

## contents

### Novartis Medal Lecture

<b>Antibodies: a Paradigm for the Evolution of Molecular Recognition</b>	M. S. NEUBERGER	341
--	-----------------	-----

### colloquia

#### 676th Meeting, Heriot-Watt University, Edinburgh

#### colloquium: I4-3-3 Proteins in Cell Regulation

<b>Specificity of I4-3-3 isoform dimer interactions and phosphorylation</b>	A. AITKEN, H. BAXTER, T. DUBOIS, S. CLOKIE, S. MACKIE, K. MITCHELL, A. PEDEN AND E. ZEMLICKOVA	351
<b>Survival-promoting functions of I4-3-3 proteins</b>	S. C. MASTERS, R. R. SUBRAMANIAN, A. TRUONG, H. YANG, K. FUJII, H. ZHANG AND H. FU	360
<b>I4-3-3 Proteins and photoneuroendocrine transduction: role in controlling the daily rhythm in melatonin</b>	D. C. KLEIN, S. GANGULY, S. COON, J. L. WELLER, T. OBSIL, A. HICKMAN AND F. DYDA	365
<b>Plant I4-3-3 protein families: evidence for isoform-specific functions?</b>	M. R. ROBERTS AND G. L. DE BRUXELLES	373
<b>Affinity purification of diverse plant and human I4-3-3-binding partners</b>	F. C. MILNE, G. MOORHEAD, M. POZUELO RUBIO, B. WONG, A. KULMA, J. E. HARTHILL, D. VILLADSEN, V. COTELLE AND C. MACKINTOSH	379
<b>Use of I4-3-3 in the diagnosis of Creutzfeldt-Jakob disease</b>	A. J. E. GREEN	382
<b>Specific I4-3-3 isoform detection and immunolocalization in prion diseases</b>	H. C. BAXTER, J. R. FRASER, W.-G. LIU, J. L. FORSTER, S. CLOKIE, P. STEINACKER, M. OTTO, E. BAHN, J. WILTFANG AND A. AITKEN	387
<b>Effect of multiple phosphorylation events on the transcription factors FKHR, FKHLI and AFX</b>	Y. L. WOODS AND G. RENA	391
<b>I4-3-3s are DNA-replication proteins</b>	M. ZANNIS-HADJOPOULOS, O. NOVAC, D. ALVAREZ AND G. B. PRICE	397
<b>Exoenzyme S binds its cofactor I4-3-3 through a non-phosphorylated motif</b>	B. HALLBERG	401
<b>Transgenic I4-3-3 isoforms in plants: the metabolite profiling of repressed I4-3-3 protein synthesis in transgenic potato plants</b>	J. SZOPA	405

<b>Phosphorylation-independent interaction between 14-3-3 protein and the plant plasma membrane H<sup>+</sup>-ATPase</b>	J. BORCH, K. BYCH, P. ROEPSTORFF, M. G. PALMGREN AND A. T. FUGLSANG	<b>411</b>
<b>Plant 14-3-3 proteins assist ion channels and pumps</b>	A. H. DE BOER	<b>416</b>

---

## colloquium: Lessons from the Type II Family of G-Protein-Coupled Receptors: Their Ligands, Receptor Structure and Function

