



# NEWS FROM THE SCIENTIFIC DIRECTOR, NIEHS

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## **TRAINING COURSES**

Communication and Learning Styles: A Course for the Modern Scientist -- Written by Arti Patel

Have you ever wondered why you “click” with some people and why some people just “tick” you off? Why some personal interactions are effortless, while others drain every last bit of your energy? At the root of the “interactions” are basic principles of communication which are directly connected to “how one learns” and what we as individuals “value”.

In September 1998, principal investigators and trainees were given an opportunity to participate in a course on communication and learning styles taught by Stephanie Shipper of Expert Outcomes in Chapel Hill, NC. Four principal investigators and seven trainees signed up for the eight-session course which began on October 14, 1998. The course was designed to identify learning styles, to discover how learning styles influence communication with others, to explore how to improve communication styles, and to learn about decision making strategies was based upon the concept of Neuro-Linguistic Programming (NLP). The fundamental tenets of NLP transcend culture, gender, age, sex and other perceived obstacles to effective communication. The techniques of NLP are so fundamental that they are integrated into the training of all United Nations diplomats.

The following are comments from course participants:

*It is ironic that we spend so much valuable time “studying” biological processes, but spend very little time “studying” how to communicate this information. Being able to convey our ideas and concepts to our colleagues is a fundamental part of being a modern scientist. Stephanie’s [Stephanie Shipper] class has given us the tools to complete our scientific process.*

*The NLP techniques I learned in this course are incredibly effective and have greatly enhanced my communication abilities...no more boring seminars!*

*A wonderful opportunity – I learned a lot from this class and it has benefited me both personally and professionally. This course has enabled me to interact and communicate more effectively with individuals inside and outside of my laboratory. I am glad that I had the opportunity to take this class and I hope that ALL scientists have the same opportunity.*

The first eight sessions were so informative and captivating that 9 of the attendees chose to take part in 4 additional sessions that focused on applying the techniques learned in the first part of the course to giving and evaluating presentations. The techniques taught in this course are invaluable to any scientist who is eager to pursue a career in a growing and challenging international scientific community.

If you are interested in taking this course, please contact Janis Mullaney at 1-4900.

#### Research Laboratory Seminar Series -- Written by Dr. Jim Putney

From October of last year, ending this April, a course on Management for Scientists was given at NIEHS. The idea for such a course originated from discussions of the Council of the Assembly of Scientists who noted that little or no such training was available for junior, tenure-track faculty at the Institute. The Council reasoned that there are basic skills useful to all practicing scientists and that even more seasoned members of the Institute had picked up these skills (and to varying degrees) through the OJT mechanism. We involved the OSD in these discussions, and as a result Janis Mullaney learned of a course on Management for Scientists offered for graduate credit through the FAES graduate school in Bethesda, taught by Thomas Hoffman from the FDA. Janis arranged to have Dr. Hoffman come to the NIEHS on a regular basis and deliver an abbreviated version of his course for our scientist. The course was attended by a number of junior and senior NIEHS scientists as well as by three members of the Assembly of Scientists Council.

The course consisted of 13 sessions, two hours each, held roughly every two weeks. The format of the course was meant to be seminar and discussion rather than didactic lecture. The discussions depended to a large extent on reading assignments provided by Dr. Hoffman; copies of articles from books and journals dealing with issues of management relevant to the topic at hand. The volume of reading was not particularly onerous given the two week spacing between sessions, but could be a bit much if put off until the night before! Class time was spent discussing, criticizing and debating the principles espoused by the various authors. Members of the class were encouraged to relate relevant anecdotal experiences, and on occasion, some role playing was utilized to illustrate points.

