Secretary informed the membership about current/future BSMB meetings.

- The Spring 2001 BSMB meeting on '**Cellular and Molecular Mechanism in Tissue Engineering**' where this AGM was taking place. The organisers of the meeting were Professors Tim Hardingham and Cay Keilty. Four BSMB bursaries were awarded for this meeting as well as an IJEP poster competition.
- The Autumn 2001 BSMB was to be held at the University of Norwich on the 3rd - 4th of September. The topic of the meeting was '**The Impact of Proteinases on Matrix Biology**' and was being organised by Dr. Ian Clark. BSMB bursaries would be awarded for this meeting.

- The Secretary noted that there would be no Spring or Autumn 2002 meeting due to the fact the BSMB was hosting the XVIIth FECTS (July 27th - 31st 2002). The Secretary noted that if any member wanted to help with the organisation they should contact her immediately.
 - Sally Roberts questioned why the Committee had decided not to hold a BSMB meeting as she thought that many students, for financial reasons, might not be able to attend. The Secretary replied that the cost of the meeting was being kept low to encourage student attendance and that any surplus money would be used as a rebate to these students. Additionally the Committee felt that they did not have enough energy to devote to both the organisation of the FECTS and BSMB annual meetings.
 - SR then asked if the BSMB would sponsor one day meetings to which the Secretary/Chairman replied that the BSMB would support and publicise but not organise these one day meetings.
 - Vic Duance asked whether the BSMB held annual meetings in 1986 when they previously sponsored the FECTS. As no one knew the answer the Secretary was actioned.

There was no other questions.

4. Treasurer's report

The Treasurer's report is attached. There was some discussion over the amount of money we had in surplus and several suggestions were received from the floor as to how we could utilise the spare funds (e.g. fund more Bursaries, increase the number of International Speakers, fund wine and cheese at the poster viewing). TH noted that we should be less cautious. However RM suggested that as we may lose money on the FECTS that we should review the financial status of the BSMB after that meeting. This was agreed by the membership in attendance.

Action: The Secretary to ensure that this is revisited after the finances of the FECTS are completed.

5. Election of Chairman and New Committee Members

The Secretary reported that the current BSMB Committee is as follows:

Officers: Chairman, Prof. Tim Hardingham (University of Manchester); Honorary Treasurer, Dr. Jay Dudhia (The Royal Veterinary College, London); Honorary Secretary Dr. Rose Maciewicz (AstraZeneca Pharmaceuticals).

Elected Members: Dr. Jo Lewthwaite (Eastman Dental Institute, UCL); Dr. Ian Clark (University of East Anglia); Dr. Anthony Day (University of Oxford); Dr. Alison Reith (University of Bergen, Norway) and Dr. Norman McKie (Medical School, University Newcastle-upon-Tyne) and Dr. Anthony Hollander (University of Bristol).

One Committee member, Dr. Jo Lewthwaite was due to retire in Spring 2001. The Committee received only one nomination for this position: Dr. Graham Riley (Soft Tissue Injury and Repair Group, Addenbrookes Hospital). As this was the only nomination a postal ballot was not held. The Secretary thus welcomed Dr. Riley to the Committee and thanked Dr. Jo Lewthwaite for all her work on behalf of the BSMB Committee.

The Secretary noted that the Chairman, the Treasurer and four Committee members (Dr. Ian Clark (University of East Anglia); Dr. Anthony Day (University of Oxford); Dr. Alison Reith (University of Bergen, Norway) and Dr. Norman McKie (Medical School, University Newcastle-upon-Tyne) were due to retire in Spring 2002. She noted that such a large re-organisation during the year we were organising FECTS was problematic and sought feedback from the membership. Several suggestions were noted:

- extend the position of Chairman and Treasurer by 1 year
- keep 2 out of the 4 Committee members
- co-opt departing committee members for the FECTS year.

It was agreed that the Committee would come up with an acceptable way forward (bearing in mind our Constitution); circulate this to the membership seeking general agreement.

Action: The Secretary to ensure the Committee implements this plan.

6. Any other business

The Secretary noted that the 2002 BSMB AGM would be held at the XVIIth FECTS as there was not to be a Spring BSMB meeting. However in 2003 the AGM would be held at the Spring meeting.

There was no other business.

The meeting was concluded at 17:52.

The Impact of Proteinases on Matrix Biology
British Society for Matrix Biology, Autumn 2001 BSMB Meeting
3rd / 4th September 2001
University of East Anglia, Norwich

Monday 3rd September

Registration: from 11:00, LCR, Student's Union Bldg

Introduction Lecture Theatre 3, 1300 - Ian Clark

Session 1:

- 13:15 - 14:00 Voon Wee Yong, U. Calgary, Canada: MMPs in the CNS - friend or foe?
- 14:00 - 14:45 Drew Rowan, U. Newcastle, UK: The effects of IL-17 on cartilage and chondrocytes
- 14:45 - 15:30 John Iredale, U. Southampton, UK: Recovery from liver fibrosis: matrix degradation and the fate of the hepatic stellate cell
- 15:30 - 16:10 Coffee and Poster viewing

Session 2:

- 16:10 - 16:50 Shu Ye, U. Southampton, UK: Polymorphisms in MMP and TIMP genes
- 16:50 - 17:30 Vince Ellis, UEA, Norwich, UK: Mechanisms regulating plasmin generation in the pericellular environment
- 18:30 - 20:00 Wine reception and SCVA gallery viewing
- 20:00 Conference dinner, Sainsbury Centre

