

REPORT ON THE BRITISH CONNECTIVE TISSUE SOCIETY MEETING Leicester University, 21st and 22nd September, 1998

Leicester University hosted the Biochemical Society Glycobiology Group/BCTS joint colloquium entitled, 'The Biology of Hyaluronan' on the main campus. Up to 100 delegates from all corners of the world registered for the meeting. Speakers were invited from laboratories in the UK, USA, Sweden, Finland, Canada and Germany. The meeting was organised by Professor Tim Hardingham and Dr. John Sheehan from The Wellcome Trust Centre for Cell Matrix Research, Manchester. Financial support for the Symposium was provided by Arthritis Research Campaign, Seikagaku Corporation, Biomatrix Inc., Pfizer and Zeneca.

The scientific programme was divided into sessions describing (1) the bacterial and mammalian hyaluronan synthase (HAS) family (2) the biosynthesis of HA (3) the structure and biophysical behaviour of HA (4) biomedical applications of HA (5) interactions of HA with the HA binding protein, TSG-6, and the HA receptors, CD44 and RHAMM, in the role of HA in the regulation of cell differentiation during embryogenesis and in extracellular matrix organisation.

Paul Weigel (Oklahoma, USA) presented data on hyaluronan synthases from *Streptococcus pyogenes*. Radiation induced inactivation of the bacterial HAS predicted a higher molecular weight for the active species than would be expected from the amino acid sequence. Bovine cardiolipin could stimulate bacterial HAS activity and was shown to be important for HAS function. A pore consisting of HAS protein and 16 cardiolipin molecules (responsible for the extra mass in the inactivation experiments) was put forward as a possible model for the membrane bound complex.

Andrew Spicer (Davis, USA) continued the discussion of the HAS family focussing on mammalian HAS1, 2 and 3. HAS cDNA expression in transfected mammalian cells indicated different catalytic activities for the 3 enzymes and a much shorter HA chain length synthesised by HAS 3, which was independent of substrate concentration. All three HAS genes had been inactivated by gene targeting to produce HAS1, 2 or 3 deficient mice. HAS 1 and 3 null mutants appeared normal, whereas the HAS 2 knockout was lethal at around embryonic day 10 of development. Embryos had a very poor blood supply, due to inadequate yolk sac blood vessel development, and massively enlarged hearts and pericardial sacs.

In the following session **Evi Heldin** (Uppsala, Sweden) discussed how TGF- β , PDGF and TPA affected the regulation of HA-synthases. All three agents stimulated HA synthesis in mesenchymal cells. In mesothelial cells and human lung fibroblasts, PDGF BB upregulated the steady state mRNA level for HAS 2. HAS 1 expression monitored by in situ hybridisation was strong in the epithelium of skin. Some additional signal was seen in the papillary dermis following burn injury, and in inflammatory cells and around sweat glands and blood vessels in healing skin.

Vince Hascall (Cleveland, USA) then outlined the aetiology of inflammatory bowel disease which leads to a loss of structural organisation of colonic crypts. Using an assay where leucocyte adhesion to the pericellular coat of smooth muscle cells was measured it was shown that TNF α and Poly I:C (a synthetic dsRNA used as a virus mimic), could increase leucocyte binding. The TNF induced binding could be inhibited by an anti VCAM-1 antibody indicating a probable VCAM - integrin binding. The Poly I:C induced binding was not inhibited by this antibody, but was reduced with a hyaluronidase digestion. This binding was probably mediated through CD44 (leucocyte) and increased by upregulating the HAS-2 system (smooth muscle cells). A separate investigation of mouse cumulus oocyte cells using quantitative PCR demonstrated that the copy number of HA-synthases was comparatively low at 50 per cell reaching a maximum of 350 per cell during expansion of cumulus cell layer matrix.

The role of inter-cellular HA in the epidermal compartment was then discussed by **Markku Tammi** (Kuopio, Finland) using results from a human keratinocyte culture model. The half-life of HA in the epidermis was shown to be comparatively short at 1 day. Displacement of the HA network could be achieved by incubating tissue with HA decamers but not hexamers, although the maximum displacement was only 50%, and 2 pools of HA were proposed. Quantitative microscopy showed that some anti-CD44 antibodies could reduce the proportion of bound HA in the epidermis, suggesting a role for this receptor in stabilising hyaluronan pericellular networks.

The first afternoon session focused on the biophysical aspects of hyaluronan behaviour. **Tony Day** (Oxford, UK) gave an overview of the hyaladherin family and its common structural domain, the link binding module. Data from isothermal scanning calorimetry demonstrated that HA oligosaccharides of octamer size or larger bind recombinant link module with a K_d of 0.3 μ M. Mutation studies showed 4 amino acids were critical to this binding and that the fully folded protein gave maximal binding efficiency. Further NMR structural studies showed the binding surface to be conserved. Binding was also shown to be pH sensitive and mechanisms for the inhibition of aggrecan aggregation during the inflammatory response were discussed.

John Sheehan (Manchester, UK) then reminded the audience of fibre X-ray crystallography studies which showed the counterion dependence of HA helical structural arrangements. He then presented a new computational molecular modelling approach to understanding the role of intra-chain hydrogen bonding and the interaction of water molecules with hyaluronan and demonstrated that although stiff, hyaluronan has comparatively high intra-chain mobility over short time scales.

The hydrodynamic and network properties of higher molecular weight HA and aggrecan, measured using the confocal-FRAP technique, were then compared by **Tim Hardingham** (Manchester, UK) and related to their structural

properties. The relative contributions of electrostatic repulsion and hydrogen bonding to the intrinsic chain stiffness of hyaluronan was measured in experiments at high pH and the impact of hydrogen bonding was shown to be more important. Divalent counterions, especially Ca^{2+} , were also able to significantly further de-stiffen hyaluronan.