The earlier sessions of the course dealt with very general issues, and in some cases their relevance to the scientific laboratory were not all that evident. Dr. Hoffman stated from the outset that management is basically interpersonal interactions, and understanding interpersonal

interactions involves to varying degrees basic psychology. Thus, we discussed how attitudes and philosophies can translate into success or failure, at the level of large, multinational corporations, at the level of individuals; we asked what are the bases of authority; of leadership, for example. In later sessions, issues of more obvious relevance were discussed: effective communication, control vs supervision, meetings, conflicts, negotiations, recruiting, effective problem choice, peer review. Interestingly, as these more directly applicable topics were undertaken, we came to realize the relevance of the principles from earlier sessions. In short, the idea as to develop management skills by understanding the principles, not just “formulae” for specific situations. This is the kind of scholarly approach that should be well received by most scientists.

This particular style was not universally appreciated by all participants in the course. Some left the course after the first few sessions; I believe they would say that they failed to see the applicability of the material to managing their laboratories. But some stayed in the course despite developing the same misgivings in the beginning. These individuals indicated at the end of the course that they found it much more useful than they would have predicted after the first few sessions.

Because the course deals with principles rather than specific problems, it should be helpful to those seeking to be successful managers of a new laboratory of only two or three people, as well as larger groups, a Laboratory, a Program or a Division.

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## **CHANGES IN WASTE PICKUP REQUESTS**

The web-based electronic waste pickup request form developed by the Health and Safety Branch (HSB) has been available to NIEHS personnel since August 1998. With very few reported problems and at least 60-70 percent of requests coming in electronically, the HSB has decided to go paperless. Paper copies of the Chemical and Radioactive Waste and Surplus Materials forms will be accepted until July 31.

There have been several demo sessions offered by HSB to Institute personnel in recent months, however, if you were unable to attend one of these sessions HSB will provide additional sessions or individual assistance as needed. Contact Kent Stone, Ext. 1-7713, for a demo.

After July 31<sup>st</sup>, paper requests will be accepted only for the following cases:

- 1) Lab cleanouts involving large numbers of chemicals (>20)
- 2) Any significant time period that the web form is unavailable
- 3) Special circumstances pre-arranged on a case-by-case basis (e.g., on-site contractors that may not have computer access)

HSB will continue to provide waste tags and labels at the C-mall location across from the Self-Service Store and in F-basement around the corner from the Health and Safety offices.

If you have any questions or concerns, please call 1-7713.

The electronic waste pickup request form is available at  
<http://www.niehs.nih.gov/odhsb/forms/hazwst/pickup.htm>

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## **SHIPPING OF HAZARDOUS MATERIALS AT NIEHS**

Recently, the NIH has had interactions with the Federal Aviation Administration (FAA) regarding the shipment of materials classified as Hazardous Goods under United Nations (UN), International Civil Aviation Organization (ICAO), International Air Transport Association (IATA), and/or Department of Transportation (DOT) regulations from the NIH. Recently NIH was cited for shipping UN Class 9 Hazardous Goods (dry ice) improperly and for packers not being trained and certified to ship Hazardous Goods. In response NIH is re-examining their process that is currently in place and looking for ways to improve compliance. NIEHS has specific instructions on shipping all Hazardous Materials. Pertinent information and instructions from the Health and Safety Branch (HSB) are listed below and will be posted on the NIEHS website. Questions regarding this topic should be referred to Scott Merkle at extension 1-7933.

### Information/Instructions

Under US Department of Transportation (DOT) regulations, Hazardous Materials or “Dangerous Goods” can include:

- ❑ **Diagnostic specimens** – any human or animal material shipped for the purposes of diagnosis (e.g. blood, blood components, tissues, tissue fluids, excreta, secreta).
- ❑ **Biological materials** which contain pathogens in Risk Group 1; those which contain pathogens under such conditions that their ability to produce disease is very low to none; and those known not to contain pathogens.
- ❑ **Infectious specimens** – viable micro-organisms, or their toxins, that cause or may cause disease in humans or animals.
- ❑ **Chemicals** – any material listed in the DOT Hazardous Material Table, including dry ice.
- ❑ **Radiactive materials** – any material with a specific activity greater than 0.002 microcurie/gram.

