ON THE COVER

**GPCRs**
Biasing agonism
Article, p692

**AMYLOIDS**
A toxic diversion
Article, p730

**POST-TRANSLATIONAL MODIFICATIONS**
The amine next door
Brief Communication, p667

---

**EDITORIAL**

649  Our professional opinion

**COMMENTARY**

650  SAS-6 oligomerization: the key to the centriole?
Matthew A Cottee, Jordan W Raff, Susan M Lea & Hélio Roque

**RESEARCH HIGHLIGHTS**

654  Our choices from the recent literature

**NEWS AND VIEWS**

657  Receptors: GPCR-G protein preassembly?
   R A John Challiss & Jürgen Wess  ►  Article p740

658  Glycobiology: Challenging reaction equilibria
   Robert A Field  ►  Article p685

660  RNA structure: Riboswitch strikes a chord
   Charles E Dann III  ►  Article p748

661  Channels: A TR(i)P in the air
   Peter M Zymunt  ►  Article p701

663  Epigenetics: Targeting leukemia on the DOT
   Jon Travers, Julian Blagg & Paul Workman

665  Plant chemical biology: Florigen takes two to tango
   Joshua S Mylne & Philip A Wigge

**BRIEF COMMUNICATIONS**

667  The tRNA synthetase paralog PoxA modifies elongation factor-P with \((R)\)-\(\beta\)-lysine

PoxA is a lysyl-tRNA synthetase paralog that post-translationally modifies elongation factor-P (EF-P) with a lysine moiety. Further biochemical analysis reveals that \((R)\)-\(\beta\)-lysine, rather than the more abundant \(\alpha\)-amino acid, is the preferred substrate for PoxA.
ARTICLES

671 A genetically incorporated crosslinker reveals chaperone cooperation in acid resistance
M Zhang, S Lin, X Song, J Liu, Y Fu, X Ge, X Fu, Z Chang & P R Chen

The ribosomal incorporation of a new, more flexible photocrosslinking amino acid allows the identification of client proteins for a chaperone that works during acid stress as well as the discovery of a chaperone-cooperation mechanism that enhances protein refolding upon pH neutralization.

678 Twisted Schiff base intermediates and substrate locale revise transaldolase mechanism
A Lehwess-Litzmann, P Neumann, C Parthier, S Lüdtke, R Golbik, R Ficner & K Tittmann

The first high-resolution structures of transaldolase with bound intermediates both define active site residues that necessitate a revision of the current reaction pathway and point to a high-energy intermediate structure and protein conformational changes as mechanisms to promote product formation.

685 Using simple donors to drive the equilibria of glycosyltransferase-catalyzed reactions
R W Gantt, P Peltier-Pain, W J Cournoyer & J S Thorson

A systematic analysis of possible substrates for reverse glycosyltransferase reactions reveals thermodynamically favored pathways to the traditional “activated” sugar donors, enabling high-yielding enzymatically coupled sugar transfers and a general colorimetric assay for sugar nucleotide formation and utilization.

692 Multiple ligand-specific conformations of the β2-adrenergic receptor
A W Kahsai, K Xiao, S Rajagopal, S Ahn, A K Shukla, J Sun, T G Oas & R J Lefkowitz

A quantitative covalent labeling strategy reveals that multiple ligand-specific conformational states are present in the G protein–coupled β2-adrenergic receptor. Their existence may underlie ‘biased agonism’, which describes the differential abilities of agonists to activate distinct signaling mechanisms downstream of GPCRs.

701 TRPA1 underlies a sensing mechanism for O2

The redox-sensitive TRP channel TRPA1 is activated in hyperoxic and hypoxic conditions directly through modification of cysteine residues by O2 and indirectly through prolyl hydroxylation by PHDs, enzymes related to the hypoxia-inducible factor HIF-1, thus helping to explain how O2 is sensed by sensory and vagal neurons.

© 2011 Nature America, Inc. All rights reserved.
Chemical inhibition of RNA viruses reveals REDD1 as a host defense factor
M A Mata, N Satterly, G A Versteeg, D Frantz, S Wei, N Williams, M Schmolke, S Peña-Llopis, J Brugarolas, C V Forst, M A White, A García-Sastre, M G Roth & B M A Fontoura
A screen for compounds that alleviate the inhibitory effect of influenza NS1 on host gene expression and suppress viral toxicity found naphthalimides that could upregulate REDD1, an mTORC1 inhibitor, revealing that viruses inhibit REDD1 to activate the mTORC1 pathway.

High-frequency transposition for determining antibacterial mode of action
H Wang, D Claveau, J P Vaillancourt, T Roemer & T C Meredith
A transposon-generated mutation strategy used to find targets of eight antibacterial compounds and compound combinations in Staphylococcus aureus identifies known targets as well as new mechanisms of resistance.

Ligand binding to distinct states diverts aggregation of an amyloid-forming protein
The aromatic compound rifamycin SV binds to expanded and partially compact assembly intermediates and inhibits amyloid fibril formation of β2-microglobulin by diverting assembly toward soluble, toxic spherical aggregates lacking the classical structure of amyloid.

Inactive-state preassembly of Gq-coupled receptors and Gq heterotrimers
K Qin, C Dong, G Wu & N A Lambert
Monitoring preassembly of the G protein-coupled receptor M3 muscarinic acetylcholine receptor M3R–Gq heterotrimers by FRAP reveals that agonist- and antagonist-insensitive preassembly of inactive-state complexes via a polybasic motif in M3R increases the sensitivity and accelerates the onset of GPCR signaling.

Structural principles of nucleoside selectivity in a 2′-deoxyguanosine riboswitch
O Pikovskaya, A Polonskaia, D J Patel & A Serganov
Purine base binding specificity in adenine and guanine riboswitches is governed primarily by specific base pairing interactions in the ligand-binding site. A series of 2′-deoxyguanosine riboswitch structures reveals remodeling of the ligand-binding site and remote regions of the structure to accommodate the sugar moiety of the nucleoside substrate.