In the special lecture that followed **Endre Balazs** (New Jersey, USA) introduced the audience to some of the medical applications of hyaluronan and cross-linked hyaluronan gels, including viscosupplementation, viscoprotection and viscoaugmentation. The importance of using non-inflammatory material with the minimum proportion of protein contaminants was emphasised, as was ensuring that the molecular weight chosen matched the property required of the gel or solution. The pharmaceutical action of hyaluronan in viscosupplementation studies was then postulated to arise from the temporary return of correct joint articulation which gives an opportunity for the joint to restore homeostasis.

Andrew Pitsillides (London, UK) discussed the role of HA in joint cavitation using embryonic chick diarthrodial joints as a model system. Data were presented demonstrating that effective joint cavitation involved co-ordinated changes in synthesis of HA, CD44 expression and molecules involved in cytoskeletal assembly. Manipulation of joint cavity development, using HA oligosaccharides or immobilisation, disrupted joint formation, decreased HA synthesis and expression of CD44 and actin filaments. Movement-induced stimuli played an essential role in both formation and maintenance of the joint cavity.

Gary Douthwaite (Cardiff, UK) gave the first of four short presentations. He continued with the theme of the role of movement-induced stimuli in joint cavitation, showing changes in the phosphorylation status of CD44 and cytoskeletal organisers when developing joints were placed under strain.

Paul Noble (Yale, USA) described the differential biological properties of high and low molecular weight HA on the regulation of mouse alveolar macrophage activation. Low molecular weight HA (<200, 000 Da), but not high molecular weight HA, induced the expression of several genes including $\text{TNF}\alpha$, $\text{IL-1}\beta$, VEGF, IL-12 and iNOS. Anti-CD44 monoclonals abrogated HA fragment-induced gene expression.

David Jackson (Oxford, UK) described a novel 80 kDa HA receptor on human lymph vessel endothelium (LYVE-1) which shares 30% sequence identity with CD44. Discovered by homology searching expressed sequence tag databases, recombinant LYVE-1 was shown to bind HA in a solid phase plate assay. A polyclonal antiserum was prepared and used to screen tissue for LYVE-1 distribution. LYVE-1 was expressed in large amounts on lymphatic vessels suggesting a role for this HA receptor in the transport and clearance of HA from the lymphatic system.

Rod Levick (St. Georges, London, UK) discussed the function of HA in the synovial cavity and its role in determining the flow and diffusion of fluids and solutes. In-vivo kinetic studies showed hyaluronan was selectively maintained in the joint cavity, probably through the action of a molecular sieving mechanism. Hyaluronan also acted as a flow limiter, resisting the efflux of water through the synovial membrane, probably because of concentration polarisation. A mathematical model was presented which appeared to accurately describe many of the experimental observations.

Eva Turley (Toronto, Canada) concentrated her presentation on HA binding molecules that do not contain the link module binding motif, in particular the molecule RHAMM. The complicated splice variant pattern encoding multiple protein forms of RHAMM could vary greatly with cell culture conditions. Two receptors were found for RHAMM isoforms that encode an alternatively spliced exon 4; RHAMM and RHAMMv4. RHAMM occurs both on the cell surface and in the cytoplasm. Epitope tagging experiments showed that RHAMMv4 occurs only in the cytoplasm. RHAMM and RHAMMv4 are involved in the regulation of extracellular-regulated kinase (ERK) activity. Over expression of RHAMMv4 enhances expression of ERK.

Cheryl Knudson (Chicago, USA) described the role of HA in chondrocyte pericellular matrix assembly. HA hexamers or CD44 antibodies could inhibit chondrocyte matrix assembly. Pericellular HA, but not CD44, could be removed using *Streptomyces* hyaluronidase. CD44 was shown to be localised predominantly to the cytoskeleton suggesting a role for intracellular signalling in chondrocyte-matrix interactions.

Hans-Georg Wisniewski (New York, USA) gave an update on the structure and functions of TNF-stimulated gene 6 (TSG-6). The TSG-6 gene encodes a 28 kDa polypeptide which is secreted as a 35 kDa glycoprotein. There are two structural domains; an N-terminal link module with HA binding activity and a C-terminal CUB domain. The TSG-6 gene can be induced 3-4 h after exposed to inflammatory cytokines such as $\text{IL-1}\beta$ or $\text{TNF}\alpha$. Recombinant TSG-6 exerted anti-inflammatory effects in a murine air pouch model of inflammation. Link module mutants, prepared using site-directed mutagenesis, abrogated anti-inflammatory properties of TSG-6. TSG-6 forms a stable complex with the plasma protein inter- α -inhibitor ($\text{I}\alpha\text{I}$). The function of TSG-6/ $\text{I}\alpha\text{I}$ remains unclear.

Helmut Ponta (Karlsruhe, Germany) described the complex variants of CD44 and how CD44 / HA interactions may be important in haematopoietic differentiation. Long term bone marrow culture experiments suggested that HA was important for myelogenesis in this system, possibly as a result of HA stimulated production of IL-6 by bone marrow macrophages, although it was still effective in CD44 knockout mice.

**REPORT ON THE XVIth MEETING OF THE FEDERATION OF THE EUROPEAN
CONNECTIVE TISSUE SOCIETIES (FECTS)
1st to 6th August 1998, University of Uppsala, Sweden.**

The recent XVIth FECTS meeting was held in the picturesque university town of Uppsala in Sweden. The opening lecture and plenary lectures were given in the Main University Building, which was located within the heart of Uppsala, while the poster sessions and workshops were conducted in the new Biomedical Centre on the edge of the city.