---

<b>Transcriptional regulation of the calcitonin receptor gene</b>	M. D. PONDEL, C. JAGGER, C. HEBDEN, G. PARTINGTON AND R. MOULD	<b>423</b>
<b>Corticotropin-releasing hormone receptors</b>	E. W. HILLHOUSE, H. RANDEVA, G. LADDS AND D. GRAMMATOPOULOS	<b>428</b>
<b>Adrenomedullin: receptor and signal transduction</b>	D. M. SMITH, H. A. COPPOCK, D. J. WITHERS, A. A. OWJI, D. L. HAY, T. P. CHOKSI, P. CHAKRAVARTY, S. LEGON AND D. R. POYNER	<b>432</b>
<b>Identification of secretin, vasoactive intestinal peptide and glucagon binding sites: from chimaeric receptors to point mutations</b>	M. WAELBROECK, J. PERRET, P. VERTONGEN, M. VAN CRAENENBROECK AND P. ROBBERECHT	<b>437</b>
<b>Additional signals from VPAC/PAC family receptors</b>	D. A. MCCULLOCH, C. J. MACKENZIE, M. S. JOHNSON, D. N. ROBERTSON, P. J. HOLLAND, E. RONALDSON, E. M. LUTZ AND R. MITCHELL	<b>441</b>
<b>A small sequence in the third intracellular loop of the VPAC<sub>1</sub> receptor is responsible for its efficient coupling to the calcium effector</b>	I. LANGER, P. VERTONGEN, J. PERRET, M. WAELBROECK AND P. ROBBERECHT	<b>447</b>
<b>Interaction of calcitonin-gene-related peptide with its receptors</b>	A. C. CONNER, D. L. HAY, S. G. HOWITT, K. KILK, Ü. LANGEL, M. WHEATLEY, D. M. SMITH AND D. R. POYNER	<b>451</b>
<b>Functional relevance of G-protein-coupled-receptor-associated proteins, exemplified by receptor-activity-modifying proteins (RAMPs)</b>	J. A. FISCHER, R. MUFF AND W. BORN	<b>455</b>
<b>Receptor component protein (RCP): a member of a multi-protein complex required for G-protein-coupled signal transduction</b>	M. A. PRADO, B. EVANS-BAIN AND I. M. DICKERSON	<b>460</b>
<b>Interaction of G-protein-coupled receptors with synaptic scaffolding proteins</b>	H.-J. KREIENKAMP, M. SOLTAU, D. RICHTER AND T. BÖCKERS	<b>464</b>
<b>Development and potential of non-peptide antagonists for calcitonin-gene-related peptide (CGRP) receptors: evidence for CGRP receptor heterogeneity</b>	D. WU, H. DOODS, K. ARNDT AND M. SCHINDLER	<b>468</b>
<b>Bioinformatics and type II G-protein-coupled receptors</b>	S. M. FOORD, S. JUPE AND J. HOLBROOK	<b>473</b>

---

## colloquium: Mediation and Modulation of Antibody Function

---

<b>X-ray crystallographic studies of IgG-Fcγ receptor interactions</b>	P. SONDERMANN AND V. OOSTHUIZEN	<b>481</b>
--	---------------------------------	------------

<b>Engineering therapeutic antibodies for improved function</b>	L. G. PRESTA, R. L. SHIELDS, A. K. NAMENUK, K. HONG AND Y. G. MENG	<b>487</b>
<b>The human IgA–Fc<math>\alpha</math> receptor interaction and its blockade by streptococcal IgA-binding proteins</b>	J. M. WOOF	<b>491</b>
<b>The contrasting IgG-binding interactions of human and herpes simplex virus Fc receptors</b>	K. L. ARMOUR, A. ATHERTON, L. M. WILLIAMSON AND M. R. CLARK	<b>495</b>
<b>Troybodies and Pepbodies</b>	E. LUNDE, V. LAUVRAK, I. B. RASMUSSEN, K. W. SCHJETNE, K. M. THOMPSON, T. E. MICHAELSEN, O. H. BREKKE, L. M. SOLLID, B. BOGEN AND I. SANDLIE	<b>500</b>
<b>Bispecific antibodies targeting cancer cells</b>	M. PEIPP AND T. VALERIUS	<b>507</b>
<b>Formatting antibody fragments to mediate specific therapeutic functions</b>	A. N. C. WEIR, A. NESBITT, A. P. CHAPMAN, A. G. POPPLEWELL, P. ANTONIWI AND A. D. G. LAWSON	<b>512</b>
<b>Amino acid sequence requirements in the human IgA1 hinge for cleavage by streptococcal IgA1 proteases</b>	B. W. SENIOR, M. R. BATTEN, M. KILIAN AND J. M. WOOF	<b>516</b>
<b>Targeted cytokine delivery to neuroblastoma</b>	P. K. DEHAL, M. J. EMBLETON, J. T. KEMSHEAD AND R. E. HAWKINS	<b>518</b>