Tuesday 4th September

Session 3:

- 09:15 - 09:55 Micky Tortorella, Kennedy Institute, UK: The role and regulation of ADAM-TS4 (Aggrecanase-1) and ADAM-TS5 (Aggrecanase-2) in cartilage catabolism
- 09:55 - 10:15 Deepa Nath, UEA, Norwich, UK: Regulation of ectodomain shedding through activation of different cell surface receptors
- 10:15 - 10:35 Zara Poghosyan, UEA, Norwich, UK: Adamalysins and tyrosine kinases: a tale of tails
- 10:35 - 11:15 Coffee and Poster viewing
- 11:15 - 12:15 4 x poster talks
- 12:15 - 13:45 Lunch LCR

Session 4:

- 13:45 - 14:30 Andy Baker, U. Glasgow, UK: Death by TIMP-3: Insights into mechanisms and exploitation in gene therapy for disease
- 14:30 - 15:15 Kevin Leco, U. Western Ontario, Canada: Development of the mouse lung in the absence of TIMP-3

BSMB AUTUMN MEETING, 3RD & 4TH SEPTEMBER 2001
UNIVERSITY OF EAST ANGLIA, NORWICH
THE IMPACT OF PROTEINASES ON MATRIX BIOLOGY

Registration Form:- (*Please write or type in CAPITALS*)

Family Name:.....**First**

Name:.....(**Prof/Dr/Mr/Mrs/Ms**)

Correspondence

Address:.....

.....

.....**Postcode:**.....

Country.....

Tel:**Fax:**.....**E-mail~:**.....

Special Dietary Requirements (e.g. vegetarian):.....

REGISTRATION FEES:

Registration

BSMB members: £30

(Fee includes coffee both days; lunch on Tuesday)

Non-members: £40

(registration includes 1 year membership of BSMB)

Accommodation: £20 per night including Breakfast

Sunday 2nd

Monday 3rd

Tuesday 4th

Wine Reception, Art Gallery & Conference Dinner: £20

(Monday 3rd September, Sainsbury Centre for Visual Arts, Norwich)

TOTAL ENCLOSED = *£.....

(All cheques should be made payable to "British Society for Matrix Biology")

Please return registration form to:-

Dr Ian M Clark
AstraZeneca Pharmaceuticals
Room 2F5
Alderley Park
Macclesfield
Cheshire. SK10 4TG.

For further information, call Ian Clark on: 01625-519834 or e-mail: Ian.M.Clark@astrazeneca.com

CLOSING DATE FOR RECEIPT OF REGISTRATION FORM: FRIDAY 3rd AUGUST 2001.

INSTRUCTIONS FOR SUBMISSION OF ABSTRACTS

THE BRITISH SOCIETY FOR MATRIX BIOLOGY
University of East Anglia, Norwich, September 3rd/4th 2001

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

Abstracts with incomplete information (e.g. complete references) will NOT be published

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 Friday 3rd August 2001. Abstracts (4 hard copies PLUS electronic copy, either on floppy disc, or by email as an attached file) should be submitted to:

Dr Ian M Clark,
AstraZeneca Pharmaceuticals,
Room 2F5,
Alderley Park,
Macclesfield
Cheshire. SK10 4TG.

e-mail: Ian.M.Clark@astrazeneca.com

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**).

Those selected for oral presentations (10 min + 5 min discussion) will be notified in the week commencing 20th August 2001. **Poster boards and fixings will be supplied.**

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
- a one page *curriculum vitae*, to:

BSMB Secretary
 Dr Rose Maciewicz, Senior Principal Scientist
 Respiratory and Inflammation Research Department, AstraZeneca 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 the start date of the meeting for which the bursary application is being applied. Applicants will be informed as soon as possible and should not await such notification before submitting their Conference application.

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

Address.....

.....

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.....

APPLICATION FOR MEMBERSHIP

To be completed in **BLOCK CAPITALS** and returned to the Secretary

Secretary: Dr Rose Maciewicz, Respiratory and Inflammation Research Department, AstraZeneca Pharmaceuticals, Alderley Park, Macclesfield, Cheshire, SK10 4TG UK

email: rose.maciewicz@astrazeneca.com

Please include appropriate membership fee.

Name.....
ADDRESS.....
TEL.....FAX.....
EMAIL.....

SPONSORING MEMBERS (*Should you not know any member of the Society personally, please write to the Secretary.*)

Name.....Name.....
Signature.....Signature.....

SIGNATURE OF APPLICANT.....

Please indicate ✓

MEMBERSHIP FEES: **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.

DO NOT DETACH

BANKER’S ORDER

To: (name and address of your bank)

Please pay on the **1st January** to **National Westminster Bank plc**, City of London Office, P.O. Box 12258, 1 Princess St., London, WC2R 8PA

Code No. 60-00-01T, the sum of £.....(.....POUNDS)

for credit to the account of the **BRITISH SOCIETY MATRIX BIOLOGY**, Account No.

09670343 quoting reference no.(leave blank, for BSMB records only)and make similar payment annually on the 1st January until this order is cancelled in writing, charging such payments to:

my/our.....account numbered.....

Signature.....Date.....