The meeting opened in the majestic main auditorium of the Main University Building, with its high domed gault painted ceilings dating from 1887. We were given a historical introduction to the University of Uppsala which, since its foundation in 1477, has produced an environment for the advancement of science through people such as Carolus Linnaeus, Anders Celsius and Anders Ångström and has been the home of several Nobel Prize winners.

The opening lecture was given by **Erikki Ruoslahti (USA)** who addressed the question of how normal cells find their specific location in the body, while tumour cells locate less specifically. Phage techniques were used to isolate peptides which were capable of homing to the vasculature of a range of normal tissues. These peptide motifs, displayed on phage, were injected into mice and their tumour homing abilities assessed. The peptide motifs RGD, NGR and GSL directed the phage to the tumour. The process of tumour homing was shown to be independent of the tumour origin but dependant upon the angiogenic characteristics of the tumour vasculature. These therapeutically important findings showed that coupling the drug doxorubicin to the tumour homing peptides, RGD and NGR, enhanced anti-tumour activity while decreasing toxicity of this drug in mice.

The main programme commenced on Sunday 2nd August with a series of lectures relating to Glycobiology. **Colin Hughes' (UK)** presentation on the Galectin family, described a group of galactose binding proteins. Galectin-3, the focus of the presentation, was detected in macrophages, branching epithelia and kidney tubules. It has an involvement in establishing epithelial polarity and regulating matrix biosynthesis in kidney development. Functioning as both an antagonist and promoter of cell adhesion, galectin-3 bound to integrins, laminin, fibronectin and tenascin. In the kidney, galectin-3 was regulated during development. A polarised distribution was observed which switched from an apical to basal location on epithelial cell maturation. In renal cysts, galectin-3 localised to the luminal apical surface where it activated other adhesion systems via cadherins.

Henric Clausen (Denmark) discussed the biosynthesis of glycoconjugates via glycosyltransferases. The formation of several glycosidic linkages are now known to be formed by multiple homologous glycosyltransferases with multiple enzymes forming the same linkage. Studies focussed on the polypeptide GalNac-transferases which initiate mucin-type O-glycosylation by attaching GalNac to selected serine or threonine residues. Kinetic studies demonstrated these transferases have specific, as well as overlapping functions. Mucin-type O-glycosylation was shown to have a complex regulation which had a large genetic back up suggesting partial redundancy of the genes.

Markku Jalkanen (Finland) described structural variations of the proteoglycan syndican-1 which was shown to be dependant upon the location of the side chains along the core protein. These side chains also modulated syndican's role as a co-receptor. The syndicans were shown to undergo signal transduction following complex formation with cell surface receptors. The expression of syndican was controlled within developing tissues and differentiating cells. The recently identified FGF-inducible response element (FiRE) was described, which was shown to be activated by FGF in mesenchymal cells. FiRE was also implicated as responsible for upregulating syndican-1 in keratinocytes during wound healing and tissue regeneration.

The proteoglycan theme was continued by **Arthur Lander (USA)** who discussed the role of the glypican heparin sulphate carrier proteins in the developing brain. Glypican 1 and 2, and syndican-3 were expressed in the brain neuron in both developing and adult tissue. Conserved protein domains within glypican-1 regulated glycosylation and directed the polymerisation of heparin sulphate but not chondroitin sulphate chains. Data from a slice culture system indicated that chondroitin sulphate proteoglycan (CSPG) could have either an inhibitory or stimulatory effect on axon growth and cell adhesion. This effect was dependant upon the location within the brain. CSPG was proposed as responsible for organising the presentation of molecules by the ECM in the developing brain.

The first day of the meeting concluded with poster sessions and workshops on Proteoglycans, Cell-cell and cell matrix adhesion and Tissue regeneration and repair.

Monday 3rd August began with a series of lectures associated with Developmental biology.

Liselotte Fessler (USA) introduced us to the ECM proteins tiggren and papilin found in the Drosophila, which are not detected in vertebrates. ECM was detected early on in Drosophila development, prior to tissue specification. Laminin, papilin and tiggren, in association with integrins, separated the mesoderm and ectoderm. These proteins regulated cell migration and differentiation. The basement membrane in Drosophila acts as a covering by surrounding nerve cord, brain, gut and muscles and is not functional in determining which cells form specific organs.

Charles Streuli (UK) discussed the importance of the basement membrane (BM) in mouse mammary epithelial cells for maintaining cellular phenotype, regulating differentiation and apoptosis and controlling cell signalling pathways.

Association of prolactin with its receptor, induced Jak2 protein tyrosine kinase activity and activated the Stat5 transcription factor in this mammary epithelial cell system. BM was shown to be required for prolactin-dependant transcription of milk protein genes via the activation of Stat5 and directly affected growth factor signalling and differentiation at the plasma membrane. Apoptosis in cultured mammary epithelial cells was inhibited in the presence of BM mediated through the $\alpha 6$ and $\beta 1$ integrin subunits. Insulin signalling was shown to be regulated by cell-matrix interactions in mammary epithelia.

The *in vivo* function of the stable complex formed between laminin and nidogen-1 in basement membrane assembly and in embryogenesis was the topic of the presentation by **Ulrike Mayer (Germany)**. Nidogen-1 was shown to bind to the laminin $\gamma 1$ chain via a single module $\gamma 1$ III4. Knockout mice, in which the nidogen-binding $\gamma 1$ III4 module of the LAMC1 gene had been deleted, did not survive at birth. The majority of these animals had no kidneys and those which had one or two kidneys present were pathologically abnormal. Small lung size and reduced epithelial branching was observed in the knockout mice. Further characterisation of this mouse model is ongoing but the preliminary studies have shown that laminin requires nidogen-1 binding for both organ development and survival.