---

## colloquium: Amyloidogenic Proteins Involved in Neurodegeneration and Therapeutic Implications

---

<b>Examining the structure of the mature amyloid fibril</b>	O. S. MAKIN AND L. C. SERPELL	<b>521</b>
<b>Cholesterol and Alzheimer's disease</b>	B. WOLOZIN	<b>525</b>
<b>Memapsin 2 (<math>\beta</math>-secretase) as a therapeutic target</b>	L. HONG, R. T. TURNER III, G. KOELSCH, A. K. GHOSH AND J. TANG	<b>530</b>
<b><math>\gamma</math>-Secretase inhibition</b>	D. BEHER AND M. S. SHEARMAN	<b>534</b>
<b>Inhibition of toxicity and protofibril formation in the amyloid-<math>\beta</math> peptide <math>\beta</math>(25–35) using N-methylated derivatives</b>	A. J. DOIG, E. HUGHES, R. M. BURKE, T. J. SU, R. K. HEENAN AND J. LU	<b>537</b>
<b>Amyloid fibril formation by human stefin B: influence of the initial pH-induced intermediate state</b>	E. ŽEROVNIK, V. TURK AND J. P. WALTHO	<b>543</b>
<b>Glutamine repeats: structural hypotheses and neurodegeneration</b>	L. MASINO AND A. PASTORE	<b>548</b>
<b>Amyloid-<math>\beta</math> oligomers: their production, toxicity and therapeutic inhibition</b>	D. M. WALSH, I. KLYUBIN, J. V. FADEEVA, M. J. ROWAN AND D. J. SELKOE	<b>552</b>
<b>Properties of neurotoxic peptides related to the <i>BRI</i> gene</b>	B. AUSTEN, O. EL-AGNAF, S. NAGALA, B. PATEL, N. GUNASEKERA, M. LEE AND V. LELYVELD	<b>557</b>
<b>Aggregation and neurotoxicity of <math>\alpha</math>-synuclein and related peptides</b>	O. M. A. EL-AGNAF AND G. B. IRVINE	<b>559</b>

<b>Factors affecting interactions between prion protein isoforms</b>	B. CAUGHEY AND G. S. BARON	<b>565</b>
<b>Altering prion replication for therapy and diagnosis of transmissible spongiform encephalopathies</b>	C. SOTO	<b>569</b>
<b>Therapeutics in Alzheimer's and Prion Diseases</b>	T. WISNIEWSKI, D. R. BROWN AND E. M. SIGURDSSON	<b>574</b>

---

## colloquium: Tetrapyrroles: Their Life, Birth and Death

---

<b>Structure and function of glutamyl-tRNA reductase involved in 5-aminolaevulinic acid formation</b>	J. MOSER, W.-D. SCHUBERT, D. W. HEINZ AND D. JAHN	<b>579</b>
<b>5-Aminolaevulinic acid dehydratase: metals, mutants and mechanism</b>	P. M. SHOOLINGIN-JORDAN, P. SPENCER, M. SARWAR, P. E. ERSKINE, K.-M. CHEUNG, J. B. COOPER AND E. B. NORTON	<b>584</b>
<b>Terminal steps of haem biosynthesis</b>	H. A. DAILEY	<b>590</b>
<b>Structural diversity in metal ion chelation and the structure of uroporphyrinogen III synthase</b>	H. L. SCHUBERT, E. RAUX, M. A. A. MATTHEWS, J. D. PHILLIPS, K. S. WILSON, C. P. HILL AND M. J. WARREN	<b>595</b>
<b>Site-directed mutagenesis of Tyr-189 and Lys-193 in NADPH: protochlorophyllide oxidoreductase from <i>Synechocystis</i></b>	D. J. HEYES AND C. N. HUNTER	<b>601</b>
<b>Making light of it: the role of plant haem oxygenases in phytochrome chromophore synthesis</b>	M. J. TERRY, P. J. LINLEY AND T. KOHCHI	<b>604</b>
<b>Production of cobalamin and sirohaem in <i>Bacillus megaterium</i>: an investigation into the role of the branchpoint chelatases sirohydrochlorin ferrochelatase (SirB) and sirohydrochlorin cobalt chelatase (CbiX)</b>	H. K. LEECH, E. RAUX-DEERY, P. HEATHCOTE AND M. J. WARREN	<b>610</b>
<b>Biosynthesis of cobalamin (vitamin B<sub>12</sub>)</b>	A. I. SCOTT AND C. A. ROESSNER	<b>613</b>
<b>Controlling the reactivity of radical intermediates by coenzyme B<sub>12</sub>-dependent methylmalonyl-CoA mutase</b>	R. BANERJEE AND M. VLASIE	<b>621</b>
<b>Unravelling chlorophyll catabolism in higher plants</b>	B. KRÄUTLER	<b>625</b>
<b>Haem degradation in animals and plants</b>	T. J. MANTLE	<b>630</b>
<b>Cytochrome c maturation: a complex pathway for a simple task?</b>	L. THÖNY-MEYER	<b>633</b>
<b>Novel domain packing in the crystal structure of a thiosulphate-oxidizing enzyme</b>	V. A. BAMFORD, B. C. BERKS AND A. M. HEMMINGS	<b>638</b>