Proper shipping involves three elements:

- ❑ **Hazardous material identification** – determining the proper shipping name, use of appropriate markings, labels and placards, and accurate completion of shipping papers.
- ❑ **Packaging** – there are detailed requirements for packaging according to hazard classes. Packaging systems must meet specific performance criteria.
- ❑ **Operational rules** – numerous special provisions and specific carrier requirements (rail, air, highway, water). Persons involved in shipping hazardous material must receive training.

DOT Hazardous Material rules are complex and violations can result in civil and criminal penalties.

**At NIEHS:**

- All radioactive material shipments are handled by the HSB Radiation Safety Program (approx. 10 – 15 per year).
- All other “Dangerous Goods” shipments are handled by William Boyd, ASB Office Services, Ext. 1-3307 (approx. 12 – 24 per year). Anna Haydl Ext. 1-3360 is his backup.

Follows IATA (International Air Transport Association) Dangerous Goods Regulations which are equivalent to DOT.

FEDEX is typically the carrier. They perform a 51 point audit on each package.

Maintains supply of approved packaging materials.

Consults with HSB for proper hazard identification.

Few problems reported, other than an occasional scientist attempting to use regular mail to send “specimens”.

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**PROFILE OF A SENIOR INVESTIGATOR**

Ben Van Houten, Ph.D.

Dr. Van Houten is internationally recognized for his work in the field of DNA repair. He and part of his research group recently moved to NIEHS from the Sealy Center for Molecular Science, at the University of Texas Medical Branch (UTMB). While a faculty member of UTMB, Dr. Van Houten received the prestigious Burroughs Wellcome Fund Scholar Award in Toxicology.

Dr. Van Houten’s laboratory is currently studying the molecular aspects of DNA repair. Part of his group is investigating the protein-DNA interactions involved in damage recognition and repair. The other part of his laboratory is interested in the formation, repair and consequences of mitochondrial DNA damage.

1. *Action Mechanism of the UvrABC nucleotide excision repair system.* He and his group are interested in understanding how nucleotide excision repair proteins recognize DNA damage. They are currently using several biochemical and molecular biology approaches to characterize how the UvrABC nuclease system interacts with polycyclic aromatic hydrocarbons (PAH)-damaged DNA. They are comparing the activities of the *Escherichia coli* Uvr proteins with their thermophilic homologs from the bacteria, *Bacillus caldotenax*. The thermodynamic and kinetics of repair protein binding to the different site-specific stereo-specific PAH-DNA adducts are being investigated with fluorescence spectroscopy. The kinetics of repair enzyme incision for each set of stereoisomer PAH-DNA adducts is also being examined. Long term studies using X-ray diffraction and 2D-NMR techniques combined with site-directed mutagenesis will allow characterization of the pertinent amino acid-DNA contacts which provide

favorable interactions for increased specificity and stability of the protein-DNA interactions involved in damage recognition and repair.

2. *Reactive Oxygen and Mitochondrial Injury*. Using quantitative long PCR (10-30 kb) his laboratory has developed a very sensitive gene-specific DNA repair assay which can detect about one damaged base in  $10^5$  nucleotides from the equivalent of ~ 3000 cells worth of DNA. They have found that mitochondrial DNA is damaged 3-5 times more than nuclear DNA following exposure to hydrogen peroxide, glucose oxidase, and also asbestos. Prolonged oxidant treatment results in persistent mtDNA damage, loss of mitochondrial function, increase in p21<sup>Waf1/CIP</sup> and apoptosis. These observations suggest that mitochondrial injury, specifically DNA damage, is important for reactive oxygen induced toxicity. They are testing the hypothesis that reactive oxygen species (ROS) generated in the mitochondria results in mtDNA damage, which in turn causes the release of more ROS ( $O_2^-$ ,  $H_2O_2$ , and  $OH^\cdot$ ) that lead to further mitochondrial decline and many degenerative diseases associated with aging. They are studying this hypothesis using a murine model of Parkinson's disease in which mice are treated with MPTP a complex I inhibitor. Future experiments will address the fate of mRNA stability in mitochondria from cells treated with ROS. Thus one of the consequences of mitochondrial DNA damage would be the loss of transcription and subsequent alterations in the electron transport chain which could lead to further increases in ROS generation.

