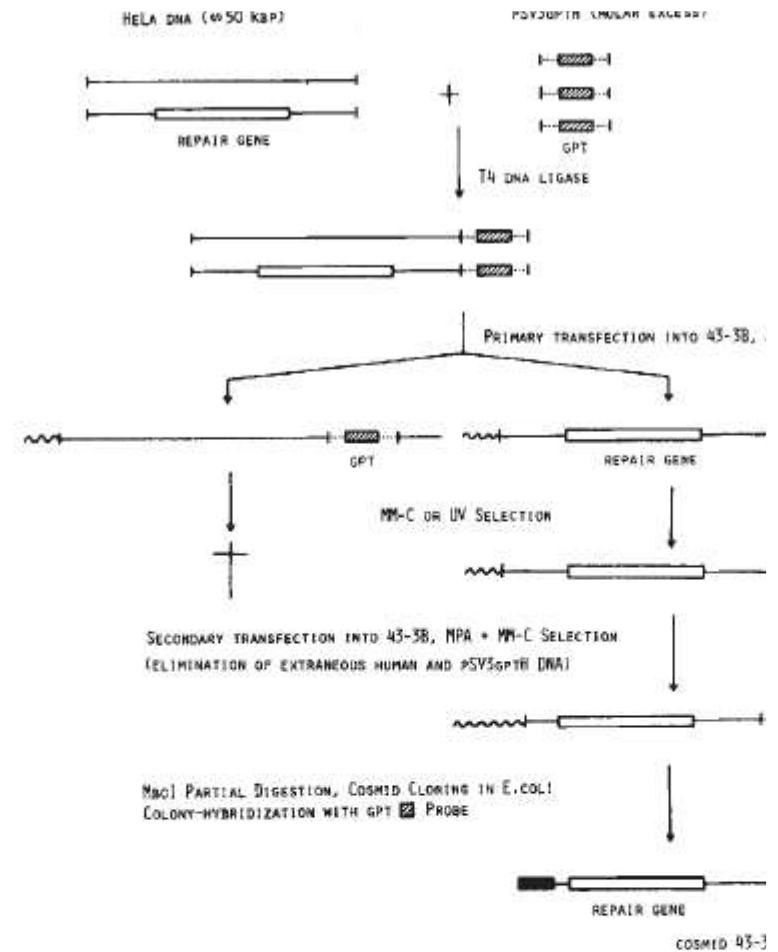


ESF data sharing workshop

Maxine Clarke, Nature

gene *ERCC1*.

Methods: For transfections, $\sim 5 \times 10^5$ 43-3B cells were seeded in 100 mm Petri dishes 1 day before DNA transformation. The cells were grown in F10/Dulbecco's minimal essential medium (DMEM) 1:1 supplemented with antibiotics and 3% fetal and 7% newborn calf serum. High-molecular weight HeLa DNA, isolated as described previously¹⁷, was partially cleaved to an average fragment size of 50–60 kbp with restriction endonuclease *Pst*I. Provided that the repair gene is not exceptionally large (>40–50 kbp), sufficient gene copies in the DNA should remain intact. The restricted DNA was subsequently ligated to a twofold molar excess of *Pst*I-linearized dominant marker pSV₃gptH using T4 DNA ligase (Biolabs). Vector pSV₃gptH is a derivative of pSV₃gpt (ref. 9), from which the simian virus 40 (SV40) early region and a 120-bp *Hind*III–*Bgl*II fragment in front of the *gpt* sequence (which contains false start codons¹⁸) were removed. After testing the ligation on agarose gels the hybrid molecules were transfected into 43-3B CHO repair mutant cells by the calcium phosphate precipitation method¹⁹. 20 μ g of DNA (vector + HeLa DNA) were applied to each Petri dish. Following overnight exposition of the DNA, cells were treated with dimethyl sulphoxide (10% for 30 min) and grown for 24–48 h on non-selecting culture medium to allow expression of the transfected markers. Selection for the dominant marker was in modified MPA medium containing: F10/DMEM 1:1, antibiotics (3% fetal, 7% newborn calf serum), aminopterin (0.2 μ g ml⁻¹), thymidine (5 μ g ml⁻¹), xanthine (10 μ g ml⁻¹), hypoxanthine (15 μ g ml⁻¹), mycophenolic acid (25 μ g ml⁻¹) and deoxycytidine (2.3 μ g ml⁻¹). The selection medium was refreshed every 3–4 days. After the appearance of MPA-resistant (MPA^r) colonies (within 2 weeks) the cells of each Petri dish were reseeded on two dishes, one of which was UV-irradiated ($3 \times 5 \text{ J m}^{-2}$ at 1-day intervals), the other exposed to mitomycin C (10^{-8} M)⁸ in MPA medium. These treatments were left 43-3B mutant, but not to repair-competent CHO cells. The UV^r and MM-C^r colonies appearing on the duplicates of one parental were expanded into mass culture (10^8 – 10^9 cells) in selective conditions (except for UV) and characterized with respect to UV and π C sensitivity (Fig. 3), UV-induced unscheduled DNA synthesis (Table 1) and Southern blot hybridization (Fig. 2). Secondary transformation and selection were done as above except that 43IUV and 43IIMM-C DNA, respectively, were used as donor DNAs for both markers (MPA^r and MM-C^r) was done simultaneously. To construct a cosmid library of 43IIMM-C DNA, a partial size-fractionated digest of 43IIMM-C DNA with an average fragment size of 40–50 kbp was ligated to *Bam*HI-cleaved pTCF-cosmid arms, packaged *in vitro* and transduced into bacterial host ED8767 essentially as described earlier²⁰. This library, which consisted of independent recombinants (equivalent to five times the diploid Chinese hamster genome), was screened by colony filter hybridization using an *Ecogpt* probe (the isolated²² small *Sph*I fragment of pSV₃gpt containing the *Ecogpt* gene and part of the SV40 early region). The *gpt* probe was labelled *in vitro* by nick-translation²³, using [α -³²P]-labelled dATP and dCTP (Amersham, 3,000 Ci mmol⁻¹) to a specific activity of 2 – 5×10^8 c.p.m. μ g⁻¹. During hybridization excess unlabelled pTCF plasmid was present as competitor. Hybridized and washed (Millipore, HA nitrocellulose, 0.45 μ m pore size) were exposed to X-ray film (Fuji Rx) at -70°C with intensifying screen (Fuji). Hybridizing *E. coli* clones were picked from the master filter, rescreened with the same probe and grown in 1 l culture medium (