<b>Current understanding of the function of magnesium chelatase</b>	J. D. REID AND C. N. HUNTER	<b>643</b>
<b>Cobalamin (vitamin B<sub>12</sub>) biosynthesis in <i>Rhodobacter capsulatus</i></b>	H. MCGOLDRICK, E. DEERY, M. WARREN AND P. HEATHCOTE	<b>646</b>
<b>Pentahaem cytochrome c nitrite reductase: reaction with hydroxylamine, a potential reaction intermediate and substrate</b>	M. RUDOLF, O. EINSLE, F. NEESE AND P. M. H. KRONECK	<b>649</b>
<b>Cytochrome <i>cbb</i><sub>3</sub> oxidase and bacterial microaerobic metabolism</b>	R. S. PITCHER, T. BRITTAIN AND N. J. WATMOUGH	<b>653</b>
<b>The membrane-bound tetrahaem c-type cytochrome <i>CymA</i> interacts directly with the soluble fumarate reductase in <i>Shewanella</i></b>	C. SCHWALB, S. K. CHAPMAN AND G. A. REID	<b>658</b>
<b>Comparison between the nitric oxide reductase family and its aerobic relatives, the cytochrome oxidases</b>	S. DE VRIES AND I. SCHRÖDER	<b>662</b>

## Focused meeting

### Biometals 2002: Third International Biometals Symposium

#### Bioremediation

<b>Molecular and atomic analysis of uranium complexes formed by three eco-types of <i>Acidithiobacillus ferrooxidans</i></b>	M. MERROUN, C. HENNING, A. ROSSBERG, G. GEIPEL, T. REICH AND S. SELENSKA-POBELL	<b>669</b>
--	---	------------

#### Mechanisms of mercury bioremediation

A. M. M. ESSA, L. E. MACASKIE AND N. L. BROWN	<b>672</b>
---	------------

#### Metal Insertion into Proteins

##### Metal insertion into NiFe-hydrogenases

M. BLOKESCH, A. PASCHOS, E. THEODORATOU, A. BAUER, M. HUBE, S. HUTH AND A. BÖCK	<b>674</b>
---	------------

##### Biosynthesis of iron-sulphur clusters is a complex and highly conserved process

J. FRAZZON, J. R. FICK AND D. R. DEAN	<b>680</b>
---------------------------------------	------------

##### *Sulfolobus* aconitase, a regulator of iron metabolism?

H. UHRIGSHARDT, S. ZOSKE AND S. ANEMÜLLER	<b>685</b>
---	------------

##### Role of proteolysis in copper homeostasis

M. SOLIOZ	<b>688</b>
-----------	------------

#### Metal Transport

##### Microbial siderophore-mediated transport

G. WINKELMANN	<b>691</b>
---------------	------------

##### Siderophore production by *Fusarium venenatum* A3/5

M. G. WIEBE	<b>696</b>
-------------	------------

##### The response to iron deprivation in *Saccharomyces cerevisiae*: expression of siderophore-based systems of iron uptake