Doris Wedlich (Germany) discussed the role of β -catenin in Xenopus development. β -catenin binds to cadherins and mediates cell adhesion. It can also transduce the Wnt/Wg signal to target genes. The Wnt/Wg signal modified the mesoderm in Xenopus development. Prior to mid blastula transition it had a dorsal function whereas after mid blastula transition it had a ventral function. The mesenchymal genes cadherin-11, $\alpha 3\beta 1$ and fibronectin were also regulated by the Wnt/Wg signal. Wnt/Wg appears to regulate cross-talk during cell-cell and cell-substrate adhesion.

The day concluded with poster sessions and workshops on Collagens, Cartilage, and ECM contacts and cell signalling.

Tuesday 4th August got underway with a series of lectures on Matrix Receptors. **Michael Henry (USA)** described the role of dystroglycan in early development. Dystroglycan has the ability to bind to numerous sites in laminin leading to a wide variety of potential complexes. The dystroglycan knockout mouse was found to die at the embryonic stage. Studies were also performed using dystroglycan null embryonic stem cells. Dystroglycan was found to be essential for early development beyond the egg cylinder stage, being required for kidney morphogenesis, laminin binding and basement membrane formation. Collagen IV, perlecan, laminin and nidogen all showed disrupted localisation patterns.

Tero Pihlajaniemi (Finland) reported findings which showed that type XIII collagen was located at the focal adhesions in cultured fibroblasts and at the myotendinous junctions and intercalated disc on human and mouse tissue. Mutant type XIII collagen in transgenic mice was embryonically lethal. It was postulated that type XIII collagen may be involved in cell adhesion to the ECM or act as a receptor for soluble ligands.

Spliced variants of the $\beta 1$ integrin were shown by **Guido Tarone (Italy)** to have important functional properties. The $\beta 1B$ isoform prevented cell adhesion, cell spreading, focal adhesion, fibronectin matrix assembly and epithelial cell organisation while the $\beta 1D$ isoform was a potent adhesive receptor which associated with the actin cytoskeleton and was actively involved in ECM assembly. Tyrosine phosphorylation was also identified as important for the organisation of adhesion molecules. Antibodies against integrin disrupted actin organisation in endothelial cells. Integrin mediated signalling pathways resulted in actin cytoskeleton organisation and regulated matrix-cytoskeleton linkage.

Arnoud Sonnenberg (The Netherlands) continued the theme of integrins in his presentation which discussed the role of the $\alpha 6\beta 4$ integrin in hemidesmosomes, which adhere epithelial cells to the basement membrane. The $\alpha 6\beta 4$ binds to laminin-5 in the ECM and to plectin, which binds directly to the keratin 5 and 14 within the cell cytoskeleton. $\beta 4$ knockout mice showed blistering and skin detachment and lacked hemidesmosomes. $\beta 4$ was shown to be responsible for the localisation of HD1/plectin and BP180 in hemidesmosomes. Studies involving the yeast hybrid system showed the actin binding region of plectin to be involved in binding $\beta 4$ as well as direct binding between BP180 and $\beta 4$. Parallel studies on patients with junctional epidermolysis bullosa showed a decreased number of hemidesmosomes and a lack of $\beta 4$ integrin.

Delegates were given the rest of the day at leisure to explore the delights of Uppsala and its surroundings.

Wednesday 5th August commenced with a series of lectures associated with Genetic Disorders. The presentations commenced with **Jacky Bonaventure (France)** who described skeletal disorders caused by mutations in FGF receptors. Crouzon syndrome, which results in facial and skeletal deformations, showed abnormalities in both the FGFR1 and FGFR2. Dwarfism was caused by mutations in the FGFR3 gene while craniosynostosis syndromes were caused by mutations in FGFR1, 2 and 3. FGFR1 and 2 were detected at the onset of bud formation in the foetus while FGFR3 was expressed later in development in mature chondrocytes. Thanatophoric dwarfism chondrocytes showed increased apoptosis with both MAPK and STAT pathways activated in these cells.

Eva Engvall (USA) gave a presentation on *in vitro* models for muscular dystrophy. Congenital muscular dystrophy shows an abnormal basement membrane as an effect of defects in the laminin $\alpha 2$ subunit. Laminin $\alpha 2$ has a role in cell survival and provides structural support for contracting myocytes in differentiating embryonic stem cells. Transgenic mice showed abnormal muscle histology and increased paralysis in their hind legs and essentially showed muscular dystrophy and extensive fibrosis. The parallels between the mouse model and the human disease make it suitable for assessment of future treatments for human muscular dystrophy.

Karl Tryggvason (Sweden) told us about the newly identified transmembrane protein nephrin, which has been identified in the glomerular basement membrane in the kidney. The leakage of proteins across the glomerular basement membrane silt diaphragm is documented in renal diseases such as nephrotic syndrome. Nephrin was immunolocalised to the podocytes in the silt membrane and is a major constituent of the glomerular basement membrane. It appears to play an important role in the glomerular size-selective filtration barrier and it is likely that it is present in other diseases which have proteinuria.

The fourth afternoon comprised poster sessions and workshops on Diseases of the ECM, Basement membranes and Metalloproteinases and their inhibitors. The conference banquet was held in the main hall of Uppsala Castle where we enjoyed an evening of traditional Scandinavian food and entertainment.

The final day of the meeting began with a series of lectures on Pathophysiology.

Harald Burkhardt (Germany) presented data on a collagen-induced arthritis as a model for rheumatoid arthritis. Collagen – induced arthritis was shown to be associated with T-cell recognition of collagen II peptides. This model was dependent upon collagen II existing in its native conformation at immunisation and upon the presence of functionally active B cells. A panel of recombinant chimeras of collagen II were used to identify the epitopes which reacted in arthritic mice. Immunodominant domains were numerous, highly organised and spread along the length of the collagen molecule. These studies provided an insight into the autoimmune response to collagen II in joints.