#### **RECENT PAPERS:**

1. Zou, Y., R. Walker, H. Bassett, N.E. Geacintov, and B. Van Houten. 1997. Formation of DNA repair intermediates and incision by the ATP-dependent UvrB-UvrC endonuclease. *J. Biol. Chem.* 272(8):4820-4827.
2. Yakes, F.M. and B. Van Houten. 1997. Mitochondrial DNA damage is more extensive and persists longer than nuclear DNA damage in human cells following oxidative stress. *Proc. Natl. Acad. Sci.* 94:514-519.
3. Fung, H., K.W. Kow, B. Van Houten, and B.T. Mossman. 1997. Patterns of 8-hydroxydeoxyguanosine (8OHdG) formation in DNA and indications of oxidative stress in rat and human pleural mesothelial cells after exposure to crocidolite asbestos. *Carcinogenesis.* 18(4):825-832.
4. Salazar, J.J., and B. Van Houten. 1997. Preferential mitochondrial DNA injury caused by glucose oxidase as a steady generator for hydrogen peroxide in human fibroblasts. *Mutation Research.* 385 (2):139-149.
5. Fung, H., Y.W. Kow, B. Van Houten, D.J. Taatjes, Z. Hatahet, Y.M.W. Janssen, P. Vacek, S.P. Faux, B.T. Mossman. 1998. Asbestos increases mammalian AP-endonuclease (APE) gene expression, protein level and enzyme activity mesothelial cells. *Cancer Res.* 58(2):189-194.
6. Zou Y, Crowley DJ, Van Houten B Involvement of molecular chaperonins in nucleotide excision repair. DnaK leads to increased thermal stability of UvrA, catalytic UvrB loading, enhanced repair, and increased UV resistance. *J Biol Chem* 1998 May 22;273(21):12887-92

7. Chen KH, Yakes FM, Srivastava DK, Singhal RK, Sobol RW, Horton JK, Van Houten B, Wilson SH Up-regulation of base excision repair correlates with enhanced protection against a DNA damaging agent in mouse cell lines. *Nucleic Acids Res* 1998 Apr 15;26(8):2001-7
8. Van Houten B, Chen Y, Nicklas JA, Rainville IR, O'Neill JP Development of long PCR techniques to analyze deletion mutations of the human hprt gene. *Mutat Res* 1998 Jul 17;403(1-2):171-5 .
9. Zou Y, Bassett H, Walker R, Bishop A, Amin S, Geacintov NE, Van Houten B. Hydrophobic forces dominate the thermodynamic characteristics of UvrA-DNA damage interactions. *J.Mol Biol* 1998 Aug 7;281(1):107-19 .
10. Ballinger, S.W., B. Van Houten, C.A. Coklin, G. Jin, and B. Godley. 1999 Hydrogen Peroxide Causes Significant Mitochondrial DNA Damage in Human RPE Cells. *Exp Eye Res.* 1999 Jun;68(6):765-772.

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#### **BEST PAPER OF THE YEAR 1998 BY A TRAINEE**

In order to recognize outstanding scientific accomplishments by NIEHS trainees, the DIR Council has created an annual award to honor the Best Paper of the Year by a Trainee. All papers published in the previous year having an NIEHS trainee as the first author are eligible for consideration.

The process for selecting the best paper of the year starts with the Scientific Director, and the Scientific Program Directors, who make an initial selection of candidate papers. Copies of these papers are distributed to all members of the DIR Council with the request for more nominations. At a subsequent meeting of the DIR Council, Council members vote to select the best paper of the year. The award consists of an additional travel allowance of up to \$1000 and a certificate, to be presented at a meeting of the DIR Council.

