Nucleic Acids Research, 2009, Vol. 37, No. 22 ***7343–7348***
doi:10.1093/nar/gkp1167

EDITORIAL: NAR Awards 2009

For the fourth year running, NAR and Oxford Journals have awarded prizes to students in recognition of their outstanding achievements. This year, prizes were awarded at eight different meetings. A detailed list of the awards is presented below. Our warm congratulations go to the prize winners.

Fifth International Society for Computational Biology (ISCB) Student Council Symposium, Stockholm, Sweden, 27 June 2009

Best Presentation Award Winner: Nils Gehlenborg

Visualization of Large Microarray Experiments with Space Map

Nils Gehlenborg and Alvis Brazma

Microarray studies that include a large number of samples have become increasingly common over the last few years. Nils presented the Space Maps visualization technique, which can visualize data sets with hundreds or thousands of samples, a task at which state-of-the-art techniques such as heat maps fail due to scalability issues.

Best Poster Award Winner: José Caldas

Probabilistic Retrieval and Visualization of Biologically Relevant Microarray Experiments

José Caldas, Nils Gehlenborg, Ali Faisal, Alvis Brazma and Samuel Kaski

As Array Express and other repositories of genome-wide experiments are reaching a mature size, it is becoming more meaningful to search for related experiments given a particular study. José introduced a model-based approach that allows for the search to be based upon actual measurement data instead of textual annotations. The method extracts information about the biological processes differentially activated in each experiment, in order to retrieve experiments where similar processes are activated. José also developed tools that allow visualization and interpretation of the model and retrieval results. Case studies on a subset of ArrayExpress show that his method indeed finds experiments relevant to particular biological aspects.

Best Poster Award Runner-Up: Inken Wohlers

PAUL: protein structural alignment using integer linear programming and Lagrangian relaxation

Inken Wohlers, Lars Petzold, Francisco S. Domingues and Gunnar W. Klau

This poster presented a protein structural alignment approach that computes alignments based on inter-residue distances. Building upon work for the alignment of protein contact maps by Caprara *et al.*, Inken used these distances to formulate the problem as an integer linear program, which was subsequently solved using Lagrangian relaxation. She assessed the performance of her program PAUL on the challenging SISY set—on this data set, she compared PAUL alignments to those computed by MATRAS, DALI, FATCAT, SHEBA, CA and CE. PAUL alignments showed higher mean and median alignment accuracies than all other methods. PAUL is thus competitive to state-of-the-art algorithms and a beneficial tool for high-quality pairwise structural alignment.

Best Poster Award Runner-Up: Nikolay Samusik

A method for validation of clustering of phenotypic gene knockdown profiles using information from protein–protein interactions

Nikolay Samusik, Yannis Kalaidzidis and Marino Zerial

Nikolay proposed a method for cross-validation of the clustering of phenotypic siRNA screening data using protein–protein interaction (PPI) data. He established a measure of cluster quality with respect to PPI and showed that this measure not only allows discrimination between optimal and suboptimal segmentation but can also be used to select clustering parameters.

BACR/EACR Symposium: Chromatin and Cancer, Cambridge, UK, 6–8 July 2009

Best Poster Award Winner: Zuzana Jasencakova

Asf1 and histone H3–H4 dynamics in chromatin replication

Zuzana Jasencakova, Annette Scharf, Katrine Ask, Armelle Corpet, Axel Imhof, Genevieve Almouzni and Anja Groth

Chromatin replication represents a critical moment in maintenance of once-established chromatin states. Supply of new and recycling of the old histones at replicating chromatin has to be tightly regulated, and histone chaperones are emerging as key players in this process. To gain more insight into the function of human histone chaperone Asf1, Zuzana profiled histone marks on Asf1-bound histones in replicating cells and cells experiencing replication stress. Her work opens up new avenues to understand how histone marks are transmitted during replication as well as how changes in chromatin could arise in disease.

BACR/EACR Symposium: Transcription and Cancer, Cambridge, UK, 8–10 July 2009

Best Poster Award Winner: Kirsteen Campbell

Myc and Mnt in lymphomagenesis

Kirsteen Campbell, Sue Bath, Darrin Smith, Peter Hurlin and Suzanne Cory

Mnt is a putative tumour suppressor protein that is thought to antagonize the proto-oncogene Myc by competitively binding to Max and repressing gene expression. Kirsteen investigated whether Mnt suppresses Myc activity *in vivo* using mouse models of Myc-induced lymphomagenesis. She hypothesized that a decrease in Mnt would increase the functional level of Myc, accelerate tumour onset and alter phenotype. However, a decrease in Mnt did not mimic increased Myc expression in these models. This suggests that the current model of Mnt antagonism of Myc is more complex than previously thought and may involve cell-type-specific effects.