Rolf Reed (Norway) described the exchange of fluid across the capillary epithelial and the resultant pressure created across the ECM. This interstitial fluid pressure (Pif) was studied during edema formation in burn injuries and in an experimental rat model where dextran was injected. In both these situations the Pif decreased. Blocking cellular responses to ECM using antibodies against $\beta 1$ integrin or $\alpha 2\beta 1$ integrin also decreased the Pif. Tissue swelling and the contractile force exerted by the ECM were in equilibrium, when the contraction process was blocked by integrin antibodies, swelling occurred and this was balanced by a further decrease in Pif. Incorporation of PDGF into this system also decreased the Pif.

The penultimate presentation by **Christer Betsholtz (Sweden)** described the role of PDGF in development. PDGF activates cell signalling via receptors PDGFR α and β . Knockout mice for PDGF-A, PDGF-B, PDGFR α and PDGFR β were lethal at either the embryonic or early neonatal stages of development due to defects associated with the mesenchymal cells. PDGF-B and its receptor were required for the development of smooth muscle and vascular endothelial cells and played an important role in cell migration. PDGF-A and its receptor were required for the development of smooth muscle cells associated with epithelial cells in the lung and intestine.

Gerard Karsenty (USA) spoke on osteoblast differentiation during bone remodeling. *Osf2*, a recently identified protein which binds OSE2 in the osteocalcin promoter, was shown to be expressed in the developing skeleton. During mesenchymal condensation it was restricted to osteoblastic cells. *Osf2* regulated the expression of many genes expressed by osteoblasts. *Osf2* was found to act as an osteoblast-specific transcription factor and as a regulator of osteoblast differentiation.

The meeting concluded with poster sessions and workshops on Inflammatory diseases of the joints, Structure and function of ECM and Development.

The FECTS meeting was well supported with 594 participants, comprising 50 delegates from the UK.

The Business Meeting the FECTS was held on Wednesday 5th August which discussed the successes and failures of the current meeting. The only criticism was that posters were displayed for only one afternoon, on the same day as the appropriate workshop, giving insufficient time for viewing as poster sessions were held in a separate location from the plenary lectures. It was felt that meeting had been well organised and had been a success. Presentations were heard from representatives from the Italian and Greek Connective Tissue Societies respectively as possible venues for the next FECTS meeting in 2000. This was put to a vote and the venue in Greece was duly selected.

Alison Reith

CONSTITUTION OF THE
BRITISH SOCIETY FOR MATRIX BIOLOGY

GENERAL

1. The Society shall be called the British Society For Matrix Biology.
2. A. The objects of the Society shall be as follows:
 - a) To advance the science of connective tissue and related subjects;
 - b) To further public education therein;
 - c) To promote study and research work on connective tissues and related areas and to publish the results of such study and research
- B. In furtherance of the above-mentioned objects but not further or otherwise, the Society shall have the following powers:
 - a) To diffuse information on all matters affecting connective tissue and related subjects and to establish, print, publish, issue, circulate and sell such papers, magazines, journals, books, periodicals and publications as shall be necessary to attain the objects or in any way beneficial to the work of the Society;
 - b) To act as an authoritative body for the purpose of consultation in matters of public and professional interest concerning connective tissue and related subjects;
 - c) To undertake and execute any charitable Trusts which may be lawfully undertaken by the Society;
 - d) To invest the moneys of the Society not immediately required for working purposes in such investments, including land, as the Executive Committee shall from time to time determine;
 - e) To establish and support or aid in the establishment and support of any charitable institutions having objects similar to those of the Society and to subscribe or guarantee money for charitable purposes in any way calculated to further the Society's objects;
 - f) To hold seminar, lectures, discussion groups, conferences and symposia;
 - g) To borrow and raise money for the purposes and for the promotion of the objects of the Society on such terms as the Executive Committee shall consider expedient in the interests of the Society;
 - h) To raise and invite and receive contributions from any person or persons whatsoever by way of subscriptions, donations and otherwise providing that the Society shall not undertake any permanent trading activities in raising funds for its primary charitable objects;
 - i) To make grants to young scientists to enable them to attend meetings;
 - j) To do all such things as shall further the above-mentioned objects or any of them.

OFFICERS AND EXECUTIVE COMMITTEE

3. The Honorary Officers of the Society shall be a Chairman, a Secretary and a Treasurer.
4. There shall be an Executive Committee of the Society consisting of the officers and of six other elected members. A quorum shall be six members, including two officers of the Society.
5. The Executive Committee shall prepare the Agenda for meetings of the Society, and between meetings shall act as necessary on behalf of the Society; it shall report on any such actions, as indicated, to the next meeting of the Society.
6. The Officers of the Society and the other six members of the Executive Committee shall be elected by ballot at an Annual General Meeting for a period of three years. Nominations may be made by the Committee or by any two ordinary members and shall be sent together with the written consent of the nominee to the Secretary, so as to reach him at least two months before the Annual General Meeting. Such nominations shall be circulated with the notice of the meeting. Members unable to attend the meeting shall be entitled to vote by post. If other nominations are not received for the filling of vacancies, the Committee's nominees shall be deemed elected.
7. The Chairman, Secretary and Treasurer shall not normally hold that office for a term of more than three years. In any case, they shall not hold that office for more than six consecutive years, but they shall be eligible for election to any other office in the Society.
8. Each year the two ordinary members of the Committee most senior in order of election shall retire from office and shall not be eligible for re-election for one year, except that he or she shall be eligible for election as one of the Officers of the Society.
9. Any vacancy occurring in the committee other than by annual retirement may be filled by another member of the Society to be elected by the Committee. The Committee will have power to co-opt additional members.