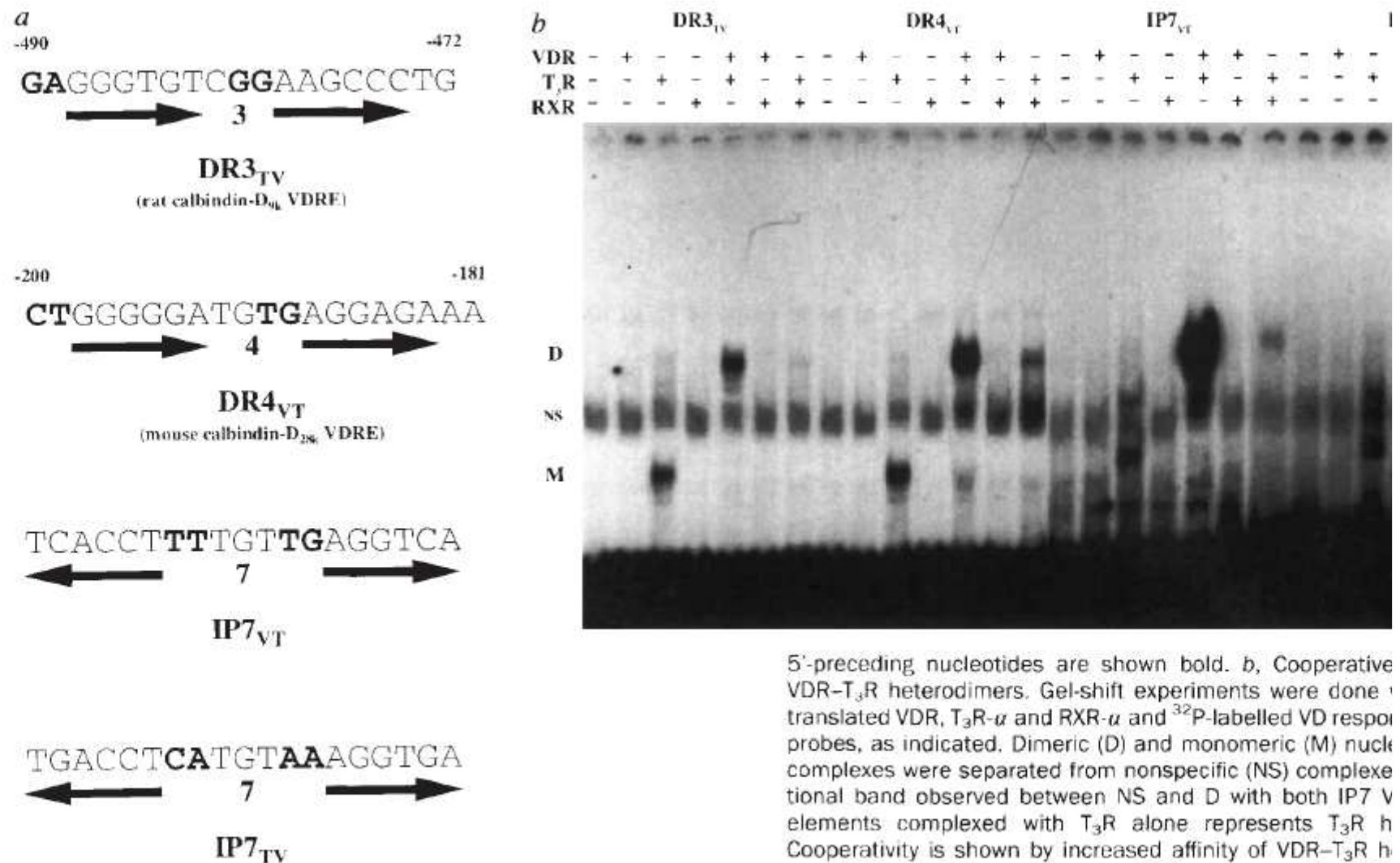


FIG. 1 Cooperativity of VDR-T₃R heterodimers. *a*, Response elements. Comparison of the binding affinity of VDR-VDR, VDR-RXR, VDR-RAR and VDR-T₃R complexes to all known natural VD response elements (VDRE) (ref. 17, and data not shown) showed that the VD response elements of rat calbindin-D_{9k} (ref. 18) and mouse calbindin-D_{28k} (ref. 19) are preferentially bound by VDR-T₃Rs. The sequences of these two natural VD response elements and of two inverted palindromic VD

5'-preceding nucleotides are shown bold. *b*, Cooperative VDR-T₃R heterodimers. Gel-shift experiments were done with translated VDR, T₃R- α and RXR- α and ³²P-labelled VD response probes, as indicated. Dimeric (D) and monomeric (M) nucleoprotein complexes were separated from nonspecific (NS) complexed material. A band observed between NS and D with both IP7 VD elements complexed with T₃R alone represents T₃R homodimer. Cooperativity is shown by increased affinity of VDR-T₃R heterodimer over VDR and T₃R homodimers and T₃R monomers. On all four response elements, the VDR-T₃R heterodimer complex is more prominent than VDR-RXR or T₃R-RXR heterodimer complexes.