2009 FASEB Meeting: Dynamic Structure of the Nuclear Hormone Receptors, Saxtons River, Vermont, USA, 9–14 August 2009

Best Poster Award Winner: Sebastien Lalevée

RARγ/Vinexinβ: Union, Phosphorylation and Separation

Sébastien Lalevée, Gaétan Bour, Marc Vitorino, Marc Quinternet, Bruno Kieffer and Cécile Rochette-Egly

The effects of retinoic acid (RA) are mediated by nuclear receptors (RARs), which function as ligand-dependent transcriptional regulators. Sébastien demonstrated that the transcriptional activity of the RARγ subtype is controlled by the phosphorylation of serine residues located in a proline-rich motif (PRM) of the N-terminal domain. He further demonstrated that this PRM interacts directly with an SH3 domain of Vinexinβ, an adaptor protein. This interaction occurs when the PRM is not phosphorylated and maintains the receptor outside of chromatin. After RA addition, the PRM becomes phosphorylated, inducing the dissociation of Vinexinβ and the recruitment of phosphorylated RARγ to RA target genes.

Third Intracellular Delivery of Therapeutic Molecules: from Bench to Bedside, Montpellier, France, 31 August–2 September 2009

Best Poster Award Winner: Laetitia Kurzawa

Imaging Cyclin-Dependent Kinases through Intracellular Delivery of the Peptide Biosensor MP72

Laetitia Kurzawa, Morgan Pellerano and May C. Morris

This work reports on the development of an innovative strategy for evaluation of relative cyclin-dependent kinase (CDK) levels in mammalian cells. Laetitia designed a fluorescent biligand peptide biosensor that recognizes recombinant as well as endogenous CDKs and cyclins. Thanks to cell-penetrating peptide carriers, it is efficiently delivered into cultured cells in a non-covalent fashion and can be followed through live-cell fluorescence imaging. This technology offers promises for the detection of alterations in levels of cell cycle regulators associated notably with tumoural progression.

Sixth International Symposium on Nucleic Acids Chemistry, Takayama, Gifu, Japan, 27 September–1 October 2009

Best Poster Award Winner: Junpei Yamamoto

Recognition and reaction mechanisms of the (6–4) photolyase as determined by using a (6–4) photoproduct analogue

Junpei Yamamoto, Kenichi Hitomi, Ryosuke Hayashi, Elizabeth D. Getzoff and Shigenori Iwai

The (6–4) photoproduct, one of the major ultraviolet radiation (UVR)-induced DNA lesions formed at bipyrimidine sites, causes carcinogenesis at high frequency. The (6–4) photolyases restore the (6–4) photoproducts to their intact bases in a light-dependent manner; however, their overall repair mechanism remains obscure. To investigate the light-dependent conversion of the (6–4) photoproduct, Junpei prepared a (6–4) photoproduct analogue with modification at 3′ pyrimidone ring, in which the carbonyl group was replaced with an imine to apply to the (6–4) photolyase assay. The (6–4) photolyase shows affinity to an oligonucleotide carrying this imine analogue of the (6–4) photoproduct, although the imine analogue is not repaired by the (6–4) photolyase.

Best Poster Award Winner: Rintaro Iwata

Stabilization of A-type nucleic acid duplexes by novel oligodiaminosaccharides

Rintaro Iwata, Masafumi Sudo, Kenta Nagafuji and Takeshi Wada

Novel oligodiaminosaccharides, {alpha}-(1->4)-linked-2,6-diamino-2,6-dideoxy-D-glucopyranose oligomers, were designed and synthesized to bind to A-type nucleic acid duplexes, such as RNA duplexes. Using properly designed glycosyl donors and glycosyl acceptors, an {alpha}-selective glycosylation was achieved. A chain elongation cycle was established and the oligodiaminosaccharides bearing the {alpha}-glycoside bonds (1–4mer) were synthesized. Analyses of their interactions with oligonucleotide duplexes were performed by using circular dichroism (CD) spectrometry and UV melting experiments. These experiments revealed that the 3mer and 4mer were found to remarkably stabilize RNA–RNA and RNA–DNA duplexes with small structural changes.