MEMBERSHIP

10. The Society shall consist of Ordinary Members engaged in or directing work of the nature indicated in Item 2A (or undertaking shortly to become so active), of Honorary Members, of Student Members and of Retired Members.
11. A candidate for Ordinary Membership or Student Membership of the Society may be proposed by two members, to whom he or she is known personally. The names and qualifications of these candidates must be sent to the Secretary on the form provided for this purpose, and the applications assessed by the Executive Committee. A list of the approved candidates will be presented for election by the membership at the Annual General Meeting or at an ordinary meeting of the Society.
12. When a person has been elected a member of the Society, the Secretary shall inform him of his election and shall send him a copy of the Rules.
13. The Executive Committee shall have the power to recommend to the AGM termination of a membership if such termination appears to them to be in the interests of the Society.
14. A student Member shall be a bona fide research student, normally under the age of 25, engaged in work of the nature indicated in Item 2A.
15. The Society may have Honorary Members. Nominations for Honorary Membership shall be presented by the Executive Committee for approval by members at the AGM.
16. Members may become Retired Members when they reach retiring age and should normally have been Ordinary Members for a least seven years.

FINANCE

17. Members shall pay to the Society an annual subscription, **payable in advance**, due on 1st January, the amount of such subscription being determined at an Annual General Meeting of the Society and continuing in force until changed at a subsequent one. The Committee shall have the power to terminate membership if a member fails to pay his subscription after due notice has been given. Honorary Members and Retired Members shall not pay the annual subscription.
18. The funds and estates of the Society shall be derived from the annual subscriptions of members, donations, grants and other endowments accepted by the Executive committee on behalf of the Society. They shall be administered by the Treasurer, acting on instructions given by the Executive Committee or by the Society at its Annual General meeting, for the furtherance of the objects of the Society.
19. The accounts of the Society shall be audited annually and a report made by the Treasurer to the Annual General Meeting.
20. In the event of the Society being dissolved for any reason, the surplus funds remaining after satisfaction of debts and liabilities shall not be distributed among the members but shall be paid or transferred to some other charitable institution of institutions having objects similar to those of the Society and which shall prohibit the distribution of its or their income among its or their members. Such institution or institutions shall be determined by the members of the Society at or before the time of dissolution, and if effect cannot be given to this provision, the surplus funds shall be devoted to some charitable object or objects.

MEETINGS

21. The Annual General Meeting (and, when necessary, an Extraordinary General Meeting) shall be held at a place and time decided by the Committee. The Secretary shall circulate the Agenda to all members at least one month before the meeting. An Extraordinary General Meeting may be called by twenty ordinary members of the Society. At least two months notice to the Secretary must be given.
22. Scientific meetings and symposia relating to the objects of the Society shall be arranged from time to time by the Committee. One such meeting may immediately precede or follow the Annual General Meeting, and at each AGM the Committee shall submit proposals for the dates of such meetings to be held during the ensuing twelve months. Reports of proceedings shall not be disclosed to the press, unless authorised by the Executive Committee.

ALTERATIONS TO CONSTITUTION

23. Any alterations to this Constitution shall be made only at a General Meeting of the Society, provided that notice of such alterations has been given on the Agenda of the meeting and that two-thirds or more of those voting on the alteration signify their assent. Members unable to attend the meeting shall be entitled to vote by post. Notice of any proposed alteration, duly seconded, shall be given to the Secretary at least two months before the meeting. No alteration shall be made to Clause 2, Clause 20 or this Clause and no alteration shall be made to the Rules which would cause the Society to cease to be a charity at law.

This constitution was approved and adopted by the Society on 19th September, 1980.

British Society for Matrix Biology & European Tissue Repair Society

The Molecular and Cell Biology of Wound Healing

St. Ann's College, Oxford

30th March -1st April, 1999

Organisers - For ETRS: Professor Keith Harding, Dr Keith Moore, Cardiff and Dr George W. Cherry, Oxford; For BSMB; Dr Malcolm Davies and Dr Robert Steadman, Cardiff

Programme

Tuesday 30th March

- 11.00-13.00 Registration and Lunch; posters to be put in place
- 12.50-13.00 Welcome and Introduction
- Session 1** Co-Chair;. Professors Mark Ferguson (Manchester) and Geoffrey Laurent (London)
- 13.00-13.25 **Professor Finn Gottrup** (Copenhagen)
Overview of the Clinical Aspects of Wound Healing
- 13.25-14.05 **Professor Richard Clark** (Stony Brook, New York)
- 14.05-14.30 Discussion
- 14.30-15.00 **Dr Keith Moore** (UWCM, Cardiff)
Inflammatory Cells in Wound healing
- 15.00-15:30 **Professor Alexis Desmouliere** (Lyon, France)
Myofibroblasts
- 15.30-16.00 TEA
- Session 2** Chairman; Professor Roger Mason
- 16.00-16.30 **Dr Jim McCarthy** (Minneapolis, Minnesota, USA)
Re-Epithelization
- 16.30-17.00 **Professor Andrew Newby** (Bristol Heart Institute, Bristol)
Response to Vascular Injury; Role of the Smooth Muscle Cell
- 17:00-17:30 **BSMB Annual General Meeting**
- 17:30-18.00 Poster viewing/ Trade Exhibition
- 19:00 Evening Meal St. Anne's College