METHODS. Pairs of oligonucleotides, each containing one of the response elements with adjacent XbaI sites, were synthesized, phosphorylated and annealed to yield double-stranded DNA, which were fused to the tk promoter to drive the expression of a reporter gene by subcloning into the XbaI site of pBLCAT2.

dependent exocytosis. Stochastic or regulated inactivation of this clamp by GTP hydrolysis or protein phosphorylation would then regulate the availability of vesicles for fusion, thereby determining how many vesicles fuse. Genetic and biochemical tests of this model are in progress.

Methods

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Molecular biology. Yeast-two hybrid bait vectors were constructed by standard techniques²¹ in pLexN using full-length Rab sequences with the indicated mutations. Yeast two-hybrid screens of a rat brain cDNA library in pVP16-3 were performed and evaluated as described^{14,22}. Two independent Rim prey clones encoding residues 1-345 (pPreyRim-100) and 11-399 (pPreyRim-52) were isolated. Liquid β -galactosidase assays were normalized for protein content²². A rat brain cDNA library in λ ZAPII was screened by standard methods²¹ using the Rim prey clone as a probe. Multiple overlapping clones covering the entire coding were sequenced to assemble the full-length sequence (GenBank accession number: AF007836). Rim-GST fusion protein vectors were obtained by cloning the *Eco*RI fragment from pPreyRim-52 into pGEX-KG²³ (pGexRIM52; N-terminal zinc-finger construct) or the 0.84-kilobase *Sma*I-*Pvu*II fragment into the *Sma*I site (pGexRim-PDZ; this encodes residues 492-772).

Sequence analysis. Initial databank searches using BLAST software identified the domains in Rim (N-terminal zinc-finger, PDZ domain, and C₂ domains). The complete Rim *C. elegans* sequence was assembled from two cosmid sequences (T10A3 and K03A1; acc. nos U41035 and U41625, respectively). In order to define the relation of the Rim zinc-finger to other databank zinc-fingers, we applied the generalized profile method²⁴. A profile was constructed from a weighted multiple alignment of the zinc-finger regions from rat and *C. elegans* Rim and rabphilin using the BLOSUM45 substitution matrix²⁵ with a gap-creation penalty of 2.1 and gap-extension penalty of 0.2. Statistical significance of profile-matching scores was derived from the analysis of the score distribution of a locally shuffled database²⁶. Significant matches ($P < 0.08$) were incorporated into subsequent rounds of profile construction for iterative profile refinement. The initial profile search found significant matches to the zinc-finger regions of the nematode open reading frames C33D9.1 ($P < 0.06$) and ZK632.12 ($P < 0.08$). The two sequences were considered related to the Rim zinc-finger domain family and incorporated into the alignment for the next round of profile refinement. Three more profile refinement cycles, accepting only proteins with error probabilities of $P < 0.01$, resulted in the protein family shown in Fig. 1c. The highest-scoring non-

the alignment for the next round of profile refinement. Three more profile refinement cycles, accepting only proteins with error probabilities of $P < 0.01$, resulted in the protein family shown in [Fig. 1c](#). The highest-scoring non-related sequences after those shown consisted of *trithorax* family members that reached error probabilities of $P > 0.5$ in all of the profile iterations.

Immunocytochemistry. Antibodies were raised in rabbits against the purified GST fusion proteins encoded by pGEX-RIM-52 and pGEX-Rim-PDZ. Double and single immunofluorescence labelling of cryostat sections from rat spinal cord and bovine retinae was performed²⁷ with two independent polyclonal Rim antibodies and multiple monoclonal antibodies to synaptic vesicle proteins. Staining was visualized by Cy2- and Cy3-conjugated secondary antibodies and viewed in a BioRad MRC1024 confocal microscope. Immuno-electron microscopy was performed by a pre-embedding protocol with silver enhancement²⁷. Controls for all immunocytochemistry experiments included the use of two independent antibodies, control stains with other antibodies, and experiments in which the first antibody was omitted.

PC12 cell transfections. PC12 cells (ATCC) were plated in collagen-coated 6-well dishes with 10^6 cells per well. Cells were transfected on day 1 with 0.2 μ g of Qiagen-purified pCMV5-hGH encoding human growth hormone and 1 μ g of the indicated expression plasmids using Lipofectamine (Life Technologies). Expression plasmids encoded the light chains of wild-type and mutant tetanus toxin in pCMV5 ([ref. 28](#)), LDL receptor and Rab3A in pCMV5, and residues 1–399 of Rim in pME18sf(-). On day 3, cells were collected, washed, and split into two portions, one of which was incubated for 20 min at 37 °C in control buffer (in mM) (145 NaCl, 5.6 KCl, 2.2 CaCl₂, 0.5 MgCl₂, 5.6 glucose, 0.5 ascorbate, 20 HEPES-NaOH, pH 7.4) and the other was incubated in the same buffer containing 56 KCl and 95 NaCl. After incubation, growth hormone in the medium and the cells was determined by radioimmunoassay (Nichols Institute). Secretion was calculated as the percentage growth hormone released as a function of stimulation. All experiments were done in triplicate at least three times.

Rim affinity chromatography. Glutathione-agarose columns without protein, with GST-Rim fusion protein encoded by pGEX-Rim-52, or with various control GST fusion proteins, were reacted with total rat brain homogenate prepared in 0.5% Triton X-100, 1 mM EDTA, 0.1 M NaCl, 0.1 g l⁻¹PMSF, and 50 mM HEPES-NaOH, pH 7.4, with either 0.5 mM GDP- β S or GTP- γ S at 4 °C overnight. Samples were washed 5 times in the same buffer without nucleotides before analysis by SDS-PAGE and immunoblotting.