Seven papers were nominated for the Best Paper of the Year 1998 by a Trainee. They were:

Altschuler, D.L., and Ribeiro-Neto, F. Mitogenic and oncogenic properties of the small G protein rap1b. *Proceedings of the National Academy of Sciences of the United States of America*, 95 (13): 7475-7479, 1998.

Beard, W.A., Bebenek, K., Darden, T.A., Li, L., Prasad, R., Kunkel, T. A., and Wilson, S. H. Vertical-scanning mutagenesis of a critical tryptophan in the minor groove binding track of HIV-1 reverse transcriptase-Molecular nature of polymerase-nucleic acid interactions. *Journal of Biological Chemistry*, 273 (46): 30435-30442, 1998.

Carballo, E., Lai, W. S., and Blackshear, P. J. Feedback inhibition of macrophage tumor necrosis factor-alpha production by tristetraprolin. *Science*, 281 (5379): 1001-1005, 1998.

Honkakoski, P., Zelko, I., Sueyoshi, T., and Negishi, M. The nuclear orphan receptor CAR-retinoid X receptor heterodimer activates the phenobarbital-responsive enhancer module of the CYP2B gene. *Molecular and Cellular Biology*, 18 (10): 5652-5658, 1998.

Krege, J. H., Hodgin, J. B., Couse, J. F., Enmark, E., Warner, M., Mahler, J. F., Sar, M., Korach, K. S., Gustafsson, J. A., and Smithies, O. Generation and reproductive phenotypes of mice lacking estrogen receptor beta. *Proceedings of the National Academy of Sciences of the United States of America*, 95 (26): 15677-15682, 1998.

Richards, R. G., Walker, M. P., Sebastian, J., and DiAugustine, R. P. Insulin-like growth factor-1 (IGF-1) receptor-insulin receptor substrate complexes in the uterus – Altered signaling response to estradiol in the IGF-1(m/m) mouse. *Journal of Biological Chemistry*, 273 (19): 11962-11969, 1998.

Yin, Y. X., Terauchi, Y., Solomon, G. G., Aizawa, S., Rangarajan, P. N. , Yazaki, Y., Kadowaki, T., and Barrett, J. C. Involvement of p85 in p53-dependent apoptotic response to oxidative stress. *Nature*, 391 (6668): 707-710, 1998.

Congratulations to Esther Carballo and Wi Lai, Laboratory of Signal Transduction, winners of the 1998 Best Paper of the Year by a Trainee Award.

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#### **AWARDS AND HONORS FOR DIR SCIENTISTS**

- Dr. Steven Akiyama (Laboratory of Molecular Carcinogenesis) was selected to serve on the independent peer review panel of the Italian Ministry for Universities and Research (May, 1999).
- Dr. J. Carl Barrett (Scientific Director) participated as a Keynote Address Speaker in the 6th Asia/Oceania Regional Congress of Gerontology in Seoul, Korea in June.
- Dr. Beth Gladen (Biostatistics Branch) has been elected a Fellow in the American Statistical Association.
- Dr. Kenneth Korach (Chief, Laboratory of Reproductive and Developmental Toxicology) and his research on the estrogen receptor knock-out mouse was the subject of a feature story on BioMedNews.
- Dr. Joan Packenham (Laboratory of Molecular Carcinogenesis) was selected to be a American Association for the Advancement of Science-EPA Environmental Science and Engineering Fellow for 1999-2000.
- Dr. Richard Philpot (Laboratory of Signal Transduction) was recognized by a session in his honor at the 1999 annual meeting of the Experimental Biology Society in April and was invited to be a guest speaker at the national meeting of the Japanese Toxicological Society in July.
- Dr. Samuel Wilson (Laboratory of Structural Biology) gave the keynote address at the Sixth International Workshop on Radiation Damage to DNA.