Wednesday 31st March

- Session 3.** Chairman; Professor John Gallager
- 09.00-09.30 **Professor Thomas Kreig** (Koln, Germany)
Collagen
- 09.30-10.00 Hyaluronan (Speaker to be announced)
- 10.00-10.30 **Professor Merton Bernfield** (Harvard Medical School Boston)
Proteoglycans
- 10.30-11.00 Coffee
- Session 4**
- 11.00-11.30 **Dr Judith Capisi** (San Francisco)
Senescent fibroblasts
- 11.30-12.00 **Professor John Savill** (Department of Medicine, Edinburgh)
Apoptosis in Tissue Remodeling
- 12.0-12.30 **Dr William C. Parkes** (St. Louis, USA)
Metalloproteinases
- 12.30-13.00 **Professor Leif Lund** (Copenhagen)
Plasmin in Wound Healing
- 13.00-14.00 Lunch
- Session 5**
- 14.00-14:30 BSMB Young Investigator Award Lecture
- 14:30-15.00 Presentations selected from posters
- 15.00-15.30 Guest lecture; **Professor Alan Hall** (London)
- 15.30-16.00 **Dr Paul Martin** (London)
Epidermal Movement in Embryonic Wound Healing
- 16.00-16.30 Tea
- Session 6**
- 16.30-17.00 **Professor Martin Humphries** (Manchester)
Fibronectin
- 17.00-17.30 **Professor Fionna Watt**
Keratinocytes
- 17.30-19.30 Drinks, posters etc.
- 20.00 Conference Dinner

Thursday 1st April

Session 7 Co-Chairman; Professors Tim Hardingham & Keith Harding

09-30-10.00 **Dr Jill Helms** (San Francisco)

Hedgehog genes in skeletogenesis and wound repair

10.00-10.30 **Professor Charlie Archer** (Cardiff)

Cartilage repair responses

10.30-11.00 Coffee

11.00-11.30 **Dr Gillian Ashcroft** (Baltimore & Manchester)

Hormones and tissue repair

11.30-12.00 **Dr Sharon O'Kane** (Manchester)

Knockout models and wound healing

12.00-13.30 Lunch

Session 8 Chairman; Dr RAF Clark & Professor Mark Ferguson

13.30-14.00 **Professor John D Williams** (UWCM, Cardiff)

Wound healing in the peritoneum

14.30-14.30 **Dr David W Thomas** (Dental School, UWCM, Cardiff)

Oral mucosal and wound healing

14.30-15.00 **DA McGrouther** (London)

Healing in Surgical Wounds

15.00-15.30 Summary and conclusions

Dr RAF Clark, Professor Mark Ferguson

End of Meeting

NOTES FOR REGISTRATION AND POSTER PRESENTATION

Registration forms with full payment must be returned by Monday 15th February 1999 to:

Dr George Cherry
Wound Healing Institute
Department of Dermatology
The Churchill Hospital
Headington
Oxford, OX3 7LJ
Tel: +44 (0)1865 228269

Abstracts and a copy of the registration form must be returned by Monday 15th February 1999 to:-

Professor Malcolm Davies
Institute of Nephrology
Royal Infirmary
Newport Road
Cardiff, CF2 1SZ
Tel: +44 (0)1222 335292
Fax: +44 (0)1222 453643
e-mail: daviesm6@cf.ac.uk

The Conference venue is St Anne's College, Oxford (accommodation and conference dinner) and The Academic Centre, John Radcliffe Hospital, Headington, Oxford. The conference fee includes registration, transport to and from St Anne's College and the John Radcliffe, coffee and tea, lunch and the conference dinner. The registration desk will be in the entrance foyer of the John Radcliffe and will be open from 10 am on Tuesday 30th March, 1999.

There are approximately 200 rooms available at St Anne's and these will be allocated on a first come basis. Please note that this meeting is being supported by the European Tissue Repair Society and there is likely to be a demand on places. In the event that St Anne's is overbooked alternative accommodation is available. The lecture theatre at the John Radcliffe can cope with up to 300 delegates.

St Anne's College is situated on the Woodstock Road and is a short taxi ride from Oxford Railway and Bus Station (approx. £3.00). Directions on how to find the Academic Centre at the John Radcliffe Hospital are enclosed. Please note that NO parking is available at St Anne's College. Parking at the John Radcliffe is limited and on a 'Pay and Display' basis.

People attending the meeting are encouraged to submit abstracts for inclusion in the abstract booklet. Abstracts should be printed on a single side of A4 at 12 or 14 point and be suitable for photocopy reproduction. They should be marked in pencil on the reverse side "for abstract booklet". Abstracts can be forwarded for publication in the International Journal of Experimental Pathology. These abstracts should be marked in pencil on the reverse side "for publication" and additionally a copy of the abstract on computer disc should be provided to facilitate timely publication. Both types of abstract with a copy of the registration form should be sent to Professor Malcolm Davies. Abstracts should be structured with separate Introduction, Materials and Methods, Results, Discussion and Reference sections. The funding organisation should be clearly indicated. Complete references should be provided including full name and initials of each author, year of publication, journal name, volume number and full page details.

There will be some opportunities for short presentations (7 minutes + 3 minutes discussion). Please indicate your wish to give a presentation on the registration form. Those selected for oral presentations will be notified in the first week in March; please limit your talk to 4 slides or overheads. Poster boards (4 ft wide by 6 ft high) and fixings will be supplied.

Bursaries are available to members of the BSMB to assist young investigators to attend this meeting. Those requesting a bursary should complete the enclosed form and mail it, together with a copy of their abstract and a one page CV, to the BSMB Secretary by Monday 15th February 1999.

Please note that for this meeting there will be a poster competition open to young BSMB members sponsored by the International Journal of Experimental Pathology. Three prizes each of £100 will be awarded. This is an open competition and is not restricted to posters dealing with the theme of the meeting, i.e. Wound Healing. Please indicate on registration form if you are interested in participating.

Registration Form

British Society of Matrix Biology in collaboration with the European Tissue Repair Society
Tuesday 30th March - Thursday 1st April 1999
The Academic Centre, John Radcliffe Hospital and St Anne's College, Oxford, England

Name:
Title:
Address:
.....