Other procedures. RNA blotting experiments were done using multiple tissue blots (Clontech). SDS-PAGE and immunoblotting were performed using standard procedures and antibodies described previously^{1 12 28 29}. Signals

Protein preparation

Cells expressing AvrPto and Pto were induced with 1 mM IPTG for 10 h at room temperature. Cells were collected, pelleted and then resuspended in buffer A (50 mM Tris, pH 8.0, 100 mM NaCl), supplemented with protease inhibitors. The cells were lysed by sonication and then centrifuged at 14,000 r.p.m. for 1 h. The soluble fraction of the AvrPto-Pto complex from co-expression was purified using Glutathione Sepharose 4B (GS4B) and further cleaned using an [anion-exchange column](#) (Source-15Q, Pharmacia) and gel filtration chromatography after removal of GST ([Superdex200](#), Pharmacia). A similar method was used to purify the free forms of AvrPto and Pto, including their various mutants. The unique NCBI identifiers for the proteins are: Pto, A49332; AvrPto, AAA25728; Prf, AAC49408; Pti1, AAC61805; PKA, P36887; PKI, NP_006814; CHK1, AAC51736; TPRI, AAH71181.

Crystallization and data collection

Crystallization conditions for the AvrPto-Pto complex were determined from the [sparse matrix screen](#) (Hamptonresearch). Screening was done using hanging drop vapour diffusion by combining 2 μ l of protein solution. The buffer containing 0.2 M potassium sodium tartrate, 0.1 M tri-sodium citrate, pH 5.6, and 2.0 M ammonium sulphate generated crystals, which were further optimized by adding 10 mM taurine (2-aminoethanesulfonic acid). Crystals grew to their maximum size ($0.3 \times 0.4 \times 0.5 \text{ mm}^3$) approximately within two days. The crystals were transferred to the mother liquor, containing 25% glycerol, then flash cooled in liquid nitrogen. The multiple anomalous dispersion (MAD) data sets from the selenium crystal were collected to 4.0 Å. The crystal belongs to space group $P2_12_12_1$ with cell dimensions $a = 75.465 \text{ Å}$, $b = 94.591 \text{ Å}$, $c = 98.741 \text{ Å}$, and contains one AvrPto-Pto complex per asymmetric unit.

Structure determination and refinement of the AvrPto-Pto complex

All the residues except the first 29 residues of Pto were built for the AvrPto-Pto complex. When justified by the electron density, the phosphate group in the phosphorylated T199 in Pto was included. The final atomic model of AvrPto-Pto was refined to a crystallographic R_{work} of 27.1% and an R_{free} of 30.3% to 3.2 Å. There were no outliers in the Ramachandran plot (79.1%, 16.3%, 4.6% in the core, allowed and generously allowed regions, respectively).

Gel filtration assay for protein-protein interaction

The Pto and AvrPto proteins purified by affinity chromatography and anion-exchange column ([Source-15Q](#), Pharmacia) were used for interaction assay.

Online Methods

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Plasmid and oligonucleotides

Endogenous miRNAs were purified as previously described²². For the generation of miR-15 reporter constructs (Acvr2a-WT and Acvr2a-mut), the luciferase cDNA was first inserted in pcDNA3.1; the first miR-15 and miR-16 binding site of *Acvr2a* 3' UTR was then cloned downstream of luciferase by inserting double-stranded oligonucleotides. Mature miR-15 sequences were: wild-type sense, 5'-UAGCAGCACAUAAUGGUUUGUGUU-3'; wild-type antisense, 5'-CACAAACCAUUAUGUGCUGGAUUU-3'; mutant sense, 5'-UUCGUCAACAUAUGGUUUGUGUU-3'; mutant antisense, 5'-CACAAACCAUUAUGUUGACCUUUU-3' (Invitrogen). [Anti-miRNA reagents](#) were purchased from Dharmacon: anti-miR-15, 5'-AAUCCACAAACCAUUAUGUGCUGCUACUUU-3'; anti-miR-16, 5'-AAUCCUCCAGUAUUUACGUGCUGCUAAGGC-3'; control anti-miR-16 sense, 5'-UAGCAGCACGUAAAACUGGAG-3'; and control scrambled anti-miRNA. Pri-miR-15/16a and pri-miR-127 were amplified from genomic DNA by PCR and cloned into pCS2 and sequenced. RNA was synthesized using [Message Machine](#) (Ambion). Of note, we found that *in vitro* transcribed miRNA was biologically effective *in vivo* only if capped and containing the SV40 polyadenylation signal. Moreover, in order to facilitate the formation of proper secondary structures (hairpins), pri-miRNAs were denatured at 65 °C for 5 min and slowly annealed to RT.

miR-15 and miR-16 [morpholino oligonucleotides](#) (Gene Tools) were 25-base oligonucleotides designed to be complementary to the mature miRNA, but extending one or two bases over the flanking sequence of guide strand, past the Drosha and Dicer cleavage sites: *mir-15b* MO, 5'-CATGCAAATCATGATGTGCTGCTAC-3'; *mir-16b* MO, 5'-TCACCCAATATTTACGTGCTGCTAA-3'; *mir-15c* MO, 5'-TCTACAAACCATGATGTGCTGCTAG-3'; *mir-16c* MO, 5'-AACTCCAGTATTTACGTGCTGCTAA-3'; control MO, 5'-CCTCTTACCTCAGTTACAATTTATA-3'.

