EDITORIAL
575  Made to measure

RESEARCH HIGHLIGHTS
576  Our choices from the recent literature

NEWS AND VIEWS
578  GPCRs: Caught in a spectroscopic trap
   Jacob Piehler
   ► Article p624
579  Biomaterials: Redox and adhesion on the rocks
   Jonathan J Wilker
   ► Article p588
581  Amyloidogenesis: FlAsH illuminates Aβ aggregation
   Tiago F Outeiro
   ► Article p602
582  Reaction design: Nature-inspired total synthesis
   Laura Furst & Corey R J Stephenson

BRIEF COMMUNICATIONS
585  An orthosteric inhibitor of the Ras-Sos interaction
   A Patgiri, K K Yadav, P S Arora & D Bar-Sagi
   A stabilized helical peptide mimic of a key helix from the guanine nucleotide exchange factor Sos interferes with Ras-Sos interaction and inhibits Ras signaling in response to receptor tyrosine kinase activation.
588  Mussel protein adhesion depends on interprotein thiol-mediated redox modulation
J Yu, W Wei, E Danner, R K Ashley, J N Israelachvili & J H Waite
Mussel adhesion depends on secreted dopa-modified proteins, but the dopa groups are prone to oxidation, which decreases their stickiness. A second mussel protein is now shown to regulate the redox state of these adhesive groups by coupling thiol oxidation to dopa reduction.
▶ N&V p579

591  The second Phytophthora mating hormone defines interspecies biosynthetic crosstalk
M Ojika, S D Molli, H Kanazawa, A Yajima, K Toda, T Nukada, H Mao, R Murata, T Asano, J Qi & Y Sakagami
Phytophthora use mating hormones to mediate reproduction between two distinct strains, but only one of the hormone has been structurally characterized. The isolation and analysis of the elusive second hormone demonstrates that the two hormones are biosynthetically linked and universally used across Phytophthora species.

ARTICLES

595  Serendipitous alkylation of a Plk1 ligand uncovers a new binding channel
F Liu, J-E Park, W-J Qian, D Lim, M Gräber, T Berg, M B Yaffe, K S Lee & T R Burke Jr
Polo-like kinase 1 (Plk1) regulates multiple processes that are important for cell proliferation, and it is a promising anticancer drug target. Efforts to inhibit Plk1 function by disrupting interactions that are essential for its proper localization identify a high-affinity alkylated phosphopeptide ligand specific for Plk1.
▶ N&V p581

602  Amyloid-β forms fibrils by nucleated conformational conversion of oligomers
J Lee, E K Culyba, E T Powers & J W Kelly
FlAsH fluorescence and thioflavin-to-FlAsH FRET are used to distinguish amyloid-β oligomer formation from fibril formation, supporting rapid oligomer formation prior to fibril formation—consistent with a nucleated conformational conversion mechanism—that can be modulated by certain Alzheimer’s disease-linked mutations or lipids.
▶ N&V p581

610  Chemical genetics identify eIF2α kinase heme-regulated inhibitor as anticancer target
T Chen, D Ozel, Y Qiao, F Harbinski, L Chen, S Denoyelle, X He, N Zvereva, J G Supko, M Chorev, J A Halperin & B H Aktas
Overabundance of the eIF2–GTP–Met-tRNAi translational initiation complex has been linked to malignant transformation. N,N'-diarylurea chemical probes that block ternary complex assembly through heme-regulated inhibitor kinase activation validate translational initiation pathways as potential anti-cancer targets.
617 Contributions of counter-charge in a potassium channel voltage-sensor domain
S A Pless, J D Galpin, A P Niciforovic & C A Ahern

Salt bridges between positively charged residues within the S4 transmembrane segment of the voltage-sensing potassium channel, Shaker, and acidic residues in S2 and S3 segments are not necessary during channel gating; rather, two of the acidic residues may occupy a hydrophilic water-filled vestibule that creates an energetically favorable environment for S4 movement during channel gating.

624 CODA-RET reveals functional selectivity as a result of GPCR heteromerization
E Urizar, H Yano, R Kolster, C Galés, N Lambert & J A Javitch

Based on a BRET readout, dopamine D2 receptor agonist NPA is more potent at activating Gαi when the D2 receptor forms a heteromer with the related D1 receptor than if it forms D2 receptor homomers, suggesting that GPCR heteromerization can result in functional selectivity.

631 Mechanistic evidence for a front-side, SNi-type reaction in a retaining glycosyltransferase
S S Lee, S Y Hong, J C Errey, A Izumi, G J Davies & B G Davis

The combination of several biochemical analyses, including determination of kinetic isotope effects and linear free energy relationships, offer the first detailed insights into a natural SNi-like reaction mechanism and provide compelling evidence for a frontal nucleophilic substitution in a retaining glycosyltransferase.

639 Natural products reveal cancer cell dependence on oxysterol-binding proteins

The identification of cellular targets for natural products that potently inhibit the growth of cancer cell lines implicates oxysterol-binding proteins in the growth of cancer cells. These natural products, termed ORPphilins, also affect sphingomyelin biosynthesis.

CORRECTIONS

648 ERRATA AND CORRIGENDUM