C. C. PHILPOTT, O. PROTCHENKO, Y. W. KIM, Y. BORETSKY AND M. SHAKOURY-ELIZEH	<b>698</b>
--	------------

##### A new mechanism for membrane iron transport in *Pseudomonas aeruginosa*

I. J. SCHALK, M. A. ABDALLAH AND F. PATTUS	<b>702</b>
--	------------

<b>Transferrin-mediated iron acquisition by pathogenic <i>Neisseria</i></b>	R. W. EVANS AND J. S. OAKHILL	<b>705</b>
<b>Bipartite gating in the outer membrane protein FecA</b>	D. VAN DER HELM, R. CHAKRABORTY, A. D. FERGUSON, B. S. SMITH, L. ESSER AND J. DEISENHOFER	<b>708</b>
<b>Investigations of iron uptake in <i>Halobacterium salinarum</i></b>	D. HUBMACHER, B. F. MATZANKE AND S. ANEMÜLLER	<b>710</b>
<b>Characterization of a non-haem ferritin of the Archaeon <i>Halobacterium salinarum</i>, homologous to Dps (starvation-induced DNA-binding protein)</b>	S. REINDEL, C. L. SCHMIDT, S. ANEMÜLLER AND B. F. MATZANKE	<b>713</b>
<b>Mercury transport and resistance</b>	N. L. BROWN, Y.-C. SHIH, C. LEANG, K. J. GLENDINNING, J. L. HOBMAN AND J. R. WILSON	<b>715</b>
<b>Mercury resistance (<i>mer</i>) operons in enterobacteria</b>	J. L. HOBMAN, A. M. M. ESSA AND N. L. BROWN	<b>719</b>
<b>Molecular evidence for the role of a ferric reductase in iron transport</b>	A. T. MCKIE, G. O. LATUNDE-DADA, S. MIRET, J. A. MCGREGOR, G. J. ANDERSON, C. D. VULPE, J. M. WRIGGLESWORTH AND R. J. SIMPSON	<b>722</b>
<b>Relationship between intestinal iron-transporter expression, hepatic hepcidin levels and the control of iron absorption</b>	G. J. ANDERSON, D. M. FRAZER, S. J. WILKINS, E. M. BECKER, K. N. MILLARD, T. L. MURPHY, A. T. MCKIE AND C. D. VULPE	<b>724</b>
<b>Down-regulation of liver iron-regulatory protein I in haemochromatosis</b>	M. NEONAKI, D. CUNNINGHAME GRAHAM, K. N. WHITE AND A. BOMFORD	<b>726</b>
<b>Design and applications of methods for fluorescence detection of iron in biological systems</b>	B. P. ESPÓSITO, W. BREUER AND Z. I. CABANTCHIK	<b>729</b>
<b>Intracellular Trafficking</b>		
<b>Plant copper chaperones</b>	H. WINTZ AND C. VULPE	<b>732</b>
<b>Iron targeting to mitochondria in erythroid cells</b>	P. PONKA, A. D. SHEFTEL AND A.-S. ZHANG	<b>735</b>
<b>The Wilson's disease protein expressed in Sf9 cells is phosphorylated</b>	S. M. VANDERWERF AND S. LUTSENKO	<b>739</b>
<b>Metal Toxicity and Therapeutic Intervention</b>		
<b>Copper and prion diseases</b>	D. R. BROWN	<b>742</b>
<b>Toxicity of myoglobin and haemoglobin: oxidative stress in patients with rhabdomyolysis and subarachnoid haemorrhage</b>	B. J. REEDER, M. A. SHARPE, A. D. KAY, M. KERR, K. MOORE AND M. T. WILSON	<b>745</b>
<b>Chromium(VI)-induced damage to the cytoskeleton and cell death in isolated hepatocytes</b>	M. GUNARATNAM AND M. H. GRANT	<b>748</b>
<b>Design of therapeutic chelating agents</b>	R. C. HIDER	<b>751</b>