Best Poster Award Winner: Shinzi Ogasawara

Photo-controllable Aptamer

Shinzi Ogasawara and Mizuo Maeda

Shinzi successfully developed a new method for photoregulation of G-quadruplex formation using *cis–trans* photoisomerization of the photochromic nucleobase 8FVG. His photo-controllable quadruplexes can be switched between a very stable quadruplex state and a non-structured state in a straightforward and reversible fashion. He also demonstrated reversibly control binding of a G-quadruplex aptamer to thrombin.

Best Poster Award Winner: Shun Nakano

Structural aspects for the function of ATP-binding ribonucleopeptide receptors

Shun Nakano, Masatora Fukuda, Tsukasa Mashima, Masato Katahira and Takashi Morii

Shun described analyses of the secondary structure of adenosine triphosphate (ATP)-binding ribonucleopeptide (RNP) receptors. Mapping of the RNA structure of ATP-binding RNP receptors by using hydrolytic enzymes, chemical probing with dimethyl sulphate (DMS) and in-line probing indicated that ATP-binding RNP receptors take the loop structure at the nucleotide position of the 'variable region'. In addition, it was evident that a part of the consensus region located next to the variable region directly participated in the binding to ATP. The completely preserved three U nucleotides were essential for the binding of RNP to ATP, as revealed by the affinity evaluation and the secondary structure analyses of the U nucleotides mutants of the ATP-binding RNP receptor. Interestingly, two mutants with an adenosine introduced to either of the two U nucleotides showed similar secondary structures to the original ATP-binding RNP. These results imply the possibility that the adenine base introduced at the U position acts much the same as the substrate ATP, and suggest that the U nucleotides in these positions interact directly to ATP.

Symposium on RNA Biology VIII, Research Triangle Park, North Carolina, USA, 16–17 October 2009

Best Presentation Award Winner: John Pagano

RNA recognition by the embryonic cell fate determinant and germline totipotency factor MEX-3

John M. Pagano, Brian M. Farley, Kingsley I. Essien and Sean P. Ryder

John's work focuses on how the *Caenorhabditis elegans* RNA binding protein MEX-3 recognizes its messenger RNA (mRNA) targets to maintain germ cell totipotency and control cell fate specification. He presented the results of quantitative binding experiments that defined the consensus MEX-3 binding sequence required for interaction with its mRNA targets. He further demonstrated that this element is necessary for MEX-3-dependent regulation in early embryos. Identification of the MEX-3 specificity determinant enabled prediction of several candidate regulatory targets that may contribute to its biological role in development.

Joint Symposium of Fifth Annual Meeting of Oligonucleotide Therapeutics Society and the 19th Anti-Sense Symposium, Fukuoka, Japan, 3–6 November 2009

Best Poster Award Winner: Shiho Ide

Development of Chemical Probes to Investigate the Molecular Mechanism of RNAi

Shiho Ide, Noriaki Minakawa and Akira Matsuda

Nucleic acids generally form a double helix, based on the Watson–Crick base pairs. In this helical structure, two grooves exist, a major and a minor, and the Watson–Crick base pairs face these grooves. Proteins such as enzymes and transcription factors are thought to recognize nucleic acids by the shape of their groove(s). In order to develop chemical probes for investigating RNA–protein interactions, Shiho designed and synthesized 7-bromo-7-deazaadenine and 3-bromo-3-deazaadenine ribonucleosides. To reveal the molecular mechanism of RNA interference (RNAi), he introduced these units into small interfering RNAs (siRNAs) in various positions. The results of modification pattern–RNAi activity relationships suggested that the major groove is crucial for RNAi.

Best Poster Award Winner: Reiko Waki

***In Situ* Imaging of the Immediate-Early Genes Using Bispyrene-Modified RNA probes in Living Cells**

Reiko Waki, Takako Ueda, Asako Yamayoshi, Akio Kobori and Akira Murakami

Reiko developed a real-time RNA detection system in living cells using a bispyrene-modified 2′-*O*-methyloligoribonucleotide (OMUpy2). He chose *c-fos*, *c-jun* and *c-myc* mRNAs as target mRNAs. The real-time monitoring of mRNAs was carried out in living HeLa cells. After OMUpy2 was transfected to serum-starved HeLa cells, the cells were stimulated by media containing epidermal growth factor (EGF). The cells were observed with a fluorescent microscopy and Reiko successfully detected all mRNAs in cytoplasm in a real-time manner. This method is promising to profile the cascade pathway of RNAs in living cells.