[Acvr2a silencer validated siRNA](#) was purchased from Ambion: sense, 5'-GGACUGAUUGUGUAGAAAAtt-3'; antisense, 5'-UUUUCUACACAAUCAGUCctg-3'.

Biological and biochemical assays

GGACUGAUUGUGUAGAAAAtt-3'; antisense, 5'-UUUUCUACACAAUCAGUCctg-3'.

Biological and biochemical assays

Xenopus embryo manipulations, mRNA preparation, microinjections and whole-mount *in situ* hybridizations were performed as previously described²⁵. Mature miRNAs, anti-miRNAs and morpholino oligonucleotides were re-suspended in 0.5 mM HEPES, pH 7.6. For luciferase assays, embryos were radially injected (except in Fig. 4c) with 40 pg of reporter plasmid (UTR, Mix.2 or Vent.2) plus 150 pg of *lacZ* mRNA and collected at early gastrula. Luciferase values were normalized to β -gal activity that, typically, did not oscillate more than 25% within the same batch. For each experiment, the normalized luciferase value is the mean of at least three independent embryo sets, each containing five embryos. In Fig. 5b we measured the effects of Wnt/ β -catenin on endogenous miR-15 and miR-16 considering the fold inhibition (typically 50%, as in Fig. 1b) between *Acvr2a*-mut and wild-type reporter. HepG2 cells were transfected with Lipofectamine2000 (Invitrogen) in DMEM, 10% serum with reporter plasmids (40 ng cm⁻²) and miR-15 RNA (300 ng cm⁻²); pCS2-lacZ (20 ng cm⁻²) was used as a normalizer. For experiments shown in Fig. 1d, HepG2 cells were first transfected with *Acvr2a* siRNA or control siRNA (siGFP) using RNAi max (Invitrogen); after 48 h, cells were transfected with reporter plasmids (40 ng cm⁻²) and pCS2-lacZ (20 ng cm⁻²) together with the indicated miR-15 RNA (300 ng cm⁻²) and pCS2*Acvr2a*-3'UTR deleted (400 ng cm⁻²). A detailed protocol has been uploaded to Protocols Network (doi:10.1038/nprot.2007.349). In each experiment, samples were transfected in duplicate. Treatments of cells with activinA, TGF- β 1 and Bmp2 proteins were carried out in 0.1% serum.

Western blotting was carried out as described³³. Anti-*Acvr2a*-specific polyclonal antibody was purchased from R&D. Quantifications were performed using NIH-Image software.

Immunohistochemistry

For immunostaining, embryos were fixed for 2 h at room temperature in MEMFA then in 80% methanol/20% dimethyl sulphoxide overnight at -20 °C. They were rinsed in PBS, dehydrated, embedded in paraffin and cut into 20- μ m sections. Slides were de-waxed, re-hydrated and treated for 45 min with 2% H₂O₂ to

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[Glucose sensing by POMC neurons regulates glucose homeostasis and is impaired in obesity](#)

Laura E. Parton, Chian Ping Ye, Roberto Coppari, Pablo J. Enriori, Brian Choi, Chen-Yu Zhang, Chun Xu, Claudia R. Vianna, Nina Balthasar, Charlotte E. Lee Elmquist, Michael A. Cowley & Bradford B. Lowell

Nature **449**, 228-232 (13 September 2007)

doi:10.1038/nature06098

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Giovanni D'Angelo, Elena Polishchuk, Giuseppe Di Tullio, Michele Santoro, Antonella Di Campli, Anna Godi, Gun West, Jacek Bielawski, Chia-Chen Chuang, van der Spoel, Frances M. Platt, Yusuf A. Hannun, Roman Polishchuk, Peter Mattjus & Maria Antonietta De Matteis
Nature **449**, 62-67(6 September 2007)
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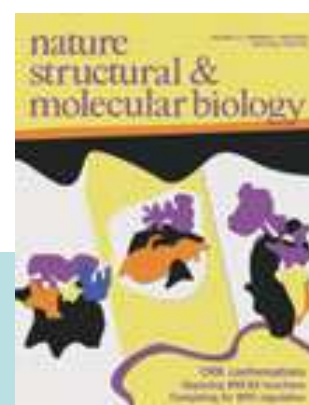
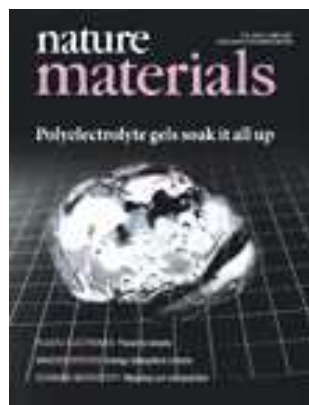
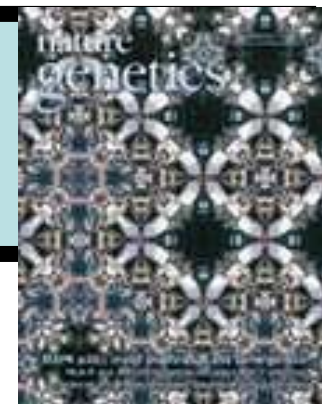
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Methods & Protocols

Microbiology

Mutant strains and cell lines

For materials such as mutant strains and cell lines, authors are expected to use established public repositories and provide relevant accession numbers (for example, [Jackson Laboratory](#), [Mutant Mouse Regional Resource Centers](#), [American Type Culture Collection](#), [UK Stem Cell Bank](#), and so on) wherever possible.

Peer-reviewers may be asked to comment on the terms of access to materials, methods and/or datasets; Nature journals reserve the right to refuse publication in cases where authors are unable to provide adequate assurances that essential resources will be made freely available to the community.