<b>The role of oxidative stress in the toxicity of pyridoxal isonicotinoyl hydrazone (PIH) analogues</b>	J. L. BUSS, J. NEUZIL AND P. PONKA	<b>755</b>
<b>Novel cytotoxic chelators that bind iron(II) selectively over zinc(II) under aqueous aerobic conditions</b>	R. P. PLANALP, A. M. PRZYBOROWSKA, G. PARK, N. YE, F. H. LU, R. D. ROGERS, G. A. BROKER, S. V. TORTI AND M. W. BRECHBIEL	<b>758</b>
<b>The influence of iron homoeostasis on macrophage function</b>	R. J. WARD, S. WILMET, R. LEGSSYER AND R. R. CRICHTON	<b>762</b>
<b>Functional Genomics and Gene Regulation in Biometals Research</b>		
<b>Responses of plants to iron, zinc and copper deficiencies</b>	H. WINTZ, T. FOX AND C. VULPE	<b>766</b>
<b>Manganese transport and its regulation in bacteria</b>	M. BHATTACHARYYA-PAKRASI, H. B. PAKRASI, T. OGAWA AND R. AURORA	<b>768</b>
<b>Structural studies of the Fur protein from <i>Rhizobium leguminosarum</i></b>	O. O. KOLADE, P. BELLINI, M. WEXLER, A. W. B. JOHNSTON, J. G. GROSSMANN AND A. M. HEMMINGS	<b>771</b>
<b>c-Myc represses the murine <i>Nramp1</i> promoter</b>	H. BOWEN, T. E. BIGGS, S. T. BAKER, E. PHILLIPS, V. H. PERRY, D. A. MANN AND C. H. BARTON	<b>774</b>
<b>Repression of ferritin expression modulates cell responsiveness to H-ras-induced growth</b>	O. KAKHLON, Y. GRUENBAUM AND Z. I. CABANTCHIK	<b>777</b>
<b>Identification of members of the <i>Aspergillus nidulans</i> SREA regulon: genes involved in siderophore biosynthesis and utilization</b>	H. OBEREGGER, I. ZADRA, M. SCHOESER, B. ABT, W. PARSON AND H. HAAS	<b>781</b>

## Focused meeting

<b>High-Throughput Screening: The Way Ahead</b>		
<b>Setting the screen: balancing quality with quantity</b>	A. CLARK AND S. HOWELL	<b>785</b>
<b>A flexible technology platform to explore valuable drug targets</b>	J. H. CONNICK	<b>786</b>
<b>Strategies to identify ligands for orphan G-protein-coupled receptors</b>	G. MILLIGAN	<b>789</b>
<b>High-throughput screening in the diagnostics industry</b>	S. WILSON AND S. HOWELL	<b>794</b>
<b>Virtual screening: a real screening complement to high-throughput screening</b>	J. MESTRES	<b>797</b>
<b>Conditionally immortalized cell lines as model systems for high-throughput biology in drug discovery</b>	N. DANIELE, R. HALSE, E. GRINYO, S. J. YEAMAN AND P. R. SHEPHERD	<b>800</b>
<b>Miniaturized screening technologies for drug discovery</b>	J. M. COOPER AND A. E. G. CASS	<b>802</b>

# Focused meeting

## Regulation of B-Lymphocytes in Health and Disease

<b>CD19–CD21 complex regulates an intrinsic Src family kinase amplification loop that links innate immunity with B-lymphocyte intracellular calcium responses</b>	T. F. TEDDER, K. M. HAAS AND J. C. POE	<b>807</b>
<b>B-cell development and antigen receptor signalling</b>	M. TURNER	<b>812</b>
<b>Hyper-IgM syndromes: a model for studying the regulation of class switch recombination and somatic hypermutation generation</b>	A. DURANDY	<b>815</b>
<b>Consequences of Fc<math>\gamma</math> receptor type III reactivity in non-organ-specific autoimmune diseases</b>	P. YOUINOU AND Y. RENAUDINEAU	<b>819</b>
<b>B-lymphocyte depletion therapy in rheumatoid arthritis and other autoimmune disorders</b>	J. C. W. EDWARDS, M. J. LEANDRO AND G. CAMBRIDGE	<b>824</b>