Best Poster Award Winner: Kazuhiro Furukawa

Photoactivation of Caged Fluorescent Oligodeoxynucleotide in Cell

Kazuhiro Furukawa, Hiroshi Abe, Satoshi Tsuneda and Yoshihiro Ito

Kazuhiro designed and synthesized new caged fluorescein derivatives containing azidomethyl-protecting groups. The new caged fluorescein derivatives are rapidly activated upon brief irradiation and show a strong increase in fluorescence. The emission was enhanced almost 1350-fold after UV irradiation. Finally, to determine the usefulness of his new molecules in a biological system, he examined the fluorescence photoactivation in living human cells. The region around the irradiation point became brightly fluorescent after a 25-s irradiation, whereas no signal was observed from the cells before irradiation. Consequently, the azidomethyl fluorescein-labelled oligonucleotide was successfully photoactivated and the resulting fluorescence signal was monitored in living human cells.

Best Poster Award Winner: Yuko Tanaka

Thermodynamics Parameters for Reliable Prediction of RNA Structures

Yuko Tanaka, Kae Kishimoto, Naoki Sugimoto and Junji Kawakami

For some stable RNA hairpins, the measured thermodynamic stability is higher than that predicted in a program. However, the correction term ΔGo(loop) for the secondary structure prediction has been settled only for the stable tetraloops, GNRA and UNCG. In this study, Yuko evaluated the ΔGo(loop) for the two stable pentaloop hairpins, NTS and boxB. As the results of UV melting analysis, the stability and the ΔGo(loop) of these RNAs, which are comparable to those of the representative stable tetraloops, were determined. Moreover, the stabilization mechanism of NTS and boxB could be explained by the relationship between ΔHo and ΔSo. The parameters determined in this study would be useful for accurate prediction of RNA secondary structures, for designing of functional RNAs, and for the target site selection in siRNA experiments and other anti-sense strategies.

Best Poster Award Winner: Kazumitsu Onizuka

Site-Selective Chemical Modification of mRNA and its Effects on Polymerization and Translation

Kazumitsu Onizuka, Yosuke Taniguchi, Mohd Shihabuddin Bin Ahmad Noorden and Shigeki Sasaki

Site-selective chemical modifications of RNA have become an important biotechnology tool, and the development of a useful method for site-specific modification is highly desired. In this study, Kazumitsu reported the functionality-transfer reaction to site-selectively modify RNA. The specific transfer to the amino group of cytosine base was achieved with *S*-functionalized-6-thioguanosine in the oligodeoxynucleotide (ODN) under neutral conditions. Interestingly, the

functionality transfer rate is greatly enhanced and the selectivity is shifted to the guanine base when the reaction is performed under alkaline conditions. Moreover, DNA polymerization was terminated efficiently and selectively at the site of the modified cytosine or guanine.

Best Poster Award Winner: Aya Ogata

Synthesis of 5′-Capped siRNA for Suppression of Off-Target Effects and Its Capability to Achieve Protein Expression

Aya Ogata, Yoshihito Ueno, Chihiro Furukawa, Kouhei Sakurai, Hideo Iba, Yoshiaki, Kitamura and Yukio Kitade

It has been reported that the phosphorylation of the 5′-end of an anti-sense strand of the siRNA duplex is an important factor for the RNAi activity of its siRNA duplex. Biaryl units comprising a bis(hydroxymethyl)benzene residue and a naphthalene or pyrene moiety can also stabilize DNA duplexes thermally and thermodynamically. Aya designed siRNAs with biaryl units comprising a bis(hydroxymethyl)benzene and a 4-dimethylaminonaphthalene residue, a naphthalene or a benzene moiety at their 5′-ends. Aya showed the synthesis of 5′-capped siRNAs for the suppression of off-target effects and their capability of protein expression. Aya found that the incorporation of biaryl units into the 5′-ends of the sense strands can suppress the off-target effects induced by the sense strands without reducing the RNAi-inducing activity of the anti-sense strands.

Best Poster Award Winner: Sharif Hossain

Efficient Delivery of siRNA by pH-Sensitive Inorganic Nanocrystals of Carbonate Apatite

Sharif Hossain, Ezharul Hoque Chowdhury and Toshihiro Akaike

siRNAs are emerging as promising therapeutic agents for the treatment of inherited and acquired diseases. However, for intracellular siRNA delivery, an ideal system, in terms of stability and endosomal trafficking, is still lacking. Sharif showed, for the first time, siRNA delivery based on pH-sensitive carbonate apatite nanoparticles being capable of strongly binding to siRNA, highly stable at the typical physiological pH and quickly degradable at the typical endosomal pH, resulting in efficient endocytosis and subsequent release of the siRNA from the particles and the endosomes. Confocal microscopy analysis revealed the endosomal localization of siRNA upon internalization and its escape from the endosome in a time-dependent manner. The gene silencing efficiency of apatite-siRNA nanoparticles was found to be more significant than cytotoxic Lipofectamine-2000.

Best Poster Award Winner: Tsuyoshi Yamamoto

Therapeutic Application of 2′,4′-BNA/LNA-Modified Oligonucleotide for the Treatment of Hypercholesterolaemia

Tsuyoshi Yamamoto, Mariko Harada-Shiba, Shunsuke Wada, Hidetaka Torigoe, Tetsuji Yamamoka, Keisuke Narukawa, Takeshi Imanishi and Satoshi Obika

Tsuyoshi developed a new anti-sense drug for hypercholesterolaemia. 2′,4′-BNA/LNA-modified oligonucleotide (BNA-antisense) was designed to target PCSK9 mRNA, which encodes a protease that promotes degradation of the low-density lipoprotein (LDL) receptor. The duplex-forming ability of BNA-anti-sense with mRNA is much higher than that of an unmodified oligonucleotide ($\Delta T_m = +34°C$). An *in vitro* transfection assay showed a significant mRNA-inhibitory activity of BNA-anti-sense. The reduction of PCSK9 protein and concomitant induction of LDL receptor were clearly observed. Similar effects of BNA-anti-sense were confirmed by *in vivo* experiments. Consequently, 30% reduction in mice serum LDL-cholesterol was successfully achieved, compared with placebo groups.

Best Poster Award Winner: Chang Ho Lee

Vector-Based Anti-miR Expression System which Inhibits miRNA Function

Chang Ho Lee, Sung Jin Kim, You sub Won and Seong-Wook Lee

In this study, Chang Ho tested various derivative forms of anti-miR-122 oligos with 2′-OH, 2′-F, 2′-OME modification or phosphothioated backbone combined with 2′-OME modification to inhibit miR-122. Of these anti-miRs, 2′-OH and 2′-F RNA were least functional. However, when he expressed variable anti-miRs, using cytoplasmic localized 7SL- or nuclear localized U6-promoter system, several forms efficiently inhibited miRNA. Interestingly, levels of miRNA inhibition through U6 promoter driven anti-miR was comparable to those by 7SL promoter driven anti-miR. Chang Ho constructed viral delivery systems encoding the 7SL or U6 promoter driven anti-miR transcript, and tested their inhibitory activities against miRNA. Processing pattern as well as expression level of the targeted miRNA in the viral infected cells are still being analyzed.

Best Poster Award Winner: Kohta Mohri

Development of Highly Structured DNA Molecules as Drug Delivery Systems with High Immunostimulatory Activity

Kohta Mohri, Makiya Nishikawa, Sakulrat Rattanakiat, Yumiko Mizuno, Nao Matsuoka, Hisakage Funabashi, Dan Luo and Yoshinobu Takakura

DNA can be used as a building block for creating nano-sized bioactive materials. In this study, Kohta developed DNA hydrogels with high immunostimulatory activity by ligating X-shaped DNA (X-DNA) containing immunostimulatory unmethylated CpG dinucleotides (CpG motifs). X-DNA monomers with a variety of structural features were successfully obtained, and the immunostimulatory activity of CpG DNA was significantly increased by the X-shape formation. The ligation of these monomers resulted in the formation of DNA hydrogels, which was effective for controlled release of intercalated doxorubicin. These results indicate that DNA hydrogels with high immunostimulatory activity can be developed as drug delivery systems for immuno- and chemotherapy.

Keith Fox, Senior Editor, *Nucleic Acids Research*
Rich Roberts, Senior Editor, *Nucleic Acids Research*