Relevant editorials in Nature journals:

Nature Genetics: [How to discuss ancestry and ethnicity](#)

Nature Genetics: [Criteria for association](#)

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Sequences, structures and 'omics'

Papers reporting protein or DNA sequences and molecular structures will not be accepted without an accession number to [Genbank/EMBL/DBJ](#), [Protein DataBank](#), [SWISS-PROT](#) or other appropriate, identified, publicly available database in general use in the field that gives free access to researchers from the date of publication, as described in the *Nature* editorials listed below. All novel sequences or structure data must be made available to editors and referees either as Supplementary Information (five copies if provided on disk) or by an accession number to an appropriate publicly accessible database that can be accessed before publication. Please note that this policy includes even short stretches of novel sequence information such as epitopes, functional domains, genetic markers, or haplotypes. Short novel sequences must include surrounding sequence information to provide context.

The sequences of all RNAi, antisense and morpholino probes must be included in the paper or deposited in a public database, with the accession number quoted. When an unpublished library is included in the paper, at minimum the sequences of probes central to the conclusions of the paper must be presented.

Only indexed public repositories are acceptable for providing this type of information. Accession numbers are provided directly to authors by these databases on deposition of data, and must be included in the Nature journal paper before publication. All such deposited material must be freely available on and after the publication date.

Papers must state that atomic coordinates and structure factor files (or comparable NMR data) have been deposited in the [Protein DataBank](#) (or [Nucleic Acids database](#) or [BioMagResBank](#), as appropriate), and must list the accession code(s). Accessibility must be designated "for immediate release on publication". Authors must provide atomic coordinates and structure-factor files upon request of peer-reviewers and editors for the purposes of evaluating the manuscript, if they are not already freely accessible in a publicly available and recognized database, via CD (five copies are required).

Proteomics databases recommended by Nature journals include the [International Molecular Exchange consortium](#); [PRIDE](#); [IntAct](#); [PeptideAtlas](#); [Tranche](#); and the [Global Proteome Machine Organization](#).

Nature journal editorials providing more detail for these policies:



(comments from authors and other scientists in the field are welcome at [this Nautilus post](#)).

Nature Structural & Molecular Biology [Name that gene!](#) ([Comments welcome on Nautilus.](#))

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Microarrays

Please see the [MGED open letter](#) specifying microarray standards. Authors submitting manuscripts containing microarray data must either provide accession number and URL or supply the data as Supplementary Information on CD at time of submission. The data must be MIAME-compliant and supplied in a form that is widely accessible, with the completed checklist also placed on the CD. If data are provided via CD at submission rather than as links to database entries, five copies are required so that they can be sent to peer-reviewers.

Nature journals require submission of microarray data to the [GEO](#) or [ArrayExpress](#) databases, with accession numbers at or before acceptance of the paper for publication.

Nature journal editorials providing more detail for these policies:

Nature: [Microarray standards at last](#)

Nature Immunology: [Microarray policy](#)

Nature Cell Biology: [Microarray data standards](#) (the third editorial on this web page)

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Other supporting data

Any supporting data sets for which there is no public repository must be made available to referees at submission and any interested reader on and after the publication date from the authors directly, the author providing a URL to be used in the paper on publication.

Such material must be hosted on an accredited independent site (URL and accession numbers to be provided by the author), or sent to the Nature journal at submission, either uploaded via the journal's online submission service, or if the files are too large or in an unsuitable format for this purpose, on CD/DVD (five copies). Such material cannot solely be hosted on an author's personal or institutional web site.

After publication, readers who encounter a persistent refusal by the authors to comply with these guidelines should contact the chief editor of the Nature journal concerned, with "materials complaint" and publication reference of the article as part of the subject line. In cases where editors are unable to resolve a complaint, the journal reserves the right to refer the correspondence to the author's funding institution and/or to publish a statement of formal correction, linked to the publication, that readers have been unable to obtain necessary materials or reagents to replicate the findings.

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The entire guide for Editorial Policies is available in [PDF format](#).

Nature's view: Materials & data sharing

- All material and data **needed to reproduce must be available** (reasonable fees for time & costs can be charged)
 - Additional restrictions must be cleared with editors before publication
 - **Licensing agreements** must be revealed before publication; addendum needs to be published if access to materials is affected by future business deals
- **Community repositories** must be used
- **Sharing** can impose burdens - funders' support needed.
- Sharing should be **encouraged and credit** be given for good citizenship

BIND

Six weeks ago, the rights to one of biology's premier public databases were quietly sold to an informatics startup. The database in question, the Biomolecular Interaction Network Database (BIND), is arguably the most comprehensive freely accessible protein-protein interaction database available to the research community. Yet through a combination of bureaucratic delays, Canadian government fiscal nitpicking and a lack of community consensus, this important resource now finds itself on life support, its survival precariously linked to that of Unleashed Informatics, a private venture founded last April with little more than \$1.0 million in seed funding from Sun Microsystems.

BIND is a database of molecular associations that collates high-throughput data submissions and hand-curated information from the scientific literature.....

From *Nature Biotechnology* **24**, 115; February 2006

Rather than arguing for the importance of long-term database funding by granting agencies, BIND's saga in fact argues for greater caution and more demanding oversight when these agencies elect to fund a database's initial development.

(W. Busa, *Nature Biotechnology* **24**, 1095; September 2006).

On March 20 this year, Thomson Scientific (Philadelphia) acquired the BIND database together with a stable of software and services through the purchase of Unleashed Informatics (Toronto). These products were originally created by my laboratory using public funds. They were the intellectual property of my former host institution, Mount Sinai Hospital, in accordance with its employment contracts and policies. Confidentiality constraints from the outset of the discussion with Thomson Scientific, which predated Busa's letter, prevented me from addressing Busa's comments at the time. I would now like to address several misapprehensions and inaccuracies in his comments.....BIND has always had the broadest scope of any interaction database (all organisms) as well as the deepest annotation (down to atomic three-dimensional structures). BIND curators extracted information from figures—a feat no text mining tool can do and 85% of hand-curated BIND records have information arising from figures. It is the breadth, depth and quality of BIND that led to its commercial acquisition. And this was pursued only after having exhausted all possible means for continued public support.....(C. Hogue, *Nature Biotechnology* **25**, 971; September 2007.)

Researchers may not mind paying for the luxury of specialized databases, but data registries that cater to a broad set of users should be broadly and freely accessible to the research community. Although the initial development of databases, such as BIND, requires caution and close oversight of budgets, an equally important aim should be to ensure that data repositories of particular utility to the research community remain sustainable and publicly accessible. Databases, such as BIND, should not be left to the private sector. Ensuring public accessibility to data essential for research progress is the responsibility of the central planner, not Adam Smith's invisible hand in the marketplace. (K. Wang, *Nature Biotechnology* **25**, 971-972; September 2007.)

Challenges for publication

Data submission of **large datasets**

Checking submission for journal's **requirements**

Finding **relevant experts** for interdisciplinary work, to evaluate experimental approach, logic of conclusions, technical validity, consistency

Image manipulation check - software development needed

Challenges for data repositories

Not universal: some fields or tools have no community-accepted repositories

Structured submissions beyond what the data's creator needs for own purposes

Tools for analysis of data need to be user-friendly and open to depositors and browsers alike

Inconsistent funding - knowledge environment surrounding the data needs upkeep, ontologies, analytical tools, links to other environments

Institutional archives- how to organize and what to include, relation to community archives

Post-publication challenges

Access to data and analysis

- Licensing of data or algorithms to third parties, not bound by author-journal agreements

Timely editorial responses to accusations

International nature of science

Lack of extensive institutional **archives**

Lack of universal unique **identifiers** for individuals & data

Summary for funding agencies

Reliable support for data and material repositories

Support **educational** efforts

Incentivize data quality and sharing

Encourage efforts to develop **universal unique identifiers** for data and researchers, useful for authors, data generators, readers and journals

Summary for journals

Align their requirements with community norms

Develop procedures for **enforcement** of requirements

Liase with scientists to ensure differences between fields considered

Publicize consequences for authors

Developments with potential to improve data integrity

1. Electronic notebooks
2. Routine, institutional archiving
3. Unique identifiers

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An extensive collection of technical essays describing the performance of interesting new products or innovative applications of laboratory technologies submitted by product suppliers.



▶ Functional Glycomics Gateway

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A comprehensive source for the latest research, news and events in neuroscience and genomics research developed collaboratively with the Allen Institute for Brain Science.



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A new interactive online resource for high-quality laboratory protocols.



▶ Nature Reports Climate Change

Nature Reports: Climate Change covers the news behind the science and the science behind the news of global climate change, arguably the most far-reaching challenge of this century.



▶ Nature Network

NPG's free Web 2.0 toolkit connecting scientists worldwide — facilitating personal homepages, networking, online discussions, open or private groups and tagging.



▶ Cell Migration Gateway

A comprehensive and regularly updated resource for anyone interested in cell migration. This Gateway represents a unique collaboration between The Cell Migration Consortium (CMC) and Nature Publishing Group (NPG).



▶ GI Motility online

A unique, comprehensive resource on the motility of the gastrointestinal tract.



▶ Omics Gateway

An extensive portal into publications relevant to large-scale biology from journals throughout NPG.



▶ Nature Reports Avian Flu

In early 2007 NPG will be launching a new avian flu website. Here, we present links to NPG's existing resources on avian flu and the H5N1 virus.



▶ Nature Reports Stem Cells

A hub of information about the science, politics, ethics and clinical applications of stem cell research.



▶ Pathway Interaction Database

An authoritative, peer-reviewed database of signaling pathways in human cells. The database is a collaboration between the U.S. National Cancer Institute and NPG.

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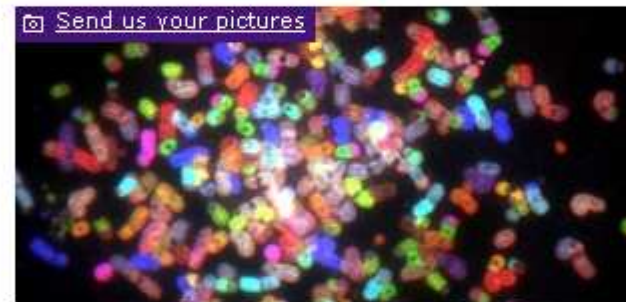
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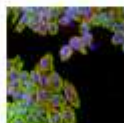
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Above image provided by Carrie Viars, Steve Goodison, and George McNamara.

Featured Protocols



GENOMICS / PROTEOMICS

Design and implementation of high-throughput RNAi screens in cultured *Drosophila* cells

Whole-genome RNAi facilitates gene discovery and enables functional networks to be derived. However, careful experimental design is critical. This protocol, provided by the *Drosophila* RNAi Screening Center, describes how to plan and implement a genome-wide RNAi screen in cultured *Drosophila* cells. It also provides guidance on data analysis.



SYNTHETIC CHEMISTRY

Synthesis of pyrimidines by direct condensation of amides and nitriles

In this protocol devised in the Movassaghi laboratory, gram-scale syntheses of pyrimidine derivatives are realized through the novel single-step condensation of *N*-vinyl or *N*-aryl amides with nitriles.

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[OTMI at BioNLP 2007](#)

I presented a talk and a poster on OTMI at BioNLP 2007 the week before last (Friday, June 29). This was a one-day workshop attached to the 45th Annual Meeting of the Association for Computational Linguistics conference held...

Posted in Nascent on July 10, 2007 05:44 AM

[Agile Descriptions](#)

Last Thursday week, March 8, Library of Congress held a public meeting of the Future of Bibliographic Control Working Group hosted at their Mountain View home. The theme of the meeting was 'Users and Uses of Bibliographic...

Posted in Nascent on March 19, 2007 10:43 AM

[Open Text Mining Interface - Update](#)

We've posted here before (here and here) about OTMI, the Open Text Mining Interface specification that we are proposing as a research-oriented, scholarly full text for text analysis purposes. This post details some recent updates. Contact email First...

Posted in Nascent on February 28, 2007 07:05 AM

[Open Text Mining Interface version 0.2](#)

A few weeks ago we floated OTMI as a suggested way of opening up subscriber-only articles to text mining research. We received feedback from that initial proposal, so we decided to update the demo, incorporating...

Posted in Nascent on June 13, 2006 12:54 PM

[Open Text Mining Interface](#)

Update: My colleague, Ben Lund, has posted about a new version of our OTMI demo here. Every now and then a scientist contacts us for a machine-readable copy of our content (i.e., the XML) to use in text-mining research...

Posted in Nascent on April 24, 2006 11:39 AM

[Web 2.0 in Science](#)

Full text of the article "Web 2.0 in Science" by Ben Lund, published in the journal "Web 2.0 in Science". The article discusses the impact of Web 2.0 on science and the role of Open Text Mining Interface (OTMI) in this context.

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AUGUST 30, 2007

[A 'rough guide' to publication.](#)

The process of getting a manuscript published can be a long and sometimes convoluted one. The more transparent it is, however, that members of the scientific community will be able to negotiate it to their benefit. In our [September editorial](#), we provide a brief overview of the steps in the process, especially those where problems are likely to be encountered.

Posted by Natalie De Souza at 0

JULY 30, 2007

[Receptor dimerization revisited](#)

Last December we published an [Article](#) by Simon Davis and colleagues challenging the conventional methodology being used in BRET to detect dimerization of G protein coupled receptors. The conclusions were contested in a [Correspondence](#) by Michel Bouvier and a new [Correspondence](#), a former member of the Bouvier lab further argues against the results and conclusions of the Davis study by using the 'Type 2' BRET assay of Davis and colleagues.

[Continue reading "Receptor dimerization revisited" »](#)

Posted by Daniel Evanko at 0

[No faulty-gene carrier need apply](#)

A bill designed to prohibit discrimination based on genetic information in terms of health insurance and employment is awaiting a vote in the Senate. There have been several similar but ultimately unsuccessful legislative attempts over the past 12 years. It is crucial that this bill be passed into law to address a public fear likely to limit patient access to predictive genetic testing and to discourage participation in gene

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"I have crossed 20,000 leagues in that submarine tour of the world, which has revealed so many wonders....And to the question asked by Ecclesiastes three thousand years ago, "That which is far off and exceeding deep, who can find it out?" two men alone of all men were right to give an answer— Captain Nemo and myself." These words, from the closing passages of Jules Verne's *20,000 Leagues Under the Sea*, are a poetic allegory for the search for scientific knowledge. At this blog we aim to provide some navigational help to enable you to publish your research in our journals.

You are welcome to contact us by e-mail at 'authors at nature dot com' with questions and suggestions of topics to feature on the blog.

Fostering responsible research

 [Bo](#)

The European Science Foundation and the US Office of Research Integrity have created a web page of resources on scientific misconduct: [References & Background Reading : European Science Foundation](#). The page contains links to relevant articles in *Nature*, *Nature Biotechnology*, *Science* and *Research Policy*, as well as information about books published on the topic. The list is part of the backlist of the [World Conference of Science Integrity](#), being held this week (16-19 September 2007) at the Calouste Gulbenkian Foundation, Lisbon. [See the Conference website:](#)

The World Conference on Research Integrity is the first global forum convened to provide researchers, research administrators, research journal editors, representatives from professional societies, policymakers, and others an opportunity to discuss strategies for handling research misconduct policies and fostering responsible conduct in research.

The Nature journals' policies on ethics in publishing can be found at our [authors' and reviewers' website](#).

Posted by Maxine Clarke on

Categories: [Ethics](#) | [Perma](#)

Technology and science

ng efforts have their genesis in a something, but their ultimate people wanting to listen, needing oices, and answering in kind."

or comment for the Nascent iscent at nature.com' and Gavin n will get back to you.



SEPTEMBER 18, 2007

Second Nature event: "Through Birds' Eyes"

Moving swiftly on from [Ancient DNA](#) to the mysteries of foraging seabirds, this week's guest in the [Second Nature events series](#) wi [Graham Martin](#) on the topic of Great Cormorants.

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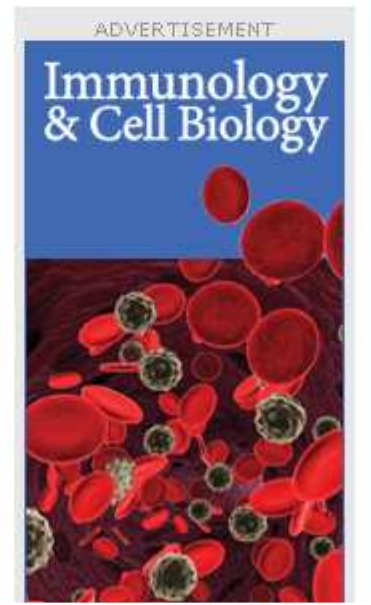
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