Tel: Fax:
e-mail:

Inclusive Conference Fee: £60.00 **£**

Are you submitting a poster? YES/NO

Would you like it to be considered for publication in IJEP
(International Journal of Experimental Pathology)? YES/NO

Would you like to be entered in the IJEP poster competition? YES/NO

Would you like to give a short presentation? YES/NO

Poster/Short presentation title:
.....
.....

I will attend the Conference Dinner: YES/NO

Are vegetarian or special meals required (please give details)?
.....

Accommodation required:

Arrival date: Departure date: Total nights:
.....

Basic room including Bed & Breakfast @ £38.00 **£**
/night

Ensuite room including Bed & Breakfast @ £65.00 **£**
/night

Total money enclosed: **£**

Cheques to be drawn on a UK Bank in pounds sterling and made payable to:
Educational Trust Fund 25027

Please return form to:
Dr George Cherry
The Oxford Wound Healing Business Office
Department of Dermatology
Churchill Hospital
Old Road, Headington, Oxford, OX3 7LJ, UK

Tel: +44 (0) 1865 228269/228264
Fax: +44 (0) 1865 228233

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.....

.....
.....
.....

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, Cardiovascular, Metabolism & Musculoskeletal Research Department, Zeneca Pharmaceuticals, Alderley Park, Macclesfield, Cheshire, SK10 4TG UK. email: rose.maciewicz@alderley.zeneca.com

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 cred it to the account of
(in words)

the **BRITISH SOCIETY MATRIX BIOLOGY**, Account No. 09670343 quoting reference no.
(leave blank, for BSMB records only)

and make similar payments annually on the 1st January until this order is cancelled in writing, charging such payments to:

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

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

AUDIT OF MEMBERSHIP DETAILS

Please fill out the following form, EVEN IF NONE OF YOUR DETAILS HAVE CHANGED and return by February 15th, 1999 to Dr. Rose Maciewicz Cardiovascular, Metabolism & Musculoskeletal Research Department, Zeneca Pharmaceuticals, Alderley Park, Macclesfield, Cheshire, SK10 4TG, UK

In order for the Society to keep accurate records of our membership it is necessary for us to ask you to complete these details however they will not be passed onto any 3rd party unless you agree to this.

Title (please tick one):	
Professor <input type="checkbox"/>	Dr. <input type="checkbox"/> Miss <input type="checkbox"/> Ms. <input type="checkbox"/> Mrs. <input type="checkbox"/> Mr. <input type="checkbox"/> Other.....
First Name(s) please print clearly in block capitals below:	
Last Name	
Department	
Organisation	
Street	
City	
County/State	
Postcode/Zip	
Country	
Email	
Tel (inc. std codes)	
Fax (inc. std codes)	
Position: (tick one of the following)	
Academia (HODm Professor, Lecturer.....)	<input type="checkbox"/>
Pharmaceutical	<input type="checkbox"/>
Postdoc.....	<input type="checkbox"/>
Research Scientist.....	<input type="checkbox"/>
Research Assistant/PhD student.....	<input type="checkbox"/>
Other.....	<input type="checkbox"/>
Please circle your choices below:	
Do you pay your membership by direct debit? Yes/No	
If yes, please can you check you are paying the correct amount	
If no, please send us a cheque immediately and consider setting up a direct debit (see section @ bottom of membership form appended to this newsletter). Please note membership fee is collected on Jan. 1 st of the year. If you fail to send us your 1999 subscription fee we will have to cancel your membership.	
Would you like to receive an email copy (attachment) of the newsletter rather than a paper copy? Yes/No	
Or would you like an email notification of when the next newsletter is published on the website? Yes/No	
Would you be happy to have your details published on the website? Yes/No	

Do you pay your membership fee by direct debit?

Please complete the following form to notify your bank of the change of the name of the society and send directly to your bank as soon as possible (do not send to the Society).

☛ If you pay your BSMB/BCTS subscription by direct debit then please complete and send this form to your bank (alternatively some banks may allow you to do this over the telephone).

☛ If you do not pay by direct debit and would like to, then please fill out the section at the bottom of the membership form which is appended to this newsletter.

If you have any queries or problems with this form please contact BSMB assistant secretary, Dr Jo Lewthwaite, Cellular Microbiology Research Group, Eastman Dental Institute, 256 Gray's Inn Road, London, WC1X 8LD, UK. Email: J.Lewthwaite@eastman.ucl.ac.uk, Tel: 0171 915 1247, Fax 0171 915 1259.

.....

To: (name and address of your bank)

.....
.....
.....
.....

I/we (my/our account name).....(account number)..... have a direct debit for £10 **full membership** or £2 **student membership** (tick as appropriate) payable to the British Connective Tissue Society on the 1st January each year. (Society bank, National Westminster Bank, code 60-00-01T, Account no. 09670343).

Please note the name of the Society has changed from the British Connective Tissue Society (BCTS) to the **British Society for Matrix Biology (BSMB)** please ensure payment is made out to the new Society name from now on and that all records pertaining to this are amended - Many thanks.

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

BALLOT FORM FOR NEW BSMB COMMITTEE MEMBERS

Please indicate your choices by placing a cross (✗) in the boxes by no more than 3 names (ballot papers voting for more than 3 names will be deemed null and void)

Please return your ballot paper by February 15, 1999.

Postal Ballot for Committee Member should be sent to:

BRITISH SOCIETY MATRIX BIOLOGY

Dr Rose Maciewicz

Cardiovascular, Metabolism & Musculoskeletal Research Department

Zeneca Pharmaceuticals

Alderley Park, Macclesfield

Cheshire, SK10 4TG UK

IAN CLARK University of East Anglia (UEA)	
ALISON REITH University of Manchester	
ANTHONY DAY University of Oxford	
ANTHONY HOLLANDER University of Sheffield	
NORMAN McKIE University